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Bile Ducts / Cholangiocarcinoma

1- **Genome wide DNA copy number analysis in cholangiocarcinoma using high resolution molecular inversion probe single nucleotide polymorphism assay**

Alexander Arnold, Marcus Bahra, Dido Lenze, Maren Bradtmöller, Katrin Guse, Claire Gehlhaar, Hendrik Bläker, Frank L. Heppner, Arend Koch

Experimental and Molecular Pathology, Oct 2015, 99(2): 344-353

... new possible target genes within regions of high significant copy number aberrations were detected using a high-density ... (MIP SNP) assay ... DNA was subjected to the Onco-Scan FFPE Express assay analysis (Affymetrix ...}

Bladder

2- **Canine urothelial carcinoma: genomically aberrant and comparatively relevant**

S.G. Shapiro1, S. Raghunath1,2, C. Williams1, A. A. Motsinger-Reif3,8, J. M. Cullen4,8, T. Liu5, D. Albertson5, M. Ruvolo6, A. Bergstrom Lucas6, J. Jin6, D.W. Knapp7, J.D. Schiffman2, M. Breen1,8,9,10

1. Dept of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, 1060 William Moore Drive, Raleigh, NC, 27607, USA; 2. Dept of Pediatrics and Huntsman Cancer Institute, University of Utah, 2000 Circle of Hope, Salt Lake City, UT, 84112, USA; 3. Dept of Statistics, College of Sciences, North Carolina State University, Raleigh, NC, USA; 4. Dept of Population Health and Pathobiology, College of Veterinary Medicine, North Carolina State University, Raleigh, NC, USA; 5. Anatomic Pathology Division Department of Pathology, University of Utah, 1950 Circle of Hope, RM N3105, Salt Lake City, UT, 84112, USA; 6. Agilent Technologies, 5301 Stevens Creek Blvd., Santa Clara, CA, 95051, USA; 7. Dept of Veterinary Clinical Sciences, Purdue University, School of Veterinary Medicine, West Lafayette, IN, USA; 8. Center for Comparative Medicine and Translational Research, North Carolina State University, Raleigh, NC, 9. Center for Human Health and the Environment, North Carolina State Univ, Raleigh, NC; 10. Lineberger Comprehensive Cancer Center, Univ of North Carolina, Chapel Hill, NC


...In the present study, we evaluated 31 primary canine UC biopsies by oligonucleotide array comparative genomic hybridization (oaCGH). Results highlighted the presence of three highly recurrent numerical aberrations: gain of dog chromosome (CFA) 13 and 36 and loss of CFA 19 ... Fluorescence in situ hybridization (FISH), using targeted bacterial artificial chromosome (BAC) clones and custom Agilent SureFISH probes, was performed to detect and quantify these regions in paraffin-embedded biopsy sections and urine-derived urothelial cells ... Affymetrix Oncoscan FFPE Express Platform (Santa Clara, CA) data for an additional 80 cases were downloaded from Gene Expression Omnibus (GEO), GSE44323 (Karolchik et al. 2004; Chekaluk et al. 2013).

3- **DNA copy number analysis of metastatic urothelial carcinoma with comparison to primary tumors**

Richard M Bambury1*,†, Ami S Bhatt23†, Markus Riester2, Chandra Sekhar Pedamallu23, Fujiko Duke23, Joaquim Bellmunt2, Edward C Stack2, Lillian Werner2, Rachel Park2, Gopa Iyer1, Massimo Lodam23, Philip W Kantof2, Franziska Michor2, Matthew Meyerson23 and Jonathan E Rosenberg1

1 Memorial Sloan Kettering Cancer Center/Weill Cornell Medical College, New York; 2 Dana-Farber Cancer Institute/Harvard Medical School, Boston, MA ; 3 The Broad Institute of MIT and Harvard, Cambridge, MA

BMC Cancer, 9 April 2015, 15:242

Background—To date, there have been no reports characterizing the genome-wide somatic DNA chromosomal copy-number alteration landscape in metastatic urothelial carcinoma. We sought to characterize the DNA copy-number profile in a cohort of metastatic samples and compare them to a cohort of primary urothelial carcinoma samples in order to identify changes that are associated with progression from primary to metastatic disease. Methods—Using molecular inversion probe array analysis we compared genome-wide chromosomal copy-number alterations between 30 metastatic and 29 primary UC samples. Whole transcriptome RNA-Seq analysis was also performed in primary and matched metastatic samples which was available for 9 patients ... performed using MIP array technology (Affymetrix Oncoscan FFPE Express 2.0) ...

4- **Meeting abstract**

External validation of somatic copy number alteration (SCNA) at chromosome 1q23.3 in advanced urothelial carcinoma (UC).

Markus Riester, Lillian Werner, Joaquim Bellmunt Molins, Shamini Selvarajah, Barbara Weir, Edward C. Stack, Rachel S. Park, Robert O’Brien, Fabio Augusto Barros Schutz, Toni K. Choueiri, Sabina Signoretti,

3
... We obtained DNA copy number data from bladder cancer patients in two independent cohorts [Spanish cohort (n= 93, Agilent aCGH 180k array) and Brigham and Women's/Dana-Farber (BW/DF) cohort (n = 48, Affymetrix OncoScan FFPE Express 2.0)].

5- **FGFR3 expression in primary and metastatic urothelial carcinoma of the bladder**
Cancer Medicine, Aug 2014, 3(4) : 835-844.

... FGFR3 protein and mRNA expression, mutational status, and copy number variation were retrospectively analyzed in 231 patients with formalin-fixed paraffin-embedded primary UCs, 33 metastases, and 14 paired primary and metastatic tumors using the following methods: immunohistochemistry, NanoString nCounterTM, OncoMap or Affymetrix OncoScanTM array, and Gain and Loss of Analysis of DNA and Genomic Identification of Significant Targets in Cancer software...

6- **Meeting abstract**
**FGFR3 protein expression and gene mutation in primary and metastatic urothelial carcinoma (UC) tumors.**
J Clin Oncol, 2012, 30(Suppl) : Abstr# 4577. [ASCO Annual Meeting]
... FGFR3 mutation in primary tumors was assessed by iPlex and confirmed by hME sequencing (n=141) or Affymetrix OncoScan FFPE Express 2.0 (primary: n=17; metastases n=31).

7- **Genomic complexity of urothelial bladder cancer revealed in urinary cfDNA**
Fiona S Togneri1, Douglas G Ward2, Joseph M Foster3, Adam J Devall2, Paula Wojtowicz1, Sofia Alyas1, Fabiana Ramos Vasques1, Assa Oumie3, Nicholas D James4, K K Cheng5, Maurice P Zeegers6, Nayneeta Deshmukh2, Brendan O’Sullivan7, Philippe Taniere7, Karen G Spink3, Dominic J McMullan1, Mike Griffiths1, Richard T Bryan2
1West Midland Regional Genetics Laboratory, Birmingham Women’s NHS Foundation Trust, Birmingham, UK; 2Institute of Cancer & Genomic Sciences, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK; 3Affymetrix UK Ltd, High Wycombe, UK; 4Cancer Research Unit, University of Warwick, Coventry, UK; 5School of Health and Population Sciences, University of Birmingham, Birmingham, UK; 6Dept of Complex Genetics, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, The Netherlands; 7Dept of Histopathology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
European Journal of Human Genetics advance online publication 13 January 2016; doi: 10.1038/ejhg.2015.281
... In this study, we report the utilisation of Affymetrix’s OncoScan FFPE Assay Kit (Affymetrix, Santa Clara, CA, USA) for detailed genomic profiling of UBC using matched FFPE tumour-derived DNA, cellular DNA from urine cell pellets and cfDNA from urine supernatant. We demonstrate that the complex genomics and important clinically actionable aberrations that are evident in FFPE tumour material (currently the predominant diagnostic biospecimen for solid tumours) are echoed in urinary DNA, and that the tumour genome is enriched in cfDNA compared with cellular DNA. These data illustrate that urinary cfDNA may represent a reliable resource for non-invasive genomic profiling of bladder cancer.

8- **Identification of Nine Genomic Regions of Amplification in Urothelial Carcinoma, Correlation with Stage, and Potential Prognostic and Therapeutic Value**
Yvonne Chekaluk, Chin-Lee Wu, Jonathan Rosenberg, Markus Riester, Qishan Dai, Sharron Lin, Yanan Guo, W. Scott McDougal, David J. Kwiatkowski

PLoS ONE, 4 April 2013, 8(4): e60927.

... A molecular inversion probe (MIP) assay examining 330,000 single nucleotide polymorphisms (SNPs) and 412 cancer gene mutations in 46 cancer-related genes (OncoScan) was performed with the assistance of Affymetrix …

9- **Integrative Analysis of 1q23.3 Copy-Number Gain in Metastatic Urothelial Carcinoma**


Clinical Cancer Research, 1 April 2014, 20(7) : 1873-1883.

... The Cancer Genome Atlas (TCGA) bladder cancer analysis … profiled with Affymetrix Genome-Wide Human SNP Arrays 6.0. ... DNA from primary tumor and metastatic specimens in the DFCI cohort was hybridized to Affymetrix OncoScanTM FFPE Express 2.0 SNP MIP (molecular inversion probe) arrays with 334,183 copy-number and single-nucleotide polymorphism …

10- **Meeting abstract**

**BCR-ABL independent, Abl-TKI-therapy-resistant CML cells show enhanced sensitivity to GDC0941**

Marie Wagle, Matthew Wongchenko, Shan Lu, Yinghui Guan, Yulei Wang, Mark Lackner, Garret Hampton, Yibing Yan.

AACR Annual Meeting 2013, Apr 09, 2013, Abstract #3395.

Introduction: Chronic Myeloid leukemia (CML) is driven by the BCR-ABL oncogene and is initially treated with ABL tyrosine-kinase inhibitors (ABL-TKI), such as Imatinib or Dasatinib. Despite strong initial responses to these drugs, many patients acquire resistance over time through acquisition of BCR-ABL mutations such as T315I, compound BCR-ABL mutations or through BCR-ABL-independent mechanisms. Even though the next generation pan-ABL inhibitor, Ponatinib, targets all known resistant ABL mutations, some patients don’t benefit from Ponatinib and in these cases resistance to TKI therapy may be due to BCR-ABL-independent mechanisms. We analyzed the mechanism of ABL-TKI-dual-resistant CML cells independent of new BCR-ABL mutations and tested the sensitivity of these resistant cells to the PI3K inhibitor, GDC-0941 and/or the MEK inhibitor GDC-0973. Methods: We created ABL-TKI-dual-resistant cells and clones through prolonged treatment of K562 and KCL22 cells with Imatinib and then Dasatinib. The cells and clones were tested for sensitivity to Imatinib, Dasatinib, Ponatinib, GDC-0941 and GDC-0973. Whole genome copy number scan (Oncoscan) and targeted deep sequencing using GAI were used to identify BCR-ABL mutations and newly acquired somatic gene alterations. Phosphoproteomic analysis of cell lysates by Reverse Phase Protein Arrays was used to profile cell signaling pathway status associated with resistance and sensitivity to these drugs. Results: The K562 ABL-TKI-dual-resistant cells were insensitive to all three ABL-TKIs including Ponatinib suggesting that resistance was mediated by a BCR-ABL-independent mechanism. Unexpectedly, the resistant cells and clones became more sensitive to GDC-0941 but not GDC-0973 compared to the parental cells. These resistant cells and clones had acquired new somatic mutations in p53, BRCA2, PTEN, RB, SMARCA4 and PBRM1, but not in BCR-ABL. Phosphoprotein profiling showed low phosphorylation of the BCR-ABL substrates cABL, SHC and FAK indicative of BCR-ABL-independent mechanisms of resistance. Activity of the PI3K/AKT and MEK/ERK pathways varied across the resistant clones. However, high levels of the AKT substrate, FOXO-1 directly correlated with resistance and with GDC-0941 sensitivity. Sensitivity to GDC-0941 also correlated with modulation of phospho-FOXO-1. Our data suggest that GDC-0941 may be a therapeutic candidate for CML patients who progress on TKI therapy through BCR-ABL-independent mechanisms of resistance.

11- **One sentence mentions OncoScan**

**Guidelines for Genomic Array Analysis in Acquired Haematological Neoplastic Disorders**

Jacqueline Schoumans1,* , Javier Suela2, Ros Hastings3, Dominique Muehlematter1, Katrina Rack4,5, Eva van den Berg6, H. Berna Beverloo7, Marian Stevens-Kroef8

1Unité de génétique du Cancer, Service de génétique médicale, Centre Hospitalier Universitaire Vaudois, CH, Lausanne, Switzerland; 2Cytagenomics Laboratory, NIMGenetics, Madrid, Spain; 3Cytogenetic External Quality Assessment, Women's Centre, John Radcliffe Hospital, Oxford University Hospitals NHS Trust, Oxford, UK; 4Institut de pathologie et de génétique, Gosselies, Belgium; 5West Midland Regional Genetic Laboratory, Birmingham Womens Hospital, Birmingham, UK; 6Dept Genet, University Groningen, University Medical Centre Groningen, Groningen, The Netherlands; 7Dept of Clinical Genetics, Erasmus Medical Centre, Rotterdam, The Netherlands; 8Dept of Human Genetics, Radboud University Medical Centre, Nijmegen, The Netherlands.

Genes, Chromosomes and Cancer, Accepted manuscript online: 16 Jan 2016. doi: 10.1002/gcc.22350
Genetic profiling is important for disease evaluation and prediction of prognosis or responsiveness to therapy in neoplasia. Microarray technologies, including array comparative genomic hybridization and single-nucleotide polymorphism-detecting arrays have in recent years been introduced into the diagnostic setting for specific types of haematological malignancies and solid tumours ... Currently with the exception of translocation CGH (tCGH) arrays and Affymetrix Oncoscan, copy number arrays are not designed to detect recurrent molecularly balanced chromosomal rearrangements (translocations, insertions, inversions) or to screen for recurrent point mutations ....

12- Meeting abstract
IKZF1 and 22q11.22 Deletions and PDGFRA Gains Are Associated with Poor Outcome in Down Syndrome Acute Lymphoblastic Leukemia
ASH (American Society of Hematology) 54th Annual Meeting, Dec 8-11, 2012, Atlanta, GA, Abst#289. ... Copy number profiling was performed using 500K, 6.0, CytoScan HD, and OncoScan FFPE Express arrays (Affymetrix), and Human CNV370-Duo arrays (Illumina). Gene expression profiling was performed using U133 Plus2.0 arrays (Affymetrix).

13- Meeting abstract
IKZF1/CDKN2A co-deletion predicts shorter survival in adult B-ALL
Shiven Patel1, Clinton C. Mason1, Martha J. Glenn1, Christian N. Paxton2, Sara T. South3, Melissa H. Cessna4, Julie Asch5, Erin F. Cobain6, Dale L. Bixby6, Lauren B. Smith7, Joshua D. Schiffman8, and Rodney R. Miles9
1Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; 2ARUP Laboratories, Salt Lake City, UT; 3University of Utah Dept of Pathology, ARUP Laboratories, Salt Lake City, UT; 4Dept of Pathology and Intermountain Biorepository, Salt Lake City, UT; 5Sitemountain Blood and Marrow Transplant/Acute Leukemia Program, Salt Lake City, UT; 6University of Michigan Dept of Hematology, Ann Arbor, MI; 7University of Michigan Dept of Pathology, Ann Arbor, MI; 8Huntsman Cancer Institute, University of Utah Dept of Pediatrics, Salt Lake City, UT; 9Huntsman Cancer Institute, University of Utah Dept of Pathology, ARUP Laboratories, Salt Lake City, UT.
Cancer Research, 2015, 75(15 Suppl):Abstract #1723. [AACR 106th Annual Meeting 2015; April 18-22, 2015; Philadelphia, PA]

B lymphoblastic leukemia (B-ALL) in adults has a higher risk of relapse and lower long-term survival than pediatric B-ALL. Prognostic biomarkers are needed for better risk-stratification and therapy selection. Microarray-based genome-wide profiling studies in pediatric patients have revealed recurrent abnormalities in B-cell development and cell cycle regulation. IKZF1 alterations convey a negative prognostic impact in pediatric B-ALL, but their significance is not well characterized in adult B-ALL. CDKN2A alterations have also been associated with a poorer prognosis in adult Ph+ ALL, possibly by mediating resistance to targeted therapy. The copy number landscape of adult B-ALL has not been fully assessed, and given its inferior prognosis, may be distinct from its pediatric counterpart. We identified 70 adult B-ALL patients (median age 45 years, range 18-83) from 1998-2013 at three institutions. DNA was isolated from formalin-fixed, paraffin-embedded (FFPE) diagnostic bone marrow clots and assessed with the OncoScan FFPE Express genome-wide single nucleotide polymorphism (SNP) assay (Affymetrix). Copy number alteration (CNA) analysis was performed using Nexus Software V7 (Biodiscovery) and in-house coding. The most frequent CNAs called by the software were manually verified for probe evidence. Clinical data available on this cohort included age, gender, hematologic laboratory values at presentation, CSF involvement, receipt of allogeneic transplant, cytogenetic profile, presence of (9;22), event-free survival (EFS), and overall survival (OS). Estimated median survival time of the entire adult B-ALL patient cohort was 29 months. Recurrent deletions in the diagnostic samples were noted at several loci, including CDKN2A (47%), IKZF1 (40%), PAX5 (24%), BTG1 (17%), and BTLA (14%). Recurrent gains were identified at the following loci: ERG (30%), ETS2 (21%), MYB (20%), UBASH3B (20%), PRKCH (19%), CDK6 (17%), and ET6 (16%). No individual CNA heralded a significant prognostic impact in the entire cohort or in subgroup analyses stratified by presence of (9;22) for either EFS or OS, though this could be due to our relatively smaller sample size in contrast to pediatric studies that have observed a prognostic impact at some of these loci. However, the combination of both CDKN2A and IKZF1 deletions (26%) correlated with a significantly worse overall survival than having only one or neither of these deletions (both vs CDKN2A only: p = 0.028, both vs IKZF1 only: p = 0.027, both vs neither deleted: p = 0.048). Age was the only other covariate significant in univariate analyses for OS, yet
IKZF1/CDKN2A co-deletion remained significant in multivariate analysis adjusting for age. Adult B-ALL demonstrates frequent CDKN2A deletions, IKZF1 deletions, and CDKN2A/IKZF1 co-deletions. To our knowledge, the negative prognostic impact of the CDKN2A/IKZF1 co-deletion is a novel finding in adult B-ALL and requires further validation in larger cohorts.

Bone / Osteosarcoma

Copy Number Alterations and Methylation in Ewing's Sarcoma.
Jahromi MS, Jones KB, Schiffman JD.
... Previously, DNA extracted from paraffin has been too degraded to yield reliable data for analysis, but a new molecular inversion probe assay (OncoScan, Affymetrix, Santa Clara, CA) has been used successfully to identify copy number changes in formalin-fixed paraffin-embedded (FFPE) samples [65].

Molecular inversion probe analysis detects novel copy number alterations in Ewing sarcoma
... Genomic DNA (3e300 ng/sample) from the FFPE clinical samples underwent MIP analysis with the expanded OncoScan FFPE Express assay (V1.0) with 330,000 cancer gene and genome-wide probes (Affymetrix).

The molecular landscape of extraskeletal osteosarcoma: A clinicopathological and molecular biomarker study
George Jou1, Lu Wang1, Sumit Middha1, Ahmet Zehir1, Wen Chen1, Justyna Sadowska1, John Healey2, Narasimhan P Agaram1, Lisa Choi2, Khedoudja Nafa1 and Meera Hameed1,*
1Dept of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY; 2Dept of Orthopedic Surgery, Memorial Sloan Kettering Cancer Center, New York, NY
... DNA from formalin-fixed paraffin-embedded (FFPE) tissue was extracted and processed from 27 cases. Genome-wide DNA copy number (CN) alterations and allelic imbalances were analyzed by single nucleotide polymorphism array using Affymetrix OncoScan FFPE Assay.

TP53 intron 1 hotspot rearrangements are specific to sporadic osteosarcoma and can cause Li-Fraumeni syndrome
Sebastian Ribi1,*; Daniel Baumhoer2,3,*, Kristy Lee4,*; Edison5, Audrey S.M. Teo1, Babita Madan5, Kang Zhang6, Wendy K. Kohlmann7, Fei Yao1, Wah Heng Lee8, Qiangze Hoi8, Shaojiang Cai8, Xing Yi Woo9, Patrick Tan1,5,10, Gernot Jundt2,3,11, Michaela Nathrath3,11, Wing-Kin Sung8,12, Joshua D. Schiffman4, David M. Virshup5, Axel M. Hillmer1
1Cancer Therapeutics & Stratified Oncology, Genome Institute of Singapore, Singapore 138672, Singapore ; 2Bone Tumor Reference Center at the Institute of Pathology, University Hospital Basel, CH-4033 Basel, Switzerland; 3Clinical Cooperation Group Osteosarcoma, Helmholtz Zentrum Muenchen, German Research Center for Environmental Health, 85764 Neuherberg, Germany; 4Dept of Pediatrics and Oncological Sciences, Huntsman Cancer Institute, University of Utah Health Care, Utah, UT 84112, USA; 5Duke-NUS Graduate Medical School Singapore, Singapore 169887, Singapore; 6Institute for Genomic Medicine, UC San Diego, La Jolla, CA 92830, USA; 7Huntsman Cancer Institute, University of Utah Health Care, Utah, UT 84112, USA; 8Computational & Systems Biology, Genome Institute of Singapore, Singapore 138672, Singapore; 9Personal Genomics Solutions, Genome Institute of Singapore, Singapore 138672, Singapore; 10Cancer Science Inst of Singapore, Nati University of Singapore, Singapore 117599, Singapore; 11Dept of Pediatrics and Wilhelm Sander Sarcoma Treatment Unit, Technische Universitat Munchen and Pediatric Oncology Center, 81675 Munich, Germany ; 12School of Computing, National Univ of Singapore, Singapore 117417, Singapore

Somatic mutations of TP53 are among the most common in cancer and germline mutations of TP53 (usually missense) can cause Li-Fraumeni syndrome (LFS). Recently, recurrent genomic rearrangements in intron 1 of TP53 have been described in osteosarcoma (OS), a highly malignant neoplasm of bone belonging to the spectrum of LFS tumors. Using whole-genome sequencing of OS, we found features of TP53 intron 1 rearrangements suggesting a unique mechanism correlated with transcription ... Cancers in this family had loss of heterozygosity, retaining the rearranged allele and resulting in TP53 expression loss. In conclusion, intron 1 rearrangements cause p53-driven
malignancies by both germline and somatic mechanisms and provide an important mechanism of TP53 inactivation in LFS, which might in part explain the diagnostic gap of formerly classified “TP53 wild-type” LFS...To test for deletions of the second allele in tumors, copy number analysis using OncoScan FFPE Express (Affymetrix, Inc.) were performed on tumor samples of H2 (two OS lung metastases that developed six months apart), P1 (undifferentiated pleomorphic sarcoma) and P13 (lung adenocarcinoma and meningioma).

Brain / Astrocytoma / Gliomas

18- A clinicopathologic study of diencephalic pediatric low-grade gliomas with BRAF V600 mutation

...BRAF duplication/fusion status was assessed by fluorescence in situ hybridization (FISH) (probes targeting 30 and 50 BRAF obtained from Empire Genomics, Buffalo, NY, USA), exon sequencing, or OncoScan FFPE SNP array (Affymetrix, Santa Clara, CA, USA).

19- Meeting abstract
A novel gene fusion in glioblastoma and a radiation response methylation signature identified by genomic characterization of glioma sphere-forming cells
Qianghu Wang1, Ravesanker Ezhalarasan1, Lindsey D. Goodman2, Joy Gumín1, Siyuan Zheng1, Kosuke Yoshihara1, Peng Sun1, Jie Yang1, Tim Heffernan1, Giulio Draetta1, Kenneth D. Aldape3, Frederick F. Lang1, Roel G.W. Verhaak1, and Erik P. Sulman1
1The University of Texas, MD Anderson Cancer Center, Houston, TX; 2University of Pennsylvania, Philadelphia, PA; 3Princess Margaret Hospital, Toronto, Ontario, Canada.

Purpose: High fidelity models of the lethal primary brain tumor glioblastoma (GBM) are essential to develop new therapies. Glioma sphere-forming cells (GSCs) are derived from surgical specimens and are thought to play important roles in tumor maintenance and treatment resistance. We performed genomic characterization of the largest reported panel of GSCs. We hypothesized that GSCs would recapitulate the genomic alterations of their GBMs of origin while identifying novel changes identifiable only in a pure tumor cell population. Methods: All GSCs were obtained at the time of surgical resection and all analyses were conducted at early passage. We performed exome and transcriptome sequencing, DNA methylation profiling (Illumina Infinium 450K Bead Arrays) and DNA copy number determination (Affymetrix OncoScan). Radiation (RT) sensitivity was determined by clonogenic survival and in vivo survival by orthotopic xenograft. Results: We analyzed 43 GSCs, 40 of which had tissue available from their tumors of origin. Somatically mutated genes previously described in GBM, such as TP53, EGFR, PTEN, NF1, PIK3CA and RB1, were found at similar mutation frequencies. Likewise, DNA copy number variations were similar to their matched tumors and those reported by the TCGA, with novel or more pronounced alterations, such as MYC application and QKI deletion, identified in the GSCs. GSCs were classified into TCGA GBM subtypes by expression signatures, identifying a subset of GSCs with a subtype differing from their matched tumors that correlated to decreased stromal enrichment. GSCS exhibited upregulation of self-renewal pathways, such as MYC, WNT, and NOTCH, and of stem-cell factors, such as MSI1, NESTIN, OLIG2, and SOX2, consistent with the stem-like phenotype attributed to GSCs. Transcript analyses identified the previously reported FGFR3-TACC3 and EGFR-SEPT14 gene fusions as well as a novel KIF1B-KMT2A (MLL) fusion, which was found to have been retained in the matching recurrent GBM as well as the GSC derived from the recurrence. A signature derived by the differential methylation pattern of RT sensitive vs. resistant GSCs was applied to the subset of TCGA cases that received upfront RT. Survival by methylation class in this subset was significantly different (median survival 84 vs. 61 weeks; HR 1.64 adjusting for patient age, p-value<0.008), suggesting this signature is predictive of clinical RT response. Conclusions: Based on genomic analyses, GSCs are robust models of GBM which can be used for therapeutic development. We have identified a novel gene fusion involving MLL with a predicted driving role suggesting a new mode of gliomagenesis. A methylation signature predictive of RT response may have potential for personalizing RT treatment of GBM patients and provides insights into RT sensitivity phenotypes.
Changes in the EGFR amplification and EGFRvIII expression between paired primary and recurrent glioblastomas

Martin J. van den Bent, Ya Gao, Melissa Kerkhof, Johan M. Kros, Thierry Gorlia, Kitty van Zwieten, Jory Prince, Sjoerd van Duinen, Peter A. Sillevis Smitt, Martin Taphoorn and Pim J. French

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Neuro Oncol, 2015, 17(7): 935-941.

Background The efficacy of novel targeted therapies is often tested at the time of tumor recurrence. However, for glioblastoma (GBM) patients, surgical resections at recurrence are performed only in a minority of patients; therefore, molecular data are predominantly derived from the initial tumor. Molecular data of the initial tumor for patient selection into personalized medicine trials can therefore be used only when the specific genetic change is retained in the recurrent tumor. Methods In this study we determined whether EGFR amplification and expression of the most common mutation in GBMs (EGFRvIII) is retained at tumor recurrence ... The qPCR assay used correlated with EGFR amplification status as determined by copy number arrays (n = 5, Oncoscan DX, Affymetrix); examples are shown in Supplementary material, Figure S1. EGFRvIII expression ...

Choroid plexus carcinomas are characterized by complex chromosomal alterations related to patient age and prognosis


... The oncoscan molecular inversion probe single nucleotide polymorphism (MIP SNP) array allows for high-resolution analysis of formalin-fixed paraffin-embedded archival samples (Wang et al., 2012) and has been successfully employed in other rare brain tumors, ...

Disseminated Medulloblastoma in a Child with Germline BRCA2 6174delT Mutation and without Fanconi Anemia


... Genome-wide copy number determination for the diagnostic formalin-fixed paraffin embedded (FFPE) sample was carried out using OncoScan system utilizing molecular inversion probe (MIP) technology (Affymetrix, Santa Clara, CA, USA). In brief, three scrolls of FFPE material (20 μm thickness) were sent to Affymetrix for DNA extraction using the OncoScan FFPE assay kit and for generation of MIP probes followed by hybridization on the Affymetrix MIP 330K platform.

DISTINCT COPY NUMBER ALTERATIONS AND INCIDENCE OF CHROMOTHripsis ASSOCIATED WITH GRADE AND PROGNOSIS IN IDH MUTANT AND WILD-TYPE GLIOMAS

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Neuro Oncol, 2014, 16(suppl 3) : iii6. [20th Intl Conf on Brain Tumor Research and Therapy, July 20-22, 2014, Lake Tahoe, CA]

BACKGROUND: Both IDH mutated (IDHmut) and wild-type (IDHwt) lower grade gliomas can progress to GBM. However, a detailed study of alterations associated with progression of these molecularly distinct tumor types has not been described. Here we perform an analysis of copy number alterations (CNA) across all grades (Grade II-II and Grade IV) IDHmut vs IDHwt infiltrating gliomas. METHODS: DNA was extracted from 94 patient FFPE glioma samples from 4 clinical and molecular groups: Grade II-III IDHwt (n = 17), Grade II-III IDHmut (n = 28), Grade IV
IDHwt (n = 25), and Grade IV IDHmut (n = 24). CNA were detected by molecular inversion probes (OncoScan FFPE Express, Affymetrix) and analyzed with Nexus Copy Number Software (BioDiscovery). GISTIC was used to define deletions and amplifications. Chromothripsis (“chromosomal shattering”) was defined using stringent criteria of at least ten switches of CNA in individual chromosomes. RESULTS: Unsupervised clustering of CNAs demonstrated distinct clusters within IDHmut gliomas that correlated with grade. However, within IDHwt gliomas all grades clustered together regardless of grade, with Chr7 amplification (including EGFR) and loss of Chr10 (including PTEN) seen in most tumors. IDHwt Grade II-III and Grade IV tumors both displayed relatively poor prognosis (median survivals of 65.4 and 37.4 weeks). However, IDHmut gliomas had better survival for all grades (604.3 weeks for Grade II-III and 270.3 weeks for Grade IV). Grade IV IDHmut gliomas were more likely to have gains of 1q25.3 (SMG7, NCF2), 1q32.1 (KIF14, DDX59, BTG2), 6p21.1 (HSP90AB1 and other genes) and loss of 3p21 compared with Grade II-III. Functional analyses showed that IDHwt tumors had more amplifications in receptor tyrosine kinases and their downstream pathways. In terms of novel prognostic markers within IDHmut Grade II-III tumors, multivariate analysis identified loss of estrogen receptor B and loss of 10q26.3 containing part of GLRX3 as poor prognostic factors, and CDKN1C loss as a good prognostic factor. Finally, significantly higher incidence of chromothripsis events were observed in grade IV IDHmut compared to IDHwt. CONCLUSIONS: CNA analysis demonstrated significant differences in molecular ontogeny, progression, and prognosis between IDHwt and IDHmut gliomas, which may serve to further elucidate pathogenesis of these distinct tumor types. Significant CNA increases and increased chromothripsis in grade IV IDHmut support malignant transformation of IDHmut low grade gliomas through accumulation of genomic instability, that results in partial overlap of CNA alterations that are seen earlier in the development of IDHwt tumors.

24- DNA copy number analysis of Grade II-III and Grade IV gliomas reveals differences in molecular ontogeny including chromothripsis associated with IDH mutation status
Adam Cohen1†, Mariko Sato2†, Kenneth Aldape3, Clinton C. Mason1, Kristin Alfaro-Munoz3, Lindsey Heathcock3, Sarah T. South46, Lisa M. Abegglen1, Joshua D. Schiffman15† and Howard Colman1†
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... DNA was plated in a 96-well plate ... The completed plates were sent to the Affymetrix Research Services Laboratory at Santa Clara, CA, and the OncoScan™ FFPE Express MIP assay was run ...

25- Extensive therapies for extraneural metastases from glioblastoma, as confirmed with the OncoScan assay
Ming Xu1, Ying Wang1, Jian Xu1, Yu Yao1, Wei-xing Yu2, Ping Zhong1, ,
1 Dept of Neurosurgery, and, Huashan Hospital, Fudan University, Shanghai, China; 2 Dept of Maxillofacial Surgery, Huashan Hospital, Fudan University, Shanghai, China
World Neurosurgery, Available online 4 February 2016, In Press, Accepted Manuscript
... The diagnosis of lymph node metastases from glioblastoma was confirmed through an OncoScan assay and pathological analysis.

26- Genetic and chromosomal alterations in Kenyan Wilms Tumor
Harold N. Lovvorn III, Janene Pierce, Jaime Libes, Bingshan Li, Qiang Wei, Hernan Correa, Julia Gouffon, Peter E. Clark, Jason R. Axt, Erik Hansen, Mark Newton, James A. O’Neill Jr., on behalf of the Kenyan Wilms Tumor Consortium
... Genomic DNA was available from 34 of these KWT specimens for this analysis and was shipped to Affymetrix to perform the OncoScan™ FFPE Assay Kit ...

27- Genome-Wide DNA Copy Number Analysis of Desmoplastic Infantile Astrocytomas and Desmoplastic Infantile Gangliogliomas
Gessi, Marco; zur Mühlen, Anja; Hammes, Jennifer; Waha, Andreas; Denkhaus, Dorota; Pietsch, Torsten
Brain tumor entities are characterized by specific copy number alterations (CNA), allelic losses/disbalances and recurrent mutations. Emerging technologies including SNP arrays, whole exome and whole genome sequencing are not suitable for degraded DNA derived from formalin-fixed, paraffin embedded (FFPE) samples. The aim of our study was to analyse the sensitivity and robustness of molecular inversion profiling (MIP) as a tool to identify these alterations in brain tumors and to compare this method to FISH and multiplex ligation probe analysis (MLPA).

Genomic DNA extracted from up to 20 years old FFPE materials from more than 1300 brain tumors covering most WHO entities were analyzed by MIP profiling (OncoScan V2/V3, Affymetrix). MIP revealed genome-wide copy number information from as little as 20 ng of degraded DNA; drop-out rate was <5%. In contrast to FISH and MLPA, MIP allowed a genome-wide analysis, adding significant information to the differential diagnosis. Characteristic CNA were detected, including BRAF duplications in pilocytic astrocytomas, chromosome 22 loss in ATRT, chromosome 10 loss, 7 gain and amplifications of PDGFR or EGFR in glioblastoma, 1p19q codeletion in oligodendrogial tumours, chromosome 2 gain and C19MC amplification in ependymoblastoma. Novel prognostic markers including MYCN amplification in CNS-PNET were identified. Established prognostic markers including MYC/MYCN amplifications in medulloblastomas and chromosome 1q gain in ependymomas were easily detected and validated by orthogonal methods. Extended chromosomal alterations including widespread hyperdiploidy in plexus papillomas or complex alterations such as chromosomal scattering of whole chromosomes (chromotripsis) in TP53 deficient medulloblastomas were easily uncovered. MIP also detected copy-neutral LOH and recurrent tumor-associated mutations (e.g. BRAFV600E, IDH gene mutations). Our data indicate that MIP is a sensitive and robust method to assess CNA, allelic imbalances/losses and specific recurrent point mutations in FFPE tumor material, and therefore represents a novel tool for precise neuropathological tumor diagnostics and prognostic stratification.
Introduction: The current molecular classification of posterior fossa (PF) ependymomas suggests two principal subgroups, one presenting mainly in infants (PFA) and a second presenting mainly in adults and adolescents (PFB). We tested the hypothesis that PF disease in infants comprises two molecular subgroups, having observed supporting transcriptomic data from patients at St. Jude (SJ) whose tumours were analysed as part of the Pediatric Cancer Genome Project. Material and methods: Transcriptomic and methylytic data were generated on a series of PF ependymomas from SJ infants (n = 124) and children and adults from the DKFZ (n = 98) using Affymetrix U133 and Illumina 450K arrays. Copy number alterations were demonstrated using fluorescence in situ hybridization or Affymetrix SNP6 or OncoScan arrays. Associations between genomic and detailed clinicopathologic data were sought. Results: Among infants, two molecular subgroups in transcriptomic and methylytic datasets were demonstrated in cohorts from both centers. These subgroups were shown to segregate with PFA tumours when datasets for infants and the entire disease were compared. Relative over-expression of HOX genes and genes involved in angiogenesis and the immune response characterized one subgroup (PFA-1), while genes involved in the cytoskeleton and development of the mid-brain/hind-brain boundary were overexpressed in the other (PFA-2). Radiological and clinical data have identified differences in the presentation and outcome of tumours from the two subgroups. Conclusion: Infant PF ependymomas comprise two molecular subgroups with different transcriptomic and methylytic profiles that suggest a distinct histogenesis. While PFA-1 and PFA-2 present at the same age, other clinicopathological characteristics are distinct, suggesting that distinguishing tumors of the two subgroups would have clinical utility.

31- Integrated Diagnostic Approach for Adult Oligodendroglioma and Oligoastrocytoma

Jens Schittenhelm*
Institute of Pathology and Neuropathology, University Tuebingen, Tuebingen, Germany
Brain Disorders & Therapy, 2015, 4(4): 187

... Figure 1: Example for integrated diagnosis in oligodendroglioma ... The tumor however exhibited nuclear loss of ATRX and 1p/19q analysis showed no allelic losses in microsatellite-PCR (high-resolution gel bottom) as well in genome-wide copy number analysis (OncoScan FFPE top).

32- Multiomics approach showing genome-wide copy number alterations and differential gene expression in different types of North-Indian pediatric brain tumors

Neetu Singh a, Dinesh Kumar Sahu b, Archana Mishra c, Preeti Agarwal d, Madhu Mati Goel d, Anil Chandra e, Sunil Kumar Singh e, Chhiti Srivastava e, Bal Krishna Ojha e, Devendra Kumar Gupta f, Ravi Kant g
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... The study design was aimed to identify and catalog genome-wide copy number alterations and differential gene expression in different types of North-Indian pediatric posterior fossa tumors and matched control tissue through Molecular Inversion Probe (MIP) Based and Human Transcriptome Array. Experimental design—MIP based OncoScan Array and Human Transcriptome Array 2.0 were used to molecularly-categorize histopathologically and immunohistochemically proven tumor samples on the basis of copy number variations and altered gene expression patterns and/or alternative splicing events ....

33- Molecular Characterization of Choroid Plexus Tumors Reveals Novel Clinically Relevant Subgroups

Diana M. Merino1, Adam Shlien1, Anita Villani1, Malgorzata Pienkowska1, Stephen Mack1, Vijay Ramaswamy1, David Shih1, Ruth Tatevosian2, Ana Novokmet1, Sanaa Choufani1, Rina Dvir3, Myran Ben-Arush4, Brent T. Harris5, Eugene I. Hwang6, Rishi Lulla7, Stefan M. Pfister8, Maria Isabel Achatz9, Nada Jabado10, Jonathan L. Finlay11, Rosanna Weksberg1, Eric Bouffet1, Cynthia Hawkins1, Michael D. Taylor1, Uri Tabori1, David W. Ellison2, Richard J. Gilbertson2, and David Malkin1,*
1 The Hospital for Sick Children, Toronto, Ontario, Canada; 2 St. Jude Children's Research Hospital, Memphis, TN; 3 Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; 4 Rambam Health Care Campus, Haifa, Israel; 5 Georgetown University Medical Center, Washington, DC; 6 Children's National Medical Center, Washington, DC; 7 Ann & Robert H. Lurie Children’s Hospital of Chicago,
... This report is the first to dissect the aberrant complexity in copy number, methylation, and gene expression of one of the largest cohort of pediatric choroid plexus tumors (CPT) .......

An initial set of 55 tumor DNA samples was hybridized to Genome-Wide Human SNP Array 6.0 (Affymetrix), whereas an independent set of 20 tumor DNA samples was hybridized to Affymetrix OncoScan FFPE Express 2.0 arrays.

34- Molecular characterization of disseminated pilocytic astrocytomas

Marco Gessi1, Alexander C. Engels1, Sally Lambert2, Thomas Rothämel3, Stephan von Hornstein4, V. Peter Collins2, Dorota Denkhaus1, Astrid Gnekow4 and Torsten Pietsch1,*
1Inst. of Neuropathology, University of Bonn, Bonn, Germany; 2Dept. of Pathology, University of Cambridge, Cambridge, UK; 3Dept. of Forensic Medicine, University of Hannover Medical School, Hannover, Germany; 4Dept. of Pediatric Oncology, Klinikum Augsburg, Augsburg, Germany
Neuropathology and Applied Neurobiology. Accepted manuscript online: 18 JUN 2015

... To identify copy number gains and losses, we used a molecular inversion probe (MIP) array using the custom-designed OncoScan FFPE Express 330K platform (v2) (Affymetrix, Santa Clara, USA) as described previously [7]....

35- Molecular stratification of medulloblastoma: Comparison of histological and genetic methods to detect Wnt activated tumors

Tobias Goschzik1, Anja zur Mühlen1, Glen Kristiansen2, Christine Haberler3, Harald Stefanits3, Carsten Friedrich4, Katja von Hoff4, Stefan Rutkowski4, Stefan M. Pfister5 and Torsten Pietsch1,*
1Dept of Neuropathology, University of Bonn Medical Centre, Sigmund-Freud-Str. 25, 53127 Bonn, Germany; 2Dept of Pathology, University of Bonn Medical Centre, Sigmund-Freud-Str. 25, 53127 Bonn, Germany; 3Institute of Neurology, Medical University of Vienna, Währinger Gütel 18-20, 1097 Vienna, Austria; 4Dept of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany; 5Dept of Pediatric Oncology, Hematology and Immunology, Heidelberg University Hospital, Im Neuenheimer Feld 430, 69120 Heidelberg, Germany

Aims--Wnt activation in medulloblastomas is associated with good outcome. Upfront testing and risk-adapted stratification of patients will be done in future clinical studies. In a cohort of 186 pediatric medulloblastomas our aim was to identify the optimal methods in standard clinical practice to detect this subgroup ...we conclude that sequencing analysis of CTNNB1 exon 3 in combination with β-catenin IHC (possibly as pre-screening method) is a feasible and cost-efficient way for the determination of Wnt medulloblastomas .................. Molecular inversion profiling To identify copy number gains and losses, the custom-designed OncoScan FFPE Express 330K molecular inversion profiling platform, version 2 (Affymetrix, Santa Clara, CA, USA) was used.

36- Mutations in G Protein Encoding Genes and Chromosomal Alterations in Primary Leptomeningeal Melanocytic Neoplasms


Limited data is available on the genetic features of primary leptomeningeal melanocytic neoplasms (LMNs). Similarities with uveal melanoma were recently suggested as both entities harbor oncogenic mutations in GNAQ and GNA11. Whether primary LMNs share additional genetic alterations with uveal melanoma including copy number variations is unknown ...Furthermore, the lesions were tested for copy number variations of chromosomes frequently present in uveal melanoma (1p, 3, 6 and 8q) by multiplex ligation-dependent probe amplification (MLPA). Genome-wide analyses of copy number alterations of two leptomeningeal melanocytic neoplasms were performed using the OncoScan SNP-array....

37- Meeting abstract

Next generation sequencing reveals distinct prognostic classes among grade II/III gliomas

Erica Bell, Oliver Ochike, Jessica Gleming, Arup Chakraborty, Joe McElroy, Cynthia Timmers, Andrea Salavaggione, Ori Staszewski, Marco Prinz, Anca Grosu, Arnab Chakravarti
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BACKGROUND: WHO grade II and III gliomas are heterogeneous both genotypically and phenotypically. Genomic characterization and prognostic classification of grade II and III gliomas has only recently begun to be elucidated. Therefore, we retrospectively analyzed an institutional cohort of grade II/III gliomas (n = 62).

METHODS: A custom Ion Torrent next generation sequencing panel was used to sequence IDH1, IDH2, CIC, FUBP1, and ATRX. TERT promoter mutations were analyzed by Sanger sequencing. 1p/19q co-deletion status was determined by the Illumina 450K Array and the Affymetrix Oncoscan platform (in select cases). Each marker was analyzed for prognostic significance by logrank tests and multivariate (MVA) Cox regression analysis.

RESULTS: The cohort consisted of 22 grade II and 40 grade III tumors. IDH1/2 mutations were found in 87% (54/62), ATRX mutations in 24% (15/62), CIC/FUBP1 mutations in 39% (24/62), and TERT mutations in 52% (27/52) of the cases. 1p/19q co-deletions were found in 51% (31/61) of the cases. Regarding classification of 1p/19q co-deletion, four cases were discordant between FISH compared to the 450K array or Oncoscan likely due to high heterogeneity in these cases and more information gained with high-density platforms. In the logrank tests, 1p/19q co-deletion (HR 2.0; p = 0.019) and IDH1/2 mutations (HR = 8.7; p < 0.001) were associated with better PFS. IDH1/2 mutations (p < 0.001), CIC/FUBP1 mutations (p = 0.021), and 1p/19q co-deletion (p < 0.001) were found to be significantly correlated with OS. In MVA, IDH mutation and 1p/19q co-deletion were independent prognostic factors for both OS and PFS after adjustment for age and grade. Three prognostic groups were also examined (IDHwt, IDHmut/non-co-del, and IDHmut/co-del) and were found to be significantly associated (p < 0.05) with PFS and OS upon MVA.

CONCLUSIONS: Our findings confirm the favorable prognostic information of IDH mutations and 1p/19q co-deletion independent of grade in gliomas. The predictive value of these molecular alterations remains to be determined.

38- Observations of the genomic landscape beyond 1p19q deletions and EGFR amplification in glioma

Christian N. Paxton, Leslie R. Rowe, Sarah T. South
Molecular Cytogenetics, December 2015, 8:60 (First online: 07 August 2015)
... The two categories of gliomas analyzed in this study were initially identified by FISH testing and subsequently assessed for CNCs using the OncoScan® array (Affymetrix, Santa Clara, CA).

39- One comment referring to ongoing studies

PCR-Based Simple Subgrouping Is Validated for Classification of Gliomas and Defines Negative Prognostic Copy Number Aberrations in IDH Mutant Gliomas

Shunsuke Nakae, Hikaru Sasaki, Saeko Hayashi, Natsuki Hattori, Masanobu Kumon, Yuya Nishiyama, Kazuhide Adachi, Shinya Nagahisa, Takuro Hayashi, Joji Inamasu, Masato Abe, Mitsuhiro Hasegawa, Yuichi Hirose
... Given the high recurrence rate among IDH mutant gliomas with TP53 mutations, efforts are required to prevent progression to high grade gliomas or secondary glioblastomas, which are difficult to control with multidisciplinary treatments. To this end, studies are in progress now using OncoScan arrays (Affymetrix) for this type of glioma to identify specific regions with common losses, gains, or high copy number gains, and consequent changes in gene expression.

40- Meeting abstract

PEDIATRIC POSTERIOR FOSSA EPENDYMOMAS CONSIST OF TWO MOLECULAR SUBGROUPS DEFINED BY GENE EXPRESSION AND METHYLATION PROFILING

Chandnamali Punchihewa1, Ryan Lee1, Tong Lin1, Wilda Orisme1, James Dalton1, Eleonora Aronica2, Amy Smith3, Amar Gajjar1, Arzu Onarer1, Stanley Pounds1, Ruth Tatevossian1, Thomas Merchant1 and David Ellison1
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Neuro Oncol (2014) 16 (suppl 1); Abstr #EM-011. [16th Intl Symposium on Pediatric Neuro-Oncology in conjunction with the 8th St. Jude-VIVA Forum, June 28 - July 2, 2014, Singapore]

Gene expression or methylation profiling has been used to delineate molecular subgroups of pediatric brain tumors, each having specific clinicopathologic and genetic correlates. Using these methods, we sought to define clinicopathologic and genetic correlates of molecular subgroups among pediatric posterior fossa ependymomas. The
study cohort comprised 161 pre-treatment tumors, available as freshly frozen or formalin-fixed paraffin-embedded (FFPE) samples. DNA methylation profiles were generated from 160 tumors on the illumina 450K platform. Expression profiling using Affymetrix U133 arrays was undertaken on 57 tumors, 40 of which were also analyzed by transcriptome sequencing on the illumina HiSeq platform. Highly over-expressed genes in two molecular subgroups defined by array profiling were also evaluated by the Quantigene™ assay in 63 FFPE tumors. Copy number alterations (CNAs) were assessed on Affymetrix SNP 6.0 (frozen samples) or OncoScan™ (FFPE samples) arrays. Two molecular subgroups were consistently recapitulated in recurrent cluster analyses using gene expression and methylation profiles for boot-strap datasets obtained by resampling of subjects. One subgroup was characterized by up-regulation of multiple HOX genes (subgroup A). Analysis of CNAs showed that loss of chromosome 22q was found only in subgroup A. Significantly more tumors with necrosis (p < 0.00001) or microvascular proliferation (p < 0.027) belonged to subgroup A. Subgroups A and B did not differ with respect to age at diagnosis or gender.

Outcome analyses were performed on 115 patients from the St. Jude RT1 trial. Outcome was not associated with molecular subgroup, but extent of surgical resection and gain of chromosome 1q were significant outcome indicators in a multivariate analysis. Using gene expression and methylation profiling, we have shown that pediatric posterior fossa ependymomas fall into two molecular subgroups. These may have different oncogenic origins and pathologic features, but have similar clinical associations.

41 Meeting abstract

REL A FUSION DEFINES CLINICOPATHOLOGIC SUBSETS OF SUPER TENTORI AL EPENDYOMA: A STUDY FROM THE COLLABORATIVE EPENDYOMA RESEARCH NETWORK

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Neuro Oncol, 2014, 16(suppl 2) : Abstr # P04.01 [Abstracts 11th Congress of the European Association of Neuro-Oncology, Turin, Italy, October 9-12, 2014]

A novel fusion involving C11ORF95 and RelA was recently described in supratentorial ependymomas. We sought to further characterize the clinical relevance of this fusion. We evaluated a cohort of 98 supratentorial ependymomas from the collaborative ependymoma research network (CERN) tissue repository. Screening of fusion transcripts from FFPE-derived RNA for the 2 most common fusion breakpoints (representing over 90% of cases when a fusion is present), we found 30 fusion-positive cases and 68 cases in which either fusion transcript was not present. With a goal of comparing fusion-positive vs. fusion negative cases, we found that fusion positive-cases were most likely to be diagnosed as anaplastic-grade III compared to fusion-negative cases (67% vs. 41%, respectively). The median patient age of fusion-positive cases was younger than fusion-negative cases (9.5 vs. 24.7 years). Overall, 20/52 (38%) of pediatric cases (age <21), were fusion-positive, compared with 10/46 (22%) of adult cases. Patient outcomes (overall- and progression-free survival) were not significantly different between fusion-positive and fusion-negative cases. Thirty-six of the 98 cases included in this study were examined for changes in DNA copy number (using Oncoscan, performed by Affymetrix) showing that patterns of copy number changes differed based on fusion status: losses in 9p, 11q and 14q and gains of 16q were significantly more common in fusion- positive cases. Conversely gains in 12, 18q and 20p were more common in fusion-negative cases: for example, loss of 9p was found in 38% of fusion-positive cases but only 6% of fusion-negative cases; conversely gain of 12q was not found in fusion- positive cases but was present in 30% of fusion-negative cases. Overall, this study extends the findings of the RelA fusion in supratentorial ependymoma by showing that it is nearly twice as common in pediatric cases, tends to present more frequently as WHO grade III and exhibits distinct patterns of DNA copy number aberration. These results identify clinical, pathologic and molecular correlates of RelA fusion status and extends the findings originally reported to robustly define 2 major molecular subgroups of supratentorial ependymomas.

42 Meeting abstract

THE TREATMENT-RESISTANT MESENCHYMAL SIGNATURE IN GIOBLASTOMA DERIVES FROM TUMOR CELLS INDEPENDENT OF STROMA

Erik P. Sulman, Qianghu Wang, Ravesanker Ezhilasasan, Lindsey D. Goodman, Joy Gumen, Peng Sun, Ken Aldape, WK Alfred Yung, Timothy Heffernan, Giulio F. Draetta and Frederick F. Lang

The University of Texas MD. Anderson Cancer Center


BACKGROUND: Glioma sphere-forming cells (GSCs) derived from surgical specimens are a fundamental resource to study glioblastoma (GBM) biology. Mesenchymal-expressing GSCs have been proposed as a source of treatment resistance and mesenchymal tumors correlate with poorer survival. Recently, we found that the anti-angiogenesis drug bevacizumab appeared to provide no benefit to patients with mesenchymal tumors, in contradiction to expectations
that a mesenchymal microenvironment may benefit from anti-angiogenesis therapy. We have developed a collection of GSCs that have undergone comprehensive genomic characterization, similar to that performed by the Cancer Genome Atlas (TCGA) for whole tumor specimens. We hypothesized that the genomic landscape of GSCs would recapitulate what was observed by TCGA. METHODS: 47 GSCs were obtained from primary culture of fresh tumor specimens obtained at surgery and cultured as 3-dimensional spheres in the absence of serum. All lines were subjected to RNAseq (75bp paired-end, 100X coverage), copy number analysis (Affymetrix Oncoscan 2.0), whole methylome (Illumina Infinium 450k bead array), and targeted resequencing of known cancer-associated genes. Whole exome sequencing was performed for 22 GSCs. Gene expression was determined by reads per kilobase per million (RPKM) using an RNA sequencing data analysis pipeline (PRADA) and somatic mutations identified by a commonly used detection method (MuTech). Consensus clustering based on none-negative matrix factorization (CNMF) was performed on expression data and correlation to TCGA clusters determined by single-sample gene set enrichment analysis (ssGSEA). RESULTS: While global copy number alterations such as gain of chromosome 7 at the EGFR locus or loss of chromosome 10 at the PTEN locus were shared between tumor and matched GSC, the rate of somatic events was significantly higher in GSCs compared to tumors (range 47-570, median 124 vs range 2-255, median 65). Optimization of CNMF identified a total of 5 gene-expression clusters. GSCs in only one of these clusters showed enrichment for a unique TCGA class, mesenchymal. GSCs in other clusters were divided among multiple TCGA classes. CONCLUSIONS: Mesenchymal glioblastomas are derived from mesenchymal GSCs, suggesting that the tumor component is the largest contributor to the aggressive biology of this subtype. GSCs from other tumor subtypes correlate to multiple TCGA classes, suggesting that tumor stroma may contribute to the expression phenotype in those cases. Therapeutics targeting the microenvironment, such as anti-angiogenesis drugs, may have a greater role in non-mesenchymal tumors where the stromal contribution is more prominent. © The Author(s) 2014. Published by Oxford University Press on behalf of the Society for Neuro-Oncology. All rights reserved.

43- Meeting abstract
Two DNA tests accurately classify gliomas into five molecular groups and provide additional information on acquired alterations
Seiji Yamada, Daniel Lachance, Cristiane Ida, Thomas Kollmeyer, Jesse Voss, Corinne Praska, Emily Barr Fritcher, Caterina Cianinni, Benjamin Kipp, Jeanette Eckel-Passow and Robert Jenkins
Mayo Foundation for Medical Education and Research, Rochester, MN, USA
Neuro-Oncology, 2015, 17(supl 5):v91-v100. [20th Annual Scientific Meeting of the Society for Neuro-Oncology, Nov 19 - 22, 2015, San Antonio, TX]

BACKGROUND: It has recently been shown that adult gliomas can be categorized into five molecular groups based on IDH mutation, 1p/19q codeletion and TERT promoter mutation (Eckel-Passow et al. N Engl J Med 2015 Epub Jun 10). We developed two genomics tests to assess these alterations and the other acquired alterations that are associated with the five glioma molecular groups. METHODS: DNA was isolated from 137 formalin-fixed, paraffin-embedded (FFPE) Mayo Clinic adult gliomas. First, copy number variants (CNV) and copy neutral loss of heterozygosity (cnLOH) were evaluated using the OncoScan platform (Affymetrix). Second, 50 genes commonly mutated in brain tumors - including TERT and IDH - were evaluated by multiplex PCR and pooled next-generation sequencing. The 50-gene panel included TP53 and ATRX. RESULTS: Together, the OncoScan CNV/cnLOH array and the 50-gene panel classified 135 (99%) of the gliomas into one of the five molecular groups: 29 (21%) Triple-Negative; 6 (4%) TERT- and IDH-mutation; 36 (26%) IDH-mutation only; 2 (1%) Triple-Negative; and 62 (45%) TERT-mutation only. Two (1%) had other patterns. Interesting findings included: Among the IDH-mutation only gliomas, all (100%) acquired a TP53 alteration and 31 (86%) an ATRX alteration. CnLOH of 17p (including TP53) was observed in 22 gliomas; 19 were IDH-mutation only. Acquired TP53 alterations were observed in all 22 tumors with 17p cnLOH. While most tumors were either TERT or ATRX mutated, some had mutations in both genes and some in neither. CIC and/or FUBP1 mutations were detected in 21 (72%) of the Triple-Positive gliomas. CnLOH of 9p was observed in 4 (14%) Triple-Positive gliomas. CONCLUSIONS: Two genomics tests using FFPE material can effectively classify gliomas into one of five molecular groups. The tests also identify common acquired alterations associated with these groups. These tests will be a significant adjunct to the clinical diagnosis of adult gliomas.

44- Two mature products of MIR-491 coordinate to suppress key cancer hallmarks in glioblastoma
X Li1,2,11, Y Liu1,11, K J Granberg1,3,4, Q Wang2, L M Moore1, P Ji1, J Gumin5, E P Sulman6, G A Calin7,8, H Haapasalo4, M Nykter3,9, I Shmulevich10, G N Fuller1, F F Lang5 and W Zhang1,8
1Dept of Pathology, University of Texas MD Anderson Cancer Center, Houston, TX; 2Dept of Biochemistry and Molecular Biology, State Key Laboratory of Cancer Biology, The Fourth Military Medical University, Xi’an, China; 3Dept of Signal Processing, Tampere University of Technology, Tampere, Finland; 4Dept of Pathology, Fimlab Laboratories and University of Tampere, Tampere, Finland; 5Dept of Neurosurgery, Univ of Texas MD Anderson Cancer Center, Houston, TX; 6Dept of Radiation Oncology, Univ of Texas MD Anderson Cancer Center, Houston, TX; 7Dept of Experimental Therapeutics, Univ of Texas MD Anderson Cancer Center, Houston,
MIR-491 is commonly co-deleted with its adjacent CDKN2A on chromosome 9p21.3 in glioblastoma multiforme (GBM). However, it is not known whether deletion of MIR-491 is only a passenger event or has an important role. Small-RNA sequencing of samples from GBM patients demonstrated that both mature products of MIR-491 (miR-491-5p and -3p) are downregulated in tumors compared with the normal brain. The integration of GBM data from The Cancer Genome Atlas (TCGA), miRNA target prediction and reporter assays showed that miR-491-5p directly targets EGFR, CDK6 and Bcl-xL, whereas miR-491-3p targets IGFBP2 and CDK6. A factor (EGF) and basic fibroblast growth factor (bFGF). 24,25 Both GSC 11 and GSC 6-27 are deleted for CDKN2A, as determined by Oncoscan copy number analysis.

45- Meeting abstract
Whole Genome Copy Number Analysis of Formalin Fixed Paraffin Embedded Samples Identifies Major Genomic Aberrations in Medulloblastoma
Nathan J. Robison, Ashley S. Margol, Anju Shukla, Rebekah J. Kennedy, Eric Fung, Alexander R. Judkins, Shahab Asgharzadeh

Medulloblastoma is the most solid tumor in children. Genomic biomarkers prognostic of radiation-free survival are needed to identify children whose tumors would respond to non-radiation based treatment, avoiding the long-term neurocognitive sequelae associated with radiation. Formalin-fixed paraffinembedded (FFPE) samples were obtained retrospectively from 79 cases (localized nZ53, metastatic nZ27) with the following histologic distribution: classic (64%), nodular desmoplastic (18%), and anaplastic (18%). Molecular subgroup classification was performed for 58 using a 31-gene signature (5% WNT, 36% SHH, 22% Group 3, 22% Group 4). For the current study, genomic DNA was isolated from 2-3 scrolls of FFPE blocks using the Qiagen FFPE gDNA kit. Whole genome copy number analysis for structural changes was performed using the OncoScan assay (80ng DNA). Data were visualized using Nexus for Oncoscan. The most common structural aberrations were gains of 17q (49%) and 7q (40%), and loss of 17p (37%). The favorable prognostic feature 6q loss was present in only 7% (5 cases), 3 of which were identified as WNT.

Acquired PIK3CA amplification causes resistance to selective phosphoinositide 3-kinase inhibitors in breast cancer
L-Y Huw, C O'Brien, A Pandita, S Mohan, J M Sporke, S Lu, Y Wang, G M Hampton, T R Wilson, M R Lackner
Oncogenesis, published online 23 Dec 2013, 2 : e83; doi:10.1038/oncsis.2013.46
... Molecular Inversion Probe (MIP) arrays were run and analyzed using Oncoscan FFPE Express 2.0 Services (Affymetrix ...

47- Meeting abstract
Array Based Identification and Validation of an Optimal FISH Reference Probe (“D17S122”) for Resolution of HER2 Amplification Status in Breast Carcinomas with Putative Chromosome 17 Aneusomy

Introduction: The Affymetrix OncoScan array offers high-quality copy number and genotype data with whole-genome coverage and high resolution for cancer genes. This assay is especially designed for use with formalin-fixed, paraffin-embedded (FFPE) tissue due to its design using small molecular inversion probes. We performed this genomic array using cases with apparent chromosome 17 aneusomy identified by HER2/CEP17 dual probe FISH assay. We hypothesized that performing a genomic screen in cases with aneusomy would reveal a highly conserved region of chromosome 17 and potentially lead to generation of a FISH reference probe that would resolve HER2 amplification status in cases with putative aneusomy. Methods: ... Samples utilized in this study segregated into three groups: 1)
48 - Meeting abstract  
**Assessing reproducibility of copy number arrays to assist breast cancer biomarker discovery**  
Cindy Q Yao1, Cheryl Crozier1, Mary Anne Quintayo1, Jane Bayani1, Melanie Spears1, Julie Livingstone1, Esther Jung1, Clement Fung1, Victoria Sabine1, Paul C Boutros1, and John MS Bartlett1  
1Ontario Institute for Cancer Research (OICR)  
Cancer Research, 2015, 75(9 Suppl):Abstract #P2-03-17. [37th Annual CTRC-AACR San Antonio Breast Cancer Symp, Dec 9-13, 2014; San Antonio, TX]  

Introduction: Large-scale interrogation of the genome has emerged as an attractive method for identifying useful characteristics of cancer biology; in particular, the study of copy number aberrations (CNA) has recently received tremendous attention. A number of different technologies have been developed to assess the copy-number landscape, allowing us to better understand the role of CNA in cancer cells. The OncoScan CNA platform (Affymetrix Inc.) has been particularly appealing for oncology due of its ability to work well with formalin-fixed, paraffin-embedded (FFPE) materials, which is the primary form for storage of clinical samples. In addition, its high resolution, rapid analysis time and ability to interrogate different genomic characteristics (CNA, loss of heterozygosity or mutation) make the OncoScan platform highly popular: it has been widely cited in the literature for use in biomarker discovery, clonal evolution and sub-clonal detection, as well as population-based analyses. While CNAs identified by the OncoScan platform have shown good concordance with fluorescence in-situ hybridization (FISH) results, to date, no studies have been conducted to thoroughly assess the reproducibility of the assay. In this study, we have assessed the reproducibility of the OncoScan platform using identical samples performed in replicates across multiple chip batches. Moreover, we have assessed the effect on reproducibility of DNA treatment, including elution in water or TE buffer, as well as in the use of varying amounts of DNA. Methods: Affymetrix OncoScan FFPE Express 3.0 SNP Arrays were performed using the optimal input DNA as recommended by the manufacturer as well as fewer input amounts for comparison. CNAs were called using BioDiscovery Nexus Copy Number™ software (http://www.biodiscovery.com/software/nexus-copy-number/) using the SNP-FASTT2 algorithm with modified parameters (significance threshold of 1 x 10^-9 and minimum number of probes per segment of 10). Results: Initial reproducibility analysis involving 12 samples repeated either 2, 4 or 6 times both within a single batch and across different batches has revealed that CNA calls were concordant between replicates for the majority of the genome (ranges between 81% to 100%), suggesting high precision of the assay. In addition, we are in the process of assessing and comparing mutation calls across replicates to gain a more in-depth understanding of the platform. Conclusion: This is the first study examining the reproducibility of OncoScan FFPE assays; initial results have suggested that the assay is precise and has the potential for robust biomarker discovery. Additional characterizations would be interesting for evaluating its use as a clinical tool in the long term.

49 - Meeting abstract  
**Assessing Tumor Percentage: A Possible Solution in Evaluating HER2 Copy Number (HER2CN) Data Generated by Molecular Inversion Probe (MIP) Technology on Formalin-Fixed Paraffin-Embedded (FFPE) Sections of Breast Cancer (BC) With Low Tumor Cellularity**  
Alexis Bousamra MD, Hui Chen, Rajyalakshmi Luthra, Xinyan Lu, Gary Lu, Rajesh Singh, Ronald Abraham MS, MHA, Shumaila Virani, Melissa Robinson MBA, CG(ASCP), Dr Bal Mukund Mishra, Aysegul Sahin MD, FASCP  
MD Anderson Cancer Center  
American Journal of Clinical Pathology, 1 October 2015, 144: A239.  

MIP technology has successfully produced quantitative HER2 copy number (HER2CN) data. Studies have shown high concordance between this emerging technology and conventional methods such as fluorescence in situ hybridization (FISH) and immunohistochemistry (IHC). OncoScan, the device behind MIP technology, appraises
tumor percentage in the form of percent aberrant cells (%AC). However, inability to assess tumor heterogeneity, extensive stroma within the tumor, and prominent in situ carcinoma component constitute scenarios where %AC cannot be generated. We hypothesized that, when %AC is not generated, estimating tumor percentage on the designated slide circumvents this limitation of MIP with resultant accurate HER2CN data. We selected 27 invasive breast cancers (BCs; 17 with, 8 without, 2 equivocal for HER2 amplification by FISH) from the archives of our institution. For each tumor, 5 μm sections were cut from a representative formalin-fixed paraffin-embedded (FFPE) block and subjected to IHC, FISH, and MIP. In all 27 BCs, two breast pathologists estimated tumor percentage (%T) on H&E-stained slides. When OncoScan generates %AC, the resultant HER2CN(CNA) is the actual HER2CN(CNT). When %AC isn't produced, CNA represents the average of both CNT and HER2CN within surrounding breast parenchyma (assumed to be diploid). In the latter scenario, CNT is calculated as: CNT = (CNA - (1 - %T) × 2)/%T. Comparing HER2 overexpression (IHC) and CNA (MIP) in all cases resulted in 7 being the cut-off HER2CN(MIP) for distinguishing BCs with 3+ HER2 score from BCs with 0, 1+, or 2+ HER2 scores (P = .00076). In 13 of 27 BCs, %AC was generated. In 13 of the remaining 14 BCs without %AC, calculated CNT showed significant correlation with HER2CN by FISH (P = .0008), while CNA did not (P = .075). Our findings show that, when MIP arrays cannot assess the percentage of invasive tumor cells within the designated tumor area, a tumor percent estimate on the representative H&E slide is an important step in overcoming the limitations of this technology and establishing actual HER2CN by MIP(CNT).

50- Bayesian hierarchical structured variable selection methods with application to molecular inversion probe studies in breast cancer
Lin Zhang, Veerabhadran Baladandayuthapani, Bani K. Mallick, Ganiraju C. Manyam, Patricia A. Thompson, Melissa L. Bondy, Kim-Anh Do

We report a unique case of a 59-year-old woman diagnosed with a benign phyllodes tumor (PT), which recurred twice in the same location over a 7-year period: first as a malignant PT and then as a malignant PT with coexisting spindle cell metaplastic breast carcinoma (MBC)... Somatic mutation analysis using a next-generation sequencing platform revealed a shared mutation in F-box and WD repeat domain... Chromosomal microarray analysis showed shared genetic gains and losses between the malignant PT and MBC. This case highlights the utility of immunohistochemistry to differentiate malignant PT from spindle cell MBC, describes a novel mutation in PT, and demonstrates a biologic relationship between these 2 entities. We performed high-resolution genome-wide DNA copy number and SNP analysis on the first malignant PT and the MBC using the Affymetrix® OncoScan™ FFPE Assay... OncoScan™ microarray showed a number of shared alterations including gains in 5p and complete gains ...

52- Breast Cancer and Non-Hodgkin Lymphoma in a Young Male with Cowden Syndrome
Robert Tanner Hagelstrom PhD, MBA, FACMG1,†,*; James Ford MD2,†; Gwendolyn M. Reiser MS, LCG3, Marilu Nelson CG(ASCP)CM1, Diane L. Pickering MS1, Pamela A. Althof MS, CG(ASCP)CM1, Warren G. Sanger PhD, FFACMG1,‡; Peter F. Coccia MD4
1Human Genetics Laboratory, Munroe-Meyer Institute, University of Nebraska Medical Center, Omaha, NE; 2Pediatric Oncology/Hematology, Univ of Nebraska Medical Center, Omaha, NE; 3Genetic Medicine, Munroe-Meyer Institute, University of Nebraska Medical Center, Omaha, NE; 4Dept of Pediatrics, University of Nebraska Medical Center, Omaha, NE

... A microarray platform designed for degraded samples (OncoScan FFPE, Affymetrix), such as tumors, was used to study copy number changes in the excised breast tumor.

53- CD117 expression in breast phyllodes tumors correlates with adverse pathologic parameters and reduced survival
CD117 (c-kit) is a type III receptor tyrosine kinase encoded by the KIT gene. Deregulation of expression and mutations in the gene are implicated in various tumors. Reports of CD117 expression in phyllodes tumors have been controversial. We aim to investigate the protein expression of CD117 and mutations in the KIT gene in phyllodes tumors, and correlate the findings with pathological parameters and clinical outcome. Nineteen cases were further selected for mutation screening through the Affymetrix OncoScan platform. No mutation of the KIT gene was found. Despite a lack of mutations in the KIT gene, CD117 protein expression is associated with unfavorable pathological parameters and poorer prognosis, suggesting an underlying role in the biology of phyllodes tumors.

54- Meeting abstract
Chromosomal aberrations associated with lymphovascular invasion in breast cancer
1County Hospital, Surgery, Breast Unit, Kalmar, Sweden; 2County Hospital, Physiology, Kalmar, Sweden; 3County Hospital, Pathology, Kalmar, Sweden; 4Faculty of Health Sciences, University, Clinical and Experimental Medicine, Linköping, Sweden
European Journal of Cancer, Sep 2015, 51(3): Abst #1904. [European Cancer Congress 2015]… The tumours were ductal carcinomas of grade 3, HER2 non-amplified but with varying ER/PR status. In 19 cases LVI was present, in 22 absent. DNA was extracted from formalin fixed samples and analysed for allele-specific copy numbers using OncoScan® single nucleotide polymorphism arrays from Affymetrix and the bioinformatic tool Tumor Aberration Prediction Suite (TAPS). …

55- Clinical Actionability Enhanced through Deep Targeted Sequencing of Solid Tumors
Ken Chen1, Funda Meric-Bernstam2,3,4, Hao Zhao1, Qingxiu Zhang3, Nader Ezzeddine3, Lin-ya Tang3, Yuan Qi1, Yong Mao1, Tenghui Chen1, Zechen Chong1, Wanding Zhou1, Xiaofeng Zheng1, Amber Johnson3, Kenneth D. Aldape5, Mark J. Roubort6, Rajyalakshmi Luthra6, Scott Kopetz7, Michael A. Davies8, John de Groot9, Stacy Moulder10, Ravi Vind11, Carol J. Farhangifar12, Kenna Mills Shaw3, John Mendelsohn3, Gordon B. Mills3,13 and Agda Karina Eterovic3,13,*
1 Dept of Bioinformatics and Computational Biology and ; 2 Dept of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX; 3 Institute for Personalized Cancer Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX; 4 Dept of Surgical Oncology; 5 Dept of Pathology; 6 Dept of Hematopathology; 7 Dept of GI Medical Oncology; 8 Dept of Melanoma Medical Oncology; 9 Dept of Neuro Oncology; 10 Dept of Breast Medical Oncology, and 11 Dept of Sarcoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; 12 Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC; 13 Dept of Systems Biology, MD Anderson Cancer Center, Houston, TX.
... Our study reveals the critical importance of acquiring and utilizing high sequencing depth in profiling clinical tumor samples and presents a very useful platform for implementing routine sequencing in a cancer care institution … validated the copy number data for 6 breast cancer samples using the Oncoscan copy number platform from Affymetrix.

56- Copy number analysis of ductal carcinoma in situ with and without recurrence
Kylie L Gorringe, Sally M Hunter, Jia-Min Pang, Ken Opeskin, Prue Hill, Simone M Rowley, David Y H Choong, Ella R Thompson, Alexander Dobrovic, Stephen B Fox, G Bruce Mann, Ian G Campbell
Modern Pathology, online 19 June 2015, 28:1174-1184.
... We analysed a cohort of pure DCIS [ductal carcinoma in situ] cases treated only with wide local excision for genome-wide copy number and loss of heterozygosity using Affymetrix OncoScan MIP arrays.

57- Meeting abstract
Copy number and loss of heterozygosity (LOH) analysis in 52 breast cancer FFPE samples using molecular Inversion probe array: detailed analysis of reproducibility and performance compared to NGS platforms
Candice L. Horn1, Fabio Nunes1, John Calley1, Steven Bray1, Isabella Wulur1, Mark Farumen1, Robert Gallavan2, Iris Halfpenny3, Paul Medlow3, Keith McGreeghan-Crosby3, and Gera Jellem3

Introduction: Somatic mutations are routinely identified using NGS cancer panels but these panels lack genome-wide coverage for copy number (CN) and LOH analysis. To investigate mutation, CN, and LOH in late-stage breast cancer we tested >50 samples using the OncoScan molecular inversion probe (MIP) array and evaluated its reproducibility and performance compared to NGS platforms. Methods: 52 breast cancer samples (stage IIIA - IV) were analyzed using MIP array (OncoScan, Affymetrix). Four samples were tested in technical triplicates to determine assay reproducibility. In addition, 28 samples were sequenced by amplicon-based NGS and five of these samples were also tested using a capture-based NGS platform for mutation, CN, and LOH comparison. Results: MIP array provided highly reproducible results for CN and LOH, with >98% of calls showing CN range in the technical triplicates of < 0.5 copy for 891 cancer genes analyzed. Variability in CN seems to be proportional to absolute copy number at the tested locus, with CN range in technical triplicates of >2 copies seen in only two cases, once for ERBB2 (CN range 32 - 35 copies) and once for FLOT2 (CN range 22 - 25 copies). Gene level results were then categorized in five groups: homozygous deletion, single copy loss, diploid, low grade amplification (>6 copies), or high grade amplification (>6 copies). Using these predetermined cut points, we saw >99% concordance rate among the technical replicates in the MIP array. We found a 93% concordance rate between MIP array and CN/LOH calls by capture-based NGS. Discordant calls between NGS and MIP array were either LOH calls or single copy number change (diploid vs. single copy loss or gain). MIP array mutation analysis of 28 samples showed good sensitivity, correctly detecting the 17 PIK3CA mutations and one TP53 mutation identified by NGS in this cohort. There were seven false positive calls by MIP array, five of them occurring in two genotypes (2x NRAS G12S/C, and 3x EGFR L858R). The other two false positives occurred in PIK3CA, with one false positive (H1047L) occurring in association with a high-grade PIK3CA amplification (7 copies). Increasing CN at the mutation locus was associated with a higher mutation score provided by MIP array (p<0.0001), which may explain some false positive calls. Conclusions: MIP array platform provides a great alternative for assessing CN and LOH in FFPE samples at lower cost and using less input DNA than NGS (80ng vs. 250ng). There was good correlation between CN and LOH results from MIP array and capture-based NGS, with discordant results limited to small CN differences or LOH calls. Mutation analysis by MIP array showed no false negatives when compared to NGS, while false positives seem to occur either due to probe-specific issues or in association with amplifications at the genotyping locus.

58-  Meeting abstract
Detection of Somatic Copy Number Changes in Breast Cancer Using the OncoScan FFPE Assay
E.Z. Liu, E.I. Reader, L.J. Tafe, G.J. Tsongalis, J.A. Lefferts
... Here we evaluate the Affymetrix OncoScan FFPE Assay for evaluation of somatic copy number variation in breast cancer cases previously evaluated for ERBB2 (HER2) amplification ... The ability of the OncoScan array to accurately report ERBB2 gene amplification status in this group of patients suggests that this test could be validated as an alternative to standard FISH testing.

59-  Meeting abstract
EVALUATION OF PTEN AND PIK3CA STATUS IN BREAST CANCER FOR PATIENT SELECTION
Annals of Oncology, Sep 2012, 12(Suppl 9) : Abstr #204P. [ESMO 2012 Congress, Vienna, Austria 28 Sep - 2 Oct 2012 (Eur Soc Medical Oncology and Jap Soc Medical Oncology)]
... PTEN alterations were genotyped in 14 TNBCs by OncoScan™ platform (Affymetrix) and were correlated to immunohistochemistry (IHC).

60- Genomic copy number imbalances associated with bone and non-bone metastasis of early-stage breast cancer
... Molecular inversion probe arrays for copy number analysis. Tumor DNA was extracted from FFPE tissue and copy number data were obtained using the MIP-based, OncoScan FFPE Express (Affymetrix, Santa Clara, CA).

61. **Genomic hallmarks of homologous recombination deficiency in invasive breast carcinomas**

Elodie Maniè1,2, Tatiana Popova1,2,†, Aude Battistella1,2, Julien Tarabeux1,2, Virginie Caux-Moncoutier3, Lisa Golmard1,2,3, Nicholas K. Smith1,2, Christopher R. Mueller1,2,4, Odette Mariani3,5, Brigitte Sigal-Zafrani3, Thierry Dubois1,6, Anne Vincent-Salomon3, Claude Houdayer1,2,3, Dominique Stoppa-Lyonnet1,2,3,7, Marc-Henri Stern1,2*

1Centre De Recherche, Institut Curie, Paris, France; 2INSERM U830, Paris, France; 3Département De Biologie Des Tumeurs, Institut Curie, Paris, France; 4Queen's Cancer Research Institute, Queen's University, Kingston, Ontario, Canada; 5Centre De Ressources Biologiques, Institut Curie, Paris, France; 6Département De Recherche Translationnelle, Institut Curie, Paris, France; 7Sorbonne Paris Cité, University Paris-Descartes, Paris, France


... This analysis demonstrates the high performance of the LST [Large-scale State Transitions] genomic signature for HRD [Homologous Recombination Deficiency] detection in breast cancers, which suggests its potential as a biomarker for genetic testing and patient stratification for clinical trials evaluating platinum salts and PARP inhibitors. The publicly available data from Cisplatin-1 and Cisplatin-2 clinical trials cohorts: 54 TNBCs with suitable quality of Oncoscan (Affymetrix) array profile were obtained from public GEO repository (GSE28330).

62. **Meeting abstract**

**High risk CNIs, race and early stage breast cancer**

Patricia A Thompson1, Abenaa Brewster2, Kim-Anh Do3, Aysegul A Sahin4, Gordon Mills5 and Melissa Bondy6

1 Cellular and Molecular Medicine, University of Arizona Cancer Center, Tucson, AZ; 2 Clinical Cancer Prevention, University of Texas MD Anderson Cancer Center, Houston, TX; 3 Biostatistics, University of Texas MD Anderson Cancer Center, Houston, TX; 4 Pathology, University of Texas MD Anderson Cancer Center, Houston, TX; 5 Systems Biology, University of Texas MD Anderson Cancer Center, Houston, TX; 6 Pediatrics, Baylor College of Medicine, Houston, TX.

**FASEB J, Apr 2013; 27: 214.3.**

We determined tumor copy number imbalances in 971 stage I/II breast tumors treated at MDACC from 1985-2000 that included 123 Hispanic and 125 African American cases. CNI were obtained using Affymetrix Oncoscan™. Models of relapse containing CNIs significantly outperformed models with clinical characteristics alone. For triple negative tumors, the combination of CNIs + clinical covariates yielded a significantly better prediction of relapse (C-index: 0.79 ± 0.023) than the best clinical model (C-Index = 0.64 ± 0.034). Race/ethnicity was not associated with relapse risk after accounting for clinical covariate but high risk CNIs were more frequent in AA and Hispanic cases in luminal and TNBC models. For example, a narrow region of 7q36.1 was more commonly lost in AA than NHW and Hispanic LUM cases (p=0.01). Furthermore, loss at Xq11-12 a risk factor for recurrence in TNBC was more common among AA and Hispanic women than NHWs (p=0.009). Measures of specific CNIs add significant additional predictive information for risk of recurrence and suggest additional opportunities to refine prognostication for early stage luminal and triple-negative breast cancers. Further, specific CNIs differ in proportion by race/ethnicity, which perhaps reflects differential germline susceptibility or distinct etiologic risk factors that contribute to observed disparity among race/ethnic groups in breast cancer specific outcomes.

63. **Human primary ductal carcinoma in situ (DCIS) subtype-specific pathology is preserved in a mouse intraductal (MIND) xenograft model.**


... the cells were truly DCIS. Genomic DNA analysis (by Affymetrix's Oncoscan) is currently being performed to confirm that the remaining non-HER2-positive cells are also truly DCIS and not hyperplastic or normal human cells.

64. **Identification of copy number alterations associated with the progression of DCIS to invasive ductal carcinoma.**


... DNA (37.5ng per sample) from IDC, DCIS and matching normal cells extracted from the same tissue sample were analysed for copy number using the Affymetrix Molecular Inversion Probe 330 K array [18] performed by Affymetrix OncoScan™ FFPE Express Services.
65- **Loss of LRIG1 Locus Increases Risk of Early and Late Relapse of Stage I/II Breast Cancer**
Patricia A. Thompson, Ingrid Ljuslinder, Spyros Tsavachidis, Abenaa Brewster, Aysegul Sahin, Håkan Hedman, Roger Henriksson, Melissa L. Bondy, Beatrice S. Melin
Cancer Research, 1 June 2014, 74(11) : 2928-2935.
We analyzed 971 stage I/II breast tumors using Affymetrix Oncoscan molecular inversion probe arrays that include 12 probes located within LRIG1.

66- **Low-grade fibromatosis-like spindle cell carcinomas of the breast are molecularly exiguous**
Elena A Takano1, Sally M Hunter2, Ian G Campbell2,3,4, Stephen B Fox1,3
1Dept of Pathology, Peter MacCallum Cancer Centre, St Andrews Place, East Melbourne, Victoria, Australia ; 2Cancer Genetics Laboratory, Peter MacCallum Cancer Centre, St Andrews Place, East Melbourne, Victoria, Australia ; 3Dept of Pathology, Univ of Melbourne, Parkville, Victoria, Australia ; 4Sir Peter MacCallum Dept of Oncology, Univ of Melbourne, Parkville, Victoria, Australia
Background Low-grade fibromatosis-like spindle cell carcinomas are very rare breast carcinomas comprising <0.5% of all breast cancers. They demonstrate immunohistochemical (IHC) features of basal-like/metaplastic breast carcinomas, but the underlying molecular characteristics are unknown. We hypothesised that, as with IHC similarities, there may be common genomic alterations between spindle cell and basal-like/metaplastic carcinomas ....Copy number analyses by molecular inversion probe assays of the three spindle cell carcinoma samples revealed little overall genomic CNAs with only minor changes identified (fraction of the genome altered; 1.3%-6.4%), but with a common 9p21.3 loss in 2 out of 3 samples, with CDKN2A (p16) being a likely candidate ..................Copy number analyses of the three spindle cell carcinomas were performed by Affymetrix OncoSFFPE Express Service ...

67- **Molecular Inversion Probe Technology Generates High-Quality HER2 Copy Number Data in Formalin-Fixed Paraffin-Embedded Breast Cancer Tissue**
Alexis Bousamra1*, Hui Chen1, Rajyalakshmi Luthra1, Xinyan Lu1, Kenneth D Aldape1, Rajesh R Singh1, Gary Lu1, Ronald Abraham1, Shumaila Virani1, Melissa Robinson1, Bal Mukund Mishra1 and Aysegul A Sahin1
1Division of Pathology and Laboratory Medicine, University of Texas, Anderson Cancer Center, Houston, Texas, USA
... We applied MIP technology to all FFPE breast tumor samples. ... Using the OncoScan FFPE Assay kit and OncoScan Console software v1.1 (Affymetrix, Santa Clara, CA), we subjected DNA samples (50-80 ng) to genome-wide CN analysis and allelic imbalance calls with focus on HER2 and the pericentromeric region of chromosome 17.

68- **Novel genetic aberrations in breast phyllodes tumours: comparison between prognostically distinct groups.**
...Twenty phyllodes tumours were separated into prognostically distinct categories depending on whether they had recurred/metastasized within the follow-up period. DNA extracted from FFPE materials was subjected to Affymetrix OncoScan™ FFPE Express molecular inversion probe microarray platform for analysis of copy number changes and mutational status.

69- **Meeting abstract**
**Quantitative Assessment of ESR, PGR and Genome-Wide Copy Number Aberrations in Advanced Breast Cancer by SNP Microarray**
MD Anderson Cancer Center, Houston, TX.
Introduction: Recent discoveries have enabled us to identify common targetable genomic alterations in cancer. Application of molecular inversion probe based SNP microarray technology (OncoScan, Affymetrix) has enabled...
genome-wide copy number aberrations (CNAs) analysis of solid tumors with limited and degraded DNA purified from formalin-fixed paraffin embedded tissue (FFPE). We previously demonstrated that OncoScan can provide accurate and quantitative assessment of CNAs of the oncogenes HER2 and FGFR1 in breast cancer. In this study, we explored the genome-wide CNAs status including ESR1, ESR2 and PGR genes that encode estrogen receptor (ER) and progesterone receptor (PR) respectively. Methods: We selected 42 resection specimens of high grade, invasive mammary adenocarcinoma from our departmental archive collected between 2011 and 2014. ER and PR overexpression was tested by immunohistochemistry (IHC). ESR1/2 and PGR gene amplification was evaluated by OncoScan using genomic DNA extracted from FFPE. Data analysis was performed using the OncoScan Console Analysis Software (Affymetrix) and Nexus Express for OncoScan (BioDiscovery). A cut-off of 4 for high copy number gains by OncoScan was used for gene amplification based on preliminary concordant results between OncoScan and fluorescence in situ hybridization (FISH) for HER2 copy number (CN) analysis. 

70- 
Response to dual HER2 blockade in a patient with HER3-mutant metastatic breast cancer

F.-C. Bidard1,2,*, C. K. Y. Ng2, P. Cottu1, S. Piscuoglio2, L. Escalup3, R. A. Sakr4, F. Reya5, P. Marianni5, R. Lim2, L. Wang2, L. Norton6, V. Servois7, B. Siga8, A. Vincent-Salomon8, B. Weigelt2, J.-Y. Pierga1,9, and J. S. Reis-Filho2,10,11 
1Dept of Medical Oncology, Institut Curie, Paris, France; 2Dept of Pathology, Memorial Sloan Kettering Cancer Center, New York; 3Dept of Pharmacy, Institut Curie, Paris, France; 4Dept of Surgery, Memorial Sloan Kettering Cancer Center, New York; 5Dept of Surgery, Institut Curie, Paris, France; 6Dept of Medicine, Memorial Sloan Kettering Cancer Center, New York; 7Dept of Radiology, Institut Curie, Paris, France; 8Dept of Pathology, Institut Curie, Paris, France; 9Paris Descartes University, Paris, France; 10Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York; 11Dept of Computational Biology, Memorial Sloan Kettering Cancer Center, New York


... copy number profiling using the single-nucleotide polymorphism 6.0 (SNP6, Affymetrix) array or molecular inversion probe (MIP) array (OncoScan v 3, Affymetrix), ...

71- 
Robust BRCA1-like classification of copy number profiles of samples repeated across different datasets and platforms

Philip C. Schouten a, Anita Grigoriadis b, Thomas Kuilman c, Hasan Mirza b, Johnathan A. Watkins b, Saskia A. Cooke b, Ewald van Dyk d, Tesa M. Severson a, Oscar M. Rueda e, Marlous Hoogstraat a, d, f, g, Caroline Verhagen h, Rachael Natrajan i, Suet-Feung Chin e, Esther H. Lips a, Janneke Kruizinga j, Arno Velds j, Marja Nieuwland j, Ron M. Kerkhoven j, Oscar Krijgsman c, Conchita Vens h, Daniel Peep c, Petra M. Nederlo f, Carlos Caldas e, l, m, Andrew N. Tutt b, Lodewyck F. Wessels d, n, Sabine C. Linn a, o, p

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Molecular Oncology, August 2015, 9(7): 1274-1286.

... We investigated samples from 230 breast cancer patients for which a CN profile had been generated on two to five platforms, comprising low coverage CN sequencing, CN extraction from targeted sequencing panels (CopywriteR), Affymetrix SNP6.0, 135K/720K oligonucleotide aCGH, Affymetrix Oncoscan FFPE (MIP) technology, 3K BAC and 32K BAC aCGH ...........We observed the same classification across different platforms in over 80% of the patients and kappa values of at least 0.36. Differential classification could be attributed to CN profiles that were not strongly associated to one class. In conclusion, we have shown that the genomic regions that define our BRCA1-like classifier are robustly measured by different CN profiling technologies, providing the possibility to retro- and prospectively investigate BRCA1-like classification across a wide range of CN platforms.
Screen detected and interval cancers; genomic analysis points to different molecular etiology?
KL Gorringe, SM Hunter, D Byrne, L Devereux, SM Rowley, K Elder, R Huynh, V Pridmore, J Hopper, A Kavanagh, G Mitchell, BG Mann, SB Fox, and IG Campbell

Peter MacCallum Cancer Centre, East Melbourne, VIC, Australia; Lifepool, East Melbourne, VIC, Australia; Royal Melbourne and Royal Womens Hospital, Parkville, VIC, Australia; BreastScreen Victoria, Melbourne, VIC, Australia; The University of Melbourne, Parkville, VIC, Australia

Cancer Research, 15 Feb 2016, 76(4 Suppl):Abstract #P6-02-04. [38th CTTRC-AACR San Antonio Breast Cancer Symposium; Dec 8-12, 2015]

NOTE: Also presented at Familial Aspects of Cancer 2015 Research and Practice, Programme [combined meeting of kConFab, Australian Breast Cancer Family Study, Australasian Colorectal Cancer Family Registry, Family Cancer Clinics of Australia and New Zealand and the International Sarcoma Kindred Study, August 25-28, 2015]; Screen detected and interval cancers; genomic analysis points to different molecular etiology?

Breast cancers diagnosed after a negative mammogram but prior to the next screening episode are termed "interval cancers" and comprise as many as 25% of all cancers detected in women attending population-based screening programs. The high interval cancer rate is a major problem affecting the effectiveness of mammographic screening. It is unclear whether interval cancers represent a distinct biological entity compared to screen-detected cancers or whether their designation is simply an arbitrary outcome of screening timing. Using an Australian prospective population-based cohort of over 53,000 women (lifepool), 537 cases of breast carcinoma (in situ and invasive breast cancer) were identified, of which 293 had known screening status at time of diagnosis. Pathology reports, mammographic density data, germline DNA and tumor tissue were available for analysis. Screen and interval cases showed no significant differences in mammographic density or PR status but there were trends towards higher proportions of ER negative and HER2 positive cases in interval cancers (p<0.1). Interval cancers also had a younger age at diagnosis (p<0.01), increased tumor size (p<0.01) and higher grade (p<0.01). Copy number analysis was performed on a subset of invasive breast cancer cases using OncoScan MIP arrays. No difference in the overall number of copy number aberrations or fraction of the genome altered were observed, however specific differences were noted between interval and screen detected cases. These included copy number changes on chromosomes 8 and 11. Analysis of germline DNA was performed using a panel sequencing approach of known breast cancer genes as well as lower-penetrance SNPs. Pathogenic mutations in BRCA1, BRCA2, TP53 and PALB2 were identified in 1/13 interval cases (in BRCA2), 1/66 screen-detected cases and 8/74 cases with currently unknown screen/interval status. Screen detected cancers may thus have a reduced contribution from high-penetrance predisposing variants.

Meeting abstract

The Australian Familial Male Breast Cancer Study: Somatic Copy Number Variant Analysis
Alison H. Trainer,* † Ella Thompson,* Maria Doyle,* Sally Hunter,* Simone Rowley,* Paul A. James,* † Antonis Antoniou; † K-ConFab Breast Cancer Consortium,* Nicholas Pachter,§ Julie McGaughran,\ Il Katherine Tucker, # Jo Burke,* ** and Ian Campbell†
*Peter MacCallum Cancer Centre, VIC, Australia; †University of Melbourne, VIC, Australia; †Centre for Cancer Genetic Epidemiology, University of Cambridge, Cambridge, U.K.; §Department of Clinical Genetics, WA; Department of Clinical Genetics, QLD. #Familial Cancer Service, Prince of Wales Hospital, NSW, Australia. **Familial Cancer Service, TAS, Australia.

Current Oncogy, Apr 2014, 21(2) : Abstr #P053. [5th International Symposium on Hereditary Breast and Ovarian Cancer, BRCA: Twenty Years of Advances]

Objectives: Male breast cancer (mbc) is a rare, easily recognized subtype of breast cancer, whose risk factors include family history, sex hormone imbalance, heritable mutations in fbc predisposition genes, most notably BRCA2, and sex chromosome anomalies such as Klinefelter syndrome. The causes and molecular basis of mbc are not well elucidated, although the majority of cases (~85%) are invasive ductal carcinoma of luminal A subtype based on immunopathologic indices. Current treatment regimens are predicated on results extrapolated from female breast cancer studies. Methods: Collaboration between the Australian Familial cancer centres and K-ConFab Breast cancer foundation is currently unpinning recruitment of BRCAx mbc cases and their families with clinical and biologic data into an Australian mbc cohort study. As part of this study, genome-wide, somatic copy number variant (cnv) analysis is undertaken on dna microdissected from well-annotated ffpe mbc tumour blocks using a 330 K molecular inverse probe set, Oncoscan 2.0 (Affymetrix). Data are analyzed using Nexus copy number 7.0 Discovery Edition and Partek Genomic Suite 6.5. Results: Here, we present the cnv data from the first 20 BRCAx mbc cases compared to published datasets. Of those cases, 25% displayed a stable genome with less than 7% of the genome displaying loh, and fewer than 25 regions of cnv, with no areas of high copy number gain. There is no correlation with age/grade between these cases and the remaining cases, which demonstrate whole-arm copy number gain and loss with infrequent regions of high copy number gains. Many fbc-associated cnv leitmotifs were present, as well as unique mbc-specific cnvs. Amplification of FGRF1 and CCND1 was commonly identified. Conclusions: Increasing evidence
indicates that mbc forms a heterogeneous group of disorders despite its relatively homogenous clinical immunopathologic presentation. Further study is required to provide a more evidence-based rationale for its most effective treatment.

74- Meeting abstract
The Breast International Group (BIG) AURORA pilot study for molecular screening in metastatic breast cancer (MBC) patients
M. Maetens1, A. Irrthum2, S. Loibl3, J.F. Laes4, P. Campbell5, P. Aftimos6, A. Thompson7, J. Cortes8, S. Loi9 and C. Sotiriou1
1Breast Cancer Translational Research Laboratory, Institute Jules Bordet, Brussels, Belgium; 2Breast International Group, Brussels, Belgium; 3Breast Centre, Klinikum Offenbach, Offenbach, Germany and German Breast Group (GBG) Forschungs GmbH, Neu-Isenburg, Germany; 4OncoDNA, Gosselies, Belgium; 5Cancer Genetics and Genomics, Wellcome Trust Sanger Institute, Cambridge, UK; 6Medical Oncology, Institute Jules Bordet, Brussels, Belgium; 7Surgical Oncology, MD Anderson Cancer Center, Houston, TX, USA; 8Oncology, Vall d’Hebron University Hospital Institut d’Oncologia, Barcelona, Spain; 9Peter MacCallum Cancer Center, Melbourne, Australia.

Introduction: In 2014, the BIG set up the AURORA molecular screening program for patients with MBC. Before launching the pilot study, a pilot study was initiated with the primary aim to investigate feasibility in terms of logistics and timelines. Secondary aims were to compare somatic mutation calls between two targeted gene sequencing (TGS) platforms and somatic copy number aberrations (SCNA) calls obtained from TGS and single nucleotide polymorphism (SNP) oligonucleotide arrays. Methods: MBC patients were enrolled in 4 European centers. Eligibility criteria for TGS were: 1) at least one representative metastatic biopsy, 2) availability of a whole blood sample and 3) >10% tumor cellularity at central pathological review. Tumor and normal DNA were subjected to TGS of cancer related genes using the Ion Torrent and Illumina platforms. SCNA calls obtained from normalized coverage of TGS data were compared to the output of the ASCAT algorithm on Affymetrix OncoScan FFPE array data. Results: Forty-one patients were enrolled and 35 of them were biopsied (85%). Successful TGS results were obtained for 26/35 patients (74%). The most common biopsied metastatic sites were the liver (43%) followed by breast (20%), lymph node (14%), skin (14%), lung (6%) and bone (3%). The tumor cellularity ranged from 10 to 85%. The median turnaround time to report the TGS results was 9 working days (range: 5-17). Somatic mutations were called in exons covered at >100X based on a fixed threshold of 10% variant allele frequency in the cancer sample. The median number of mutations per patient identified from Ion Torrent was 7 (range: 0-29), with 60% of the patients harboring at least one “actionable” mutation. Preliminary results show a validation rate of 68% (range: 33-100%) from Ion Torrent by Illumina. The SCNAS are currently being analyzed and will be presented at the IMPAKT conference. Conclusion: This pilot study demonstrates the feasibility of conducting an international MS program for MBC patients in routine clinical settings. The mutation calls validation rate was deemed acceptable. Collectively, these results are reassuring for the conduct of AURORA, aiming at recruiting 1300 patients with MBC from more than 80 European sites.

75- Meeting abstract
Tumor profiling of inflammatory breast cancer: Advancing the tools needed for precision medicine
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Cancer Research, 15 Feb 2016, 76(4 Suppl):Abstract #P6-18-03. [38th CTRC-AACR San Antonio Breast Cancer Symposium; Dec 8-12, 2015]

Introduction: Inflammatory breast cancer (IBC) is a rare and highly lethal form of breast cancer, accounting for approximately 10% of breast cancer mortality in the US. The clinical presentation of IBC includes rapid onset of symptoms, erythema > 1/3 of the breast, and edema. The genomic changes underlying the clincopathologic manifestations of IBC are yet unknown. Identification of a unique molecular signature in de novo IBC may provide insight into the biology of this disease, allowing further investigation into the etiology and treatment of this aggressive disease. In previous studies, supervised analysis of gene expression data from surgical tissue specimens identified a molecular-subtype independent 79-gene signature associated with IBC compared to locally-advanced non-IBC. In this study, we propose to identify a gene expression signature associated with IBC using breast specimens collected from patients with non-metastatic IBC prior to initiating preoperative systemic treatment. Methods: Formalin fixed paraffin embedded (FFPE) core biopsy specimens were collected from patients with inflammatory breast cancer prior to initiating systemic therapy. All specimens underwent centralized pathology review at Brigham and Women's Hospital, and the clinical diagnosis was confirmed through evaluation by the Dana Farber Cancer Institute
Inflammatory Breast Cancer Program. Sufficient RNA and DNA were simultaneously extracted from 14 biopsy specimens using the Qiagen AllPrep Kit. The RNA was amplified using the Sensation kit and profiled using the Affymetrix Human Transcriptome Array (HTA) 2.0. DNA was profiled for druggable somatic mutations and genome-wide copy number variations using the Affymetrix OncoScan Array. Results: Pearson correlation coefficients for overall gene expression for 4 technical replicates included in the HTA ranged from r=0.993 - 0.994 and suggest excellent reproducibility in archival biopsy tissue. In preliminary analyses, 765 mRNA transcripts and 335 non-coding transcripts were differentially expressed based on clinical presentation features. The strongest differential association for rapid onset of disease was observed for alternately spliced variants in the TSPAN1 gene. Somatic mutations in PIK3CA were detected in 3 of the IBC patients. Additional paired assays as well as single-gene and pathway analyses, and integrated analyses of the genome and transcriptome using the R/Bioconductor packages are ongoing. Conclusion: An understanding of the genomic changes that contribute to the unique presentation and biologic features associated with IBC should lead to a significant impact on identifying etiologic risk factors and in optimizing treatment strategies. Our findings to date suggest a robust and reproducible method for genomic investigation using standard diagnostic breast core biopsies among IBC patients, and may inform profiling of biopsy specimens for other cancer types. The completion of this study will provide biological insights into the molecular mechanisms driving IBC and may identify clinically actionable targets for novel IBC therapies that warrant further exploration.

76- Meeting abstract
Unraveling breast cancer progression through geographical and temporal sequencing
Christine Desmedt1, David Brown1, Borbala Szekely2, Dominiek Smets3, Marcell A. Szasz2, Pierre-Yves Adnet1, Françoise Rothé1, Zsofia I. Nagy2, Zsofia Farago2, Anna-Maria Tookes2, Dimitrios Zardavas1, Gabriele Zoppoli1, Michail Ignatiadis1, Lajos Pusztai4, Martine Piccart1, Denis Larmsont1, Diether Lambrechts3, Janina Kulka2, Christos Sotiriou1.
1Institut Jules Bordet, Brussels, Belgium; 2Semmelweis University, Budapest, Hungary; 3VIB Vesalius Research Center, Leuven, Belgium; 4Yale Cancer Center, New Haven, DE
AACR Annual Meeting, April 5-9 2014, San Diego, CA, Abst #986.

Background: The aim of this study was to interrogate primary/metastatic breast cancer (BC) genetic heterogeneity using next generation whole exome sequencing and copy number analysis from an autopsy series of BC patients (pts). Methods: To reconstruct the trajectories of BC progression, we performed exome sequencing (Illumina HiSeq2000, Truseq DNA sample preparation kit v2 and Exome Enrichment Kit v2; alignment done with BWA, substitutions and indels called with GATK and DINDEL respectively) coupled to validation by Sequenom and deep re-sequencing (ongoing), as well as copy number (CN) analyses (Oncoscan, Affymetrix) on DNA from matched primary (n=1-6/pt), axillary lymph node (ALN, n=1-6 for 4 pts), local recurrence (for 1 pt) and distant metastatic (n=1-5/pt) FFPE samples obtained from an autopsy series of 10 BC pts. Results: 1/ The degree of primary/metastatic genetic heterogeneity is proportional to the time elapsed between the diagnosis of the primary tumor and the emergence of the metastases (mutations: corr=0.76, CN: corr=0.63); metastases from pts with a longer cancer history being genetically more different from their corresponding primary tumor than those from pts with a shorter cancer history. 2/ The phylogenetic analyses revealed that in all but 1 pt, the various distant metastases are present on the same branch of the phylogenetic tree. This suggests that the majority of the metastases arise from a single metastasizing event, with one or more distant sites further re-seeding additional organs. ALN metastases are genetically less evolved compared to distant metastases. 3/ Distant metastases from a same patient only share between 11 and 50% metastasis-specific mutations. This implies that metastasis-specific potentially targetable genetic alterations might either be present in all metastases from a given patient (such as EGFR, PDGGRA amplification for pt 3, AR amplification for pt 8) or only in some metastases (such as NOTCH2 mutation in the liver metastasis of pt 6). 4/ Primary tumor samples and metastases from one ER+/HER2- pt were hypermutated (696 unique mutations in total). The substitutions were enriched for the APOBEC3B D316N mutation observed in all samples from this pt. Conclusions: Here we report for the first time that primary/metastatic BC genetic heterogeneity is proportional to the time elapsed between the diagnosis of the primary tumor and the emergence of the metastases. These results therefore suggest that it is extremely relevant to interrogate distant metastatic lesions, multiple if possible to account for inter-metastatic heterogeneity, to guide treatment, especially but not only, in those pts relapsing a few to many years after initial diagnosis.

Central Nervous System

77- H3.3 G34R mutations in pediatric primitive neuroectodermal tumors of central nervous system (CNS-PNET) and pediatric glioblastomas: possible diagnostic and therapeutic implications?
Marco Gessi, Gerrit H. Gielen, Jennifer Hammes, Evelyn Dörner, Anja zur Mühlen, Andreas Waha, Torsten Pietsch
To identify copy number gains and losses, the custom-designed OncoScan™ FFPE Express 330 K Molecular Inversion Probe (MIP) platform (Affymetrix, Santa Clara, USA) was used. …

78- High-Resolution Genomic Analysis of Cribriform Neuroepithelial Tumors of the Central Nervous System
Gessi, Marco; Japp, Anna Sophia; Dreschmann, Verena; zur Mühlen, Anja; Goschzik, Tobias; Dörner, Evelyn; Pietsch, Torsten
... To identify copy number gains and losses, we used an MIP array using the custom-designed OncoScan formalin-fixed paraffin-embedded Express 330 K platform version 2 (Affymetrix, Santa Clara, CA).

79- MYCN amplification predicts poor outcome for patients with supratentorial primitive neuroectodermal tumors of the central nervous system
Marco Gessi, André O. von Bueren, Andras Treszl, Anja zur Mühlen, Wolfgang Hartmann, Monika Warmuth-Metz, Stefan Rutkowski, Torsten Pietsch
Neuro Oncol, published online 26 January 2014. doi:10.1093/neuonc/not302
...Probe Assay To identify copy number gains and losses, we performed a custom-designed OncoScan FFPE Express 330K MIP assay (Affymetrix) on 15 tumors, …

80- Meeting abstract
NEXT GENERATION COPY NUMBER ANALYSIS BY MOLECULAR INVERSION PROFILING - A HELPFUL TOOL IN DIAGNOSTICS AND PROGNOSTIFICATION OF TUMORS OF THE CNS
Torsten Pietsch1, Marco Gessi1, Anja zur Muehlen1, Evelyn Doerner1, Mita Mancini2, Andy Last2 and Padma Sundar2
1Department of Neuropathology, University of Bonn, Bonn, Germany; 2Affymetrix, Santa Clara, CA, USA.
Brain tumor entities are characterized by specific copy number alterations (CNA). Emerging technologies including SNP arrays, whole exome and whole genome sequencing are not suitable for degraded DNA derived from formalin-fixed, paraffin-embedded (FFPE) samples. The aim of our study was to analyse the sensitivity and robustness of molecular inversion profiling (MIP) as a tool to identify CNA in brain tumor diagnostics and to compare this method to FISH and multiplex ligation probe analysis (MLPA). Genomic DNA was extracted from up to 20 years old FFPE materials and analyzed by MIP profiling (Oncoscan V2, Affymetrix) with more than 330,000 copy number probes. More than 1100 brain tumors covering most WHO entities were analysed. MIP revealed genome-wide copy number information from as little as 20 ng of degraded DNA; the drop-out rate was lower than 5%. In contrast to FISH and MLPA which enabled the analysis of only single or few genomic loci, MIP allowed a genome-wide analysis. It added significant information to the differential diagnosis as characteristic CNA were detected even with low input DNA, including BRAF duplications in pilocytic astrocytomas, chromosome 22 loss in ATRT, chromosome 10 loss and EGFR amplification in glioblastoma, 1p19q codeletion in oligodendrogial tumors, and chromosome 2 gain, C19MC amplification in ependymoblastoma. Prognostic markers including MYCC and MYCN copy number status in medulloblastomas and chromosome 1q gain in ependymomas were easily detected and validated by orthogonal methods. MIP also detected copy-neutral LOH and tumor-associated point mutations. Our data indicate that MIP is a sensitive and robust method to assess CNA in archival FFPE tumor material.

Colon / Colorectal

81- A comprehensive characterization of genome-wide copy number aberrations in colorectal cancer reveals novel oncogenes and patterns of alterations.
... For samples that yielded less than the recommended input DNA amount (75 ng), all DNA was carried forward into the Molecular Inversion Probe (MIP) amplification, labelling, and hybridization protocols using Affymetrix’s OncoScan V1.0 FFPE Express services (Affymetrix, CA).
Meeting abstract

A transition zone showing highly discontinuous or rapidly oscillating levels of stem cell and proliferation markers characterizes the development of colorectal cancer

Kevin J. Arvai, Ya-Hsuan Hsu, Lobin A. Lee, Dan Jones.
Quest Diagnostics Nichols Institute, Chantilly, VA
AACR Annual Meeting, April 5-9 2014, San Diego, CA, Abst #3864.

Background: Stepwise acquisition of genetic changes characterize the development of colorectal cancer (CRC). These mutational events are correlated with discrete morphologic transitions from hyperplastic to adenomatous areas followed by in situ transformation and finally invasive carcinoma. The genetic drivers for each stage of this process, however, have not been fully established and can be confounded by tumor heterogeneity. The goal of this study was to identify easily assessed biomarkers of key morphogenetic transitions in CRC. Methods and Findings: We analyzed the pattern of proliferation and expression of growth regulatory and stem cell markers across distinct morphologic transition zones in 726 cases of CRC. In cases with preserved adenoma-carcinoma morphologic transitions, we identified a characteristic zone of adenomatous epithelium, often located immediately adjacent to and extending into the invasive component, that showed rapidly oscillating intraglandular stretches of Ki-67+ and Ki-67- cells. This pattern correlated with oscillating expression of other cell cycle mediators and the growth regulators PTEN and SMAD4. These multifocal stretches of adenomatous epithelium showed alternating abrupt positive/negative expression boundaries. These zones also demonstrated similar abrupt intragland oscillations in the levels and/or subcellular localization of multiple cancer stem (CSC) markers including beta-catenin/CTNNB1, MGMT and CD44. In contrast, the expression levels of most of these markers were largely homogenous in the proximal adenomatous and deeper invasive carcinoma surrounding the transitional region. This CSC-like transitional zone, as detected by PTEN IHC, was prominent in 50/726 of all CRC (6.9%) but at least focally present in 97/201 (48.2%) cases with intact adenoma-carcinoma junctions. Genomic microarray (OncoScan HD) and mutation analysis (Ampliseq) on CRC with prominent CSC-like expansions demonstrated complex genomic changes in 12/18 (66.7%) with a similar frequency of KRAS, BRAF and CTNNB1 mutations as expected in unselected CRC cases. The transition zones in these cases also frequently demonstrated unstable genomes from cell-to-cell (as assessed by FISH) indicating high genetic instability in these areas. Conclusions: We show that multiple immunohistochemical markers, including PTEN, SMAD4, CD44 and CTNNB1, highlight a localized CSC-like transition zone of rapidly alternating quiescent/proliferative adenomatous epithelium in primary CRC tumors. This transition zone often begins in pre-invasive adenomatous epithelium adjacent to invasive tumor areas that have more uniform proliferation and more homogeneous genetic and expression profiles. This easily assessed phenomenon appears to represent a commonly occurring genetically unstable forerunner or transitional stage in CRC evolution.

Meeting abstract

Comprehensive molecular characterisation of hereditary non-polyposis colorectal tumours with mismatch repair proficiency

Fernando Bellido, Marta Pined, Rebeca Sanz-Pamplon, Matilde Navarro, Marga Nada I, Conxi Lázaro, Ignacio Blanco Victor Moreno, Gabriel Capellà, Laura Valle

... Genomic alterations in 16 tumours from 14 Amsterdam I-II families were studied using the genome-wide copy number OncoScan™ FFPE microarray. ...

Meeting abstract

Comparison of Mutational Calls Obtained with Pyrosequencing and the Affymetrix OncoScan® FFPE Assay in Patients with Colon Cancer Recruited to the NCRI FOxTROT Trial

P M Taylor1; H Wood1; D Bottomley1; E Tinkler-Hundal1; G Hemmings1; P Chambers1; JM Foster2; A Oumie1; KG Spink2; D Morton3; NP West1; P Quirke1
1Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK; 2Affymetrix UK Ltd, High Wycombe, UK; 3University of Birmingham, Birmingham, UK
The Journal of Pathology, Sep 2015, 237(S1) [Supplement: Dublin Pathology 2015. 8th Joint Meeting of the British Division of the International Academy of Pathology and the Pathological Society of Great Britain & Ireland, 23-25.

... We investigated the OncoScan® FFPE Assay Kit (OncoScan) in comparison to pyrosequencing in patients with operable colon cancer recruited to the phase II component of the NCRI FOxTROT trial of pre-operative vs. post-operative chemotherapy. FFPE samples of tumour from the resection specimens of 132 cases were tested for KRAS 12/13/61 and BRAF V600E mutations using pyrosequencing. The OncoScan assay allows for the interrogation of 74 mutations across nine genes. Pre-extracted DNA was analysed on the OncoScan assay and quality control (QC) scores generated, indicating confidence in mutation calling results. ... In patients with colon cancer recruited to the NCRI FOxTROT trial, the OncoScan FFPE assay shows good correlation with pyrosequencing when determining the
mutational status of KRAS/BRAF. Although pyrosequencing has a slightly lower failure rate, the OncoScan has the added advantage of targeting more mutations, producing genome wide CN, and LOH information in one assay.

85-

Meeting abstract

Copy number differences in EGFR and other amplicons between primary colon tumors and paired lymph node metastasis.

Vassiliki Liana Tsikitis, David Larson, Christina Preece, Spyros Tsavaridis and Patricia Thompson


Background: Prior study, demonstrating differential immunohistochemical EGFR expression between the primary colon cancer and the liver metastasis, suggested possible molecular differences between the two tumor sites. This questions the relevance of obtaining genomic information from the primary tumor to guide adjuvant treatment. In this study we examine whether there are genomic differences specific to metastatic nodes versus the paired colon primary samples. Methods: Using 30 primary and lymph node metastasis pairs (dissected for >80% tumor from paraffin embedded tissue), we obtained a dataset of copy number derived from the Affymetrix Oncoscan Molecular Inversion Probe platform. Using the Nexus Copy Number software for processing, we used the default automatic segmentation of the copy number data with a threshold for calling copy number gains/losses of 2.3/1.7. Subsequently we applied the Wilcoxon signed-rank test in order to find regions showing copy number imbalance that differ between the paired nodes and tumors correcting for multiple comparisons by performing permutation-based estimation of the false discovery rate permuting the samples 100 times. Results: Using 40 ng of total DNA from paraffin embedded tumor from primary and tumor in positive nodes, we obtained high quality, genome wide copy number data. Using FDR < 0.1, we identified four chromosomal segments that showed statistically significant increased likelihood of copy number gains in the primary tumor compared to the tumor-containing node. Thirty five percent of tumor-bearing lymph nodes were copy number normal at the EGFR locus whereas the corresponding primary tumor showed amplification at 7p11.2 (includes the EGFR gene). A similar pattern was observed for 8q24, 14q11.2, and 20q12-q13; regions associated with aggressive tumor behavior. Conclusions: Our results demonstrate four significant differences between the primary tumor and lymph node metastasis and in all cases the metastasis were copy number normal compared to the copy number gain observed in the primary tumor. These results support the importance to examine differences at the genome level between the metastatic tumor site and the primary.

86-

Meeting abstract

CSF1R Amplification in Poorly Differentiated Colorectal Adenocarcinoma with Neuroendocrine Differentiation


... Genomic DNA of case 1 was subjected to molecular inversion probe array by OncoScan FFPE Assay kit (Affymetrix, CA).

87-

Deleterious Germline BLM Mutations and the Risk for Early-onset Colorectal Cancer


... Genome-wide SNP array analysis of tumour DNA was performed using the OncoScan FFPE Express service (Affymetrix, ...}

88-

HER2 overexpression and amplification as a potential therapeutic target in colorectal cancer: Analysis of 3256 patients enrolled in the QUASAR, FOCUS and PICCOLO colorectal cancer trials

Susan D. Richman1,†,* , Katie Southward1,†, Philip Chambers1, Debra Cross2, Jennifer Barrett3, Gemma Hemmings1, Morag Taylor1, Henry Wood1, Gordon Hutchins1, Joseph M. Foster4, Assa Oumie4, Karen G Spinke4, Sarah R. Brown5, Marc Jones5, David Kerr6, Kelly Handley7, Richard Gray8, Matthew Seymour9, Philip Quirke1

1Section of Pathology and Tumour Biology, Leeds Institute of Cancer and Pathology, University of Leeds, UK; 2Histopathology and Molecular Pathology, St James University Hospital, Leeds, UK; 3Section of Epidemiology and Biostatistics, Leeds Institute of
Cancer and Pathology, University of Leeds, UK; 4Affymetrix UK Ltd, High Wycombe, UK; 5Clinical Trials Research Unit, University of Leeds, Leeds, UK; 6Cancer Medicine, University of Oxford, Oxford, UK; 7Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, UK; 8University of Oxford, Oxford, UK; 9Section of Oncology, Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK.


... We assessed HER2 amplification/overexpression in stage II-III and IV CRC patients, assessing relationships to KRAS/BRAF and outcome ...

Copy number variation analysis—47 cases with over expression/amplification of Her2 (25 stage II/III and 22 stage IV), were run on the OncoScan® FFPE Assay Kit (Affymetrix, Inc.) to identify copy number alterations ...

89- Intra-tumor genetic heterogeneity in rectal cancer
Karin M Hardiman1, Peter J Ulintz2, Rork D Kuick3, Daniel H Hovelson2, Christopher M Gates2, Ashwini Bhasi2, Ana Rodrigues Grant2, Jianhua Liu1, Andi K Cani4, Joel K Greenson2, Scott A Tomlins4,5 and Eric R Fearon4,6,7
1Dept of Surgery, University of Michigan, Ann Arbor, MI; 2Dept of Bioinformatics, University of Michigan, Ann Arbor, MI; 3Dept of Biostatistics, University of Michigan, Ann Arbor, MI; 4Dept of Pathology, University of Michigan, Ann Arbor, MI; 5Dept of Urology, University of Michigan, Ann Arbor, MI; 6Dept of Human Genetics, University of Michigan, Ann Arbor, MI; 7Dept of Internal Medicine, University of Michigan, Ann Arbor, MI

Laboratory Investigation, 2016, 96: 4-15.

... We hypothesized the existence of significant intra-tumor genetic heterogeneity in rectal cancers involving variations in localized somatic mutations and copy number abnormalities. Two or three spatially disparate regions from each of six rectal tumors were dissected and subjected to the next-generation whole-exome DNA sequencing, Oncoscan SNP arrays, and targeted confirmatory sequencing and analysis....

90- Meeting abstract
Investigating the Challenges of Using Historical Formalin-Fixed Paraffin-Embedded (FFPE) Material from the MRC CR07 Rectal Cancer Trial Using the Affymetrix OncoScan® FFPE Assay and Next Generation Sequencing
P M Taylor1; H Wood1; E Tinkler-Hundal1; DS Bottomley1; G Hemmings1; U McDermott2; JM Foster3; A Oumie3; KG Spink3; D Sebag-Montefiore1; NP West1; P Quirke1
1Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK; 2Welcome Trust Sanger Institute, Cambridge, UK; 3Affymetrix UK Ltd, High Wycombe, UK

The Journal of Pathology, Sep 2015, 237(S1) [Dublin Pathology 2015. 8th Joint Meeting of the British Division of the Intl Academy of Pathology and the Pathological Society of Great Britain & Ireland, 23-25]

There is a vast amount of historical FFPE material held in archives, but due to variations in fixation and processing this presents several challenges when applying newer genomic technologies to it. In this study we compared the genomic information obtained with the OncoScan® FFPE Assay Kit (OncoScan) and next generation sequencing (NGS). ... For the OncoScan assay, copy number (CN) and somatic mutation (SM) data was further investigated. This study was part funded by a PathSoc Fellowship. In total, 272 cases (72%) passed the NGS QC and 232 (61%) passed the OncoScan QC. A total of 186 (49%) passed QC on both platforms with marked variability in sample pass rates between the 10 centres for the NGS (range 0% to 100%) and OncoScan (ranges 33% to 84%). When assessed manually, the OncoScan SM data was considered acceptable for 273 cases (72%), which included 40 initially classified as ‘failed’ by the QC data. Similarly, the OncoScan CNV data was interpretable for the majority of cases. This study has shown that whilst historical DNA held in the FFPE blocks of archival clinical trials like MRC CR07 can present challenges when using new genomic technologies, a large proportion of samples can still yield valuable genomic data. ...

91- Loss of Expression and Promoter Methylation of SLIT2 Are Associated with Sessile Serrated Adenoma Formation
Andrew D. Beggs, Angela Jones, Neil Shepherd, Abed Arnaout, Caroline Finlayson, A. Muti Abulafi, Dion G. Morton, Glenn M. Matthews, Shirley V. Hodgson, Ian P. M. Tomlinson

... In order to verify the Illumina array results, 100 ng DNA from two sessile serrated adenoma samples were analysed using the Affymetrix OncoScan FFPE Express service utilising Affymetrix whole genome molecular inversion probe (MIP) SNP arrays.

92- Meeting abstract
Loss of pTEN Expression is Strongly Associated with the Presence of the BRAF V600E Mutation, and Further Complicates Combination Treatment Strategies for Patients with Advanced Colorectal Cancer

P SD Richman1; GJ Hemmings1; P Chambers1; M Taylor1; HM Wood1; E Tinkler-Hundal1; K Southward1; JM Foster2; A Ouime2; KG Spink2; P Quirke1
1Leeds Institute of Cancer and Pathology, Leeds, UK; 2Affymetrix, High Wycombe, UK

The Journal of Pathology, Sep 2015, 237(S1) [Dublin Pathology 2015. 8th Joint Meeting of the British Division of the Intl Academy of Pathology and the Pathological Society of Great Britain & Ireland, 23-25] … Mutation status of KRAS, NRAS, PIK3CA and BRAF was assessed by pyrosequencing. Copy number variation was assessed on Oncoscan® FFPE Assay Kit (Affymetrix Inc.). …
Genes, Chromosomes and Cancer, Feb 2013, 52(2) : 214-224.

For MIP analysis, genomic DNA was extracted from GIST samples and processed using OncoScan™ Formalin-Fixed Paraffin-Embedded (FFPE) Express (Affymetrix, Santa Clara, CA). This assay uses MIP technology based ...

**Germ Cell Tumors**

**Next generation sequencing analysis of platinum refractory advanced germ cell tumor sensitive to Sunitinib (Sutent®) a VEGFR2/PDGFRβ/c-Kit/FLT3/RET/CSF1R inhibitor in a phase II trial**


Journal of Hematology & Oncology, 1 Aug 2014, 7:52

... Oncoscan MIP array were employed to validate the copy number analysis that confirmed RET gene amplification.

**Langerhans Cells**

**Langerhans Cell Sarcoma With Lineage Infidelity/Plasticity: A Diagnostic Challenge and Insight Into the Pathobiology of the Disease**

Kurai, Laszlo J.; Sanik, Eugene; Ricotti, Carlos A.; Susa, Joseph; Sinkre, Prasanna; Aleodor, Andea A.


... Analysis of genome-wide DNA copy number changes and allelic imbalances was performed using the OncoScan FFPE Assay (Affymetrix, Santa Clara, CA). The assay requires 80 ng of input template DNA.

**Liver**

**Primary Hepatic Small Cell Carcinoma: Two Case Reports, Molecular Characterization and Pooled Analysis of Known Clinical Data**

ADITI SHASTRI1, PAVLOS MSAQUEL2,* CRISTINA MONTAGNA3, SHERRY WHITE4, MARIA DELIO3, KUNJAN PATEL3, KARENZA ALEXIS5, MARIANNA STRAKHAN5, TAREK N. ELRAFEI5, LOUIS JUDEN REED5

1Dept of Oncology, Montefiore Medical Center & Albert Einstein College of Medicine, Bronx, NY; 2Dept of Internal Medicine, Jacobi Medical Center, Bronx, NY; 3Dept of Genetics and Pathology, Albert Einstein College of Medicine, Bronx, NY; 4Dept of Pathology, Jacobi Medical Center, Bronx, NY; 5Dept of Oncology, Jacobi Medical Center, Bronx, NY.


... we report on two cases of spontaneously arising, metastatic primary HSCC that were treated at our Institution...

... like pulmonary small cell tumors, these two hepatic primaries showed only locoregional spread and very few distant metastases. Formalin-fixed samples were obtained at autopsy and sequenced using single-nucleotide polymorphism arrays and whole-genome sequencing...

Sequencing of the samples was performed using the OncoScan FFPE assay. (Affymetrix, ...)

**Lung**

**Meeting abstract**

**Characterization of MET Amplification in Lung Adenocarcinomas Using OncoScan SNP Microarray**


University of Texas MD Anderson Cancer Center, Houston, TX.


... In this study, we used OncoScan SNP array to re-assess lung adenocarcinoma cases reported as negative for MET amplification by FISH but have increased MET copy numbers. Methods: FFPE tissues from selected 14 patients were obtained from the archives at the U.T. M.D. Anderson Cancer Center (2013 to 2015). Cases were separated into 3 groups based on FISH results: positive for MET amplification, increased MET copy numbers, and negative for MET amplification. OncoScan (Affymetrix) was performed ... Conclusions: Our data show that OncoScan might be useful as a reflex test for cases with increased MET copy numbers ...
Congenital peribronchial myofibroblastic tumor (CPMT) is a rare entity recognized in the WHO classification of pulmonary neoplasms. According to available literature, it is a benign tumor with a high mortality rate exceeding 50%. ... Herein we present a case of congenital peribronchial myofibroblastic tumor in a premature male infant who was born at 31 weeks gestation due to polyhydramnios and premature rupture of membranes .................. The patient expired soon after the surgery. Hence, in this report we would like to share our experience with this difficult diagnosis and treatment of this rare tumor .................................................Additionally, a Massively Parallel Sequencing (mPS) Molecular Inversion Probe Array was performed using the Affymetrix OncoScan™ FFPE Assay.

102- Meeting abstract
Evaluation of genomic profiling in the GALAXY-1 (NCT01348126), a randomized Phase 2b study of ganetespib in combination with docetaxel versus docetaxel alone as second line therapy in patients with advanced NSCLC
Dean Fennell1 Alexey Antonov, Miguel L. Martins, Sanjay Popat, Suresh S. Ramalingam, James Spicer, Vojislav M. Vukovic, Iman El-Hariry, Vienna Reichert, Rafael Rosell
AACR Annual Meeting, April 5-9 2014, San Diego, CA, Abst #4657.

Background: Inhibition of Hsp90, a key molecular chaperone required for activation of many oncoproteins, can lead to cancer cell death. Ganetespib (G) is a 2nd generation Hsp90 inhibitor (Hsp90i) that has single agent clinical activity in patients with ALK, KRAS, HER2, and BRAF mutations. G also inhibits pathways implicated in resistance to taxanes, including hypoxia pathways (HIF-1α) as well as cell-cycle and DNA repair pathways. Combination of G with docetaxel (D) has shown synergy in NSCLC xenografts and prolongation of progression-free survival (PFS) and overall survival (OS) of patients with NSCLC adenocarcinoma in interim analyses of the GALAXY-1 trial. Methods: Patients enrolled in GALAXY-1 (n=253) receive D 75 mg/m² on D1 of a 3-week treatment cycle; combination arm patients receive G 150 mg/m² on D1 and D15 in addition. The co-primary endpoints are PFS in patients with elevated baseline level of serum LDH and PFS in the mutant KRAS population. PFS and OS in all adenocarcinoma patients are key secondary endpoints. Genomic profiling using Affymetrix Oncoscan™ was performed on archival tissues obtained at baseline, with the goal of determining biomarkers predictive of ganetespib activity Results: Tumor tissue samples from 65 patients and 26 matched normal tissues were processed on the Affymetrix Oncoscan™ FFPE Express 2.0 Services assay. The OncoScan™ FFPE Express 2.0 assay contains 332941 copy number probes. After removing samples with average call rates lower than 90%, 296522 markers on chromosome 1-22 were selected for copy number analyses. For preliminary evaluation of interactions between copy number aberrations and treatment response in the G arm, a genome scale Kaplan-Meier Estimates PFS analysis at each of 296522 markers was performed. Conclusions: Genomic profiling using OncoScan™ is utilized in the GALAXY-1 trial to identify biomarkers of response/resistance to ganetespib administered in combination with docetaxel. Complete analyses will be presented at the meeting.

103- Genomic Characterization of Non-Small-Cell Lung Cancer in African Americans by Targeted Massively Parallel Sequencing
Luiz H. Araujo, Cynthia Timmers, Erica Hlavin Bell, Konstantin Shilo, Philip E. Lammers, Weiqiang Zhao, Thanemozhi G. Natarajan, Clinton J. Miller, Jianying Zhang, Ayse S. Yilmaz, Tom Liu, Kevin Coombes, Joseph Amann and David P. Carbone
1James Thoracic Center, Dept of Medicine, The Ohio State Univ Medical Center, 460 W 12th Ave, Rm 488, Columbus, OH 43210; c ARUP Laboratories, 500 Chipeta Way, Salt Lake City, UT 84108
Journal of Clinical Oncology, April 27, 2015 JCO.2014.59.2444

Purpose Technologic advances have enabled the comprehensive analysis of genetic perturbations in non-small-cell lung cancer (NSCLC); however, African Americans have often been underrepresented in these studies. This ethnic group has higher lung cancer incidence and mortality rates, and some studies have suggested a lower incidence of epidermal growth factor receptor mutations. Herein, we report the most in-depth molecular profile of NSCLC in African Americans to date. Methods A custom panel was designed to cover the coding regions of 81 NSCLC-related genes and 40 ancestry-informative markers. Clinical samples were sequenced on a massively parallel sequencing instrument, and anaplastic lymphoma kinase translocation was evaluated by fluorescent in situ hybridization ... Selected samples with amplification in major oncogenes were validated using the OncoScan FFPE Assay Kit (Affymetrix ...
**Germline BAP1 mutation in a family with high incidence of multiple primary cancers and a potential gene-environment interaction**

Mitchell Cheung a, Yuwaraj Kadariya a, Jacqueline Talarchek a, Jianming Pei a, Jill A. Ohar b, Omar R. Kayaleh c, Joseph R. Testa a

a Cancer Biology Program and Genomics Facility, Fox Chase Cancer Center, Philadelphia, PA 19111, USA; b Section of Pulmonary, Critical Care, Allergy and Immunologic Diseases, Wake Forest University School of Medicine, Winston-Salem, NC 27157-1054, USA; c University of Florida Health Cancer Center at Orlando Health, Orlando, FL 32806, USA.


We report a high-risk cancer family with multiple mesotheliomas, cutaneous melanomas, basal cell carcinomas, and meningiomas segregating with a germline nonsense mutation in BAP1 (c.1938T>A; p.Y646X). Notably, most (four of five) mesotheliomas were peritoneal rather than the usually more common pleural form of the disease, and all five mesothelioma patients also developed second or third primary cancers, including two with meningiomas. Another family member developed both cutaneous melanoma and breast cancer. Two family members had basal cell carcinomas, and six others had melanocytic tumors, including four cutaneous melanomas, one uveal melanoma, and one benign melanocytic tumor. The family resides in a subtropical area, and several members had suspected exposure to asbestos either occupationally or in the home. We hypothesize that the concurrence of a genetic predisposing factor and environmental exposure to asbestos and UV irradiation contributed to the high incidence of multiple cancers seen in this family, specifically mesothelioma and various uveal/skin tumors, respectively.

Excerpt: CMA was performed with Affymetrix Oncoscan arrays.

105- **Meeting abstract**

**KRAS Amplification in a 73-Year-Old Man with Adenocarcinoma of Lung**


...Genomic DNA was also subjected to molecular inversion probe array by OncoScan FFPE Assay kit (Affymetrix, Santa Clara, CA). Genomic copy number and allelic imbalance calls were performed by OncoScan Console Software and data reviewed by OncoScan™ Nexus Express Software (BioDiscovery, El Segundo, CA) ... Further study on copy number variation by MIP array revealed high copy number gain in KRAS (16 copies), which was in good concordance with estimated copy number information from next generation sequencing (10 copies).

106- **Meeting abstract**

**Molecular Inversion Probe analysis using OncoScan™ FFPE Assay Kit to detect copy number aberrations and somatic mutations in lung tumor DNA samples from formalin-fixed paraffin-embedded (FFPE) tissue**

Ron Sapolsky, Anju Shukla, Sumathi Venkatapathy, Chuan Chen, Carsten Bruckner, Vicky Huynh, Liansen Liu, Xuan Shen, Kent Suyenaga, Patrick Weaver, Wai Wu, Bitao Liu, Matt Ghent, Benjamin Bolstad, Faroq Siddiqui, Diana Abdueva, Mirjana Alvi, Eric Fung, Jeanette Schmidt, Lawrence Greenfield.

AACR Annual Meeting, April 5-9 2014, San Diego, CA, Abst #4655.

Body: DNA copy number (CN) studies hold great promise for the discovery of clinical biomarkers to predict disease course, recurrence risk, and response to therapy. The molecular characterization of a tumor genome across many samples helps to classify cancers in a biologically and clinically relevant manner. While exciting results have been found with genes already known to be involved in key pathways, confirming early results and genome-wide testing requires large numbers of well-characterized clinical samples. A vast collection of hundreds of millions of stored FFPE samples already exists. Unfortunately, many genomic assays fail to produce high-quality CN and genotype data from FFPE samples, given the degradation and chemical changes to the DNA and the small quantity obtained from tiny tissue samples. The higher rate of sequencing artifacts and genotyping failures in FFPE samples restricts the application of these promising whole-genome scanning technologies to the limited number of fresh-frozen samples. OncoScan™ FFPE Assay Kit is designed to interrogate the whole genome for copy number aberrations (CNAs), loss of heterozygosity (LOH), and selected somatic mutations (SMs) and captures the alleles of over 220,000 SNPs at carefully selected genomic locations. These SNPs are evenly distributed across the genome and with increased density within ~900 cancer-related genes. Based on Molecular Inversion Probe (MIP) technology, several OncoScan Assay Kit features make it highly suitable for the analysis of FFPE tissue-derived DNA. The assay uses only 80 ng input DNA with no requirement for amplification of the genomic DNA; rather, the probe itself is amplified, leading to a high signal-to-noise ratio. The entire assay can be run such that results can be obtained within 48 hours of gDNA extraction. Cancer sample data are complex because each sample is inherently mosaic,
comprised of a mixture of normal cells along with one or multiple tumor clones. OncoScan FFPE Assay Kit includes a component algorithm that specifically addresses the issue of normal contamination in the tumor sample. In this study, we will describe the characterization of genomic variations in a set of 67 lung tumor samples collected in collaboration with Cancer Research UK (CRUK). From each sample, 80 ng FFPE gDNA has been extracted and purified as input to OncoScan Assay Kit. Collectively, the tumor genomes showed frequent CN gains on chromosomes 1q, 5p, 6p, 7, 8q, and 17q and frequent CN losses on chromosomes 6q and 17p. The number of structural aberrations per sample ranged from 3 to 340, with an average of 94. The assay simultaneously interrogates 74 SMs of interest using a panel of 64 MIPs. Forty-nine samples had at least 1 SM call (1 sample having a maximum of 4).

107 - Meeting abstract
MOLECULAR PROFILING AS AN OUTCOME PREDICTOR IN THE GALAXY TRIALTM (NCT01348126): A RANDOMIZED IIB/III STUDY OF GANETESPIB (STA-9090) IN COMBINATION WITH DOCETAXEL VERSUS DOCETAXEL ALONE IN SUBJECTS WITH STAGE IIIB/IV NSCLC
Annals of Oncology, Sep 2012, 12(Suppl 9) : Abstr #1647PD. [ESMO 2012 Congress, Vienna, Austria 28 Sep - 2 Oct 2012 (Eur Soc Medical Oncology and Jap Soc Medical Oncology)]
... Genetic mutational analysis was analyzed using Affymetrix OncoScan™ FFPE Express platform, which provides information on copy number variation, allelic ration and somatic mutations ...

108 - Meeting abstract
Unusual ROS1 Translocation Pattern in a 61 Year-old Woman with Metastatic Adenocarcinoma of Lung
Hui Chen a, Rajyalakshmi Luthra b, Neda Kalhor a, John Heymach c, Ronald Abraham b, Meenakshi Mehrotra b, Bal Mukund Mishra b, Keyur P. Patel b, Rajesh R. Singh b, Xinyan Lu b
a Dept of Pathology, MD Anderson Cancer Center, Houston, TX, USA; b Dept of Hematopathology, MD Anderson Cancer Center, Houston, TX; c Dept of Thoracic/Head &Neck Medical Oncology, MD Anderson Cancer Center, Houston, TX.
... Additionally, genomic DNA from metastatic tumor was subjected to molecular inversion probe array (MIP) by OncoScan FFPE Assay kit (Affymetrix). Genomic copy number and allelic imbalance calls were performed by OncoScan Console and data reviewed by OncoScan Nexus Express (BioDiscovery). ... MIP study on lymph node metastasis showed loss of heterozygosity involving 4 chromosomes/arms including chromosome 6 where ROS1 located. In addition, MIP array detected copy number gains involving 9 chromosomes/arms. Genome instability with numerous copy number gain and allelic imbalances, and ROS1 translocation might be one of contributing factors to patient poor clinical outcome.

Lymphoid tissue / Lymphoma

109 - Meeting abstract
Chromosome Genomic Array Testing of Follicular Lymphoma from FFPE Tissue of Untreated Patients
M. Fang1, X. Qu2, O. Press1
1Fred Hutchinson Cancer Research Center, Seattle WA; 2Seattle Cancer Care Alliance, Seattle, WA
The Journal of Molecular Diagnostics, Nov 2015, 17(6) [AMP Abstracts] : #H47, p.776
... We performed CGAT on DNA extracted from formalin-fixed, paraffin embedded (FFPE) tissue specimens from 160 newly diagnosed, untreated FL patients using OncoScan ...

110 - Poster presentation
GENETIC ARRAY ANALYSIS OF FOLLICULAR DENDRITIC CELL SARCOMA

Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm of hematopoietic derivation. Until now, little has been known about the genetic changes of FDCS. Few cases have been evaluated by conventional cytogenetics or other genetic techniques. We evaluated 14 cases of FDCS using a molecular inversion probe (MIP)-based assay, which is optimized to evaluate genomic alterations in archived formalin fixed, paraffin-embedded (FFPE) tissues. A total of 14 deidentified patient samples were recruited from several institutions. Genomic DNA was isolated from FFPE tissues
and analyzed by MIP array to assess for copy number (CN) alterations and loss-of-heterozygosity (LOH) in the samples. Genomic DNA (~80 ng) was analyzed using the Affymetrix OncoScan™ kit (Affymetrix, Santa Clara, CA).

111- Meeting abstract
Genetic profile of two pediatric aggressive lymphoma cases with relapse
Maria del Mar Andres1,*, Idoia Martin-Guerrero2,*, Federico Garcia-Bragado3, Blanca Gonzalez-Farre4, Olga Balague4, Javier Molina-Garicano3, Barbara Torres-Guerola1, Yania Yanez1, Rafael Fdez-Delgado5, Itziar Salaverria4
1Pediatric Oncology Dept, Hospital Universitario y Politecnico La Fe de Valencia, Valencia, Spain; 2Department of Genetics, Physical Anthropology and Animal Physiology, Faculty of Medicine, University of the Basque Country, UPV/EHU, Leioa, Spain; 3Complejo Hospitalario de Navarra, Pamplona, Spain; 4Hematopathology Unit, Hospital Clinic, Institut d’Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; 5Pediatric Oncohematology Department, Hospital Clinico de Valencia, Valencia, Spain; *The two first authors contributed equally to the study.

British Journal of Haematology, October 2015, 171(S1): Abstract #126. [Special Issue: 5th Intl Symp on Childhood, Adolescent and Young Adult Non-Hodgkin Lymphoma Abstracts, 22 Oct 2015, Varese, Italy] …

Tumor samples at diagnosis and relapse of two patients initially diagnosed of BL were morphologically and immunophenotypically reviewed, and genetically characterized by fluorescence-in-situ-hybridization (FISH), and copy number (CN) analysis (OncoScan; Affymetrix).

112- Meeting abstract
Genome-wide analysis of follicular lymphoma pediatric type
Itziar Salaverria1, Janine-Alison Schmidt2, Shunyou Gong3, Stefania Pittaluga3, Blanca Gonzalez-Farre1, Olga Balagu e1, Teresa Maffioti4, Noelia Garcia1, Anna Mozos5, Jos e Cabecadas6, Jon Van Der Walt7, Irina Bonzheim2, Falko Fend2, Elias Campo1, Elaine S Jaffe3,*, Leticia Quintanilla-Martinez2,*
1Hematopathology Unit, Hospital Clinic, Institut d’Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; 2Institute of Pathology, University of Tubingen, Tubingen, Germany; 3Hematopathology Section, Laboratory of Pathology, National Cancer Institute, Bethesda, MD, USA; 4Dept of Cellular Pathology, Barts and The London NHS Trust, London, UK; 5Pathology Department, Hospital de Sant Pau, Barcelona, Spain; 6Pathology Dept, Instituto Portugues de Oncologia, Lisboa, Portugal; 7Dept of Histopathology, Guy’s and St Thomas Hospitals, London, UK; *Two last authors contributed equally to the study.

British Journal of Haematology, October 2015, 171(S1): Abstract #117. [Special Issue: 5th Intl Symp on Childhood, Adolescent and Young Adult Non-Hodgkin Lymphoma Abstracts, 22 Oct 2015, Varese, Italy] …

The aim of this study was to perform a complete genetic characterization of PFL cases with a consensus diagnosis. … Molecular analyses included fluorescence-in-situ-hybridization for BCL2-breaks/t(14;18), copy number (CN) (OncoScan; Affymetrix).

113- Genome wide copy number analysis of paediatric Burkitt lymphoma using formalin-fixed tissues reveals a subset with gain of chromosome 13q and corresponding miRNA over expression.
Schiffman JD, Lorimer PD, Rodic V, Jahromi MS, Downie JM, Bayerl MG, Sanmann JN, Althof PA, Sanger WG, Barnette P, Perkins SL, Miles RR.
… DNA was quantitated with PicoGreen (Invitrogen, Carlsbad, CA, USA) and submitted for OncoScan FFPE Express (Affymetrix, Santa Clara, CA, USA) and submitted for OncoScan FFPE Express (Affymetrix, Santa Clara, CA, USA), a MIP SNP assay, performed at Affymetrix (Wang et al, 2005, 2007; Schiffman et al, 2009, 2010). …

114- Meeting abstract
High-resolution copy number analysis of B-lymphoblastic lymphoma using tissue from archived glass slides
JM Downie, AM Termuhlen, MA Lones, M Abromowitch, SL Perkins, JD Schiffman, RR Miles

DNA was extracted and analyzed on the Affymetrix OncoScan FFPE Express 2.0 platform, a single nucleotide polymorphism array that utilizes Molecular Inversion Probe technology.

115- High resolution copy number analysis of IRF4 translocation-positive diffuse large B-cell and follicular lymphomas.
Gene Chromosomes Cancer, Feb 2013, 52(2) : 150-155.
... Eleven DNAs from FFPE material were hybridized on the MIP assay using the Oncoscan FFPE Express custom service (Affymetrix, Santa Clara, CA).

116- High-resolution copy number analysis of paired normal-tumor samples from diffuse large B cell lymphoma

Elena Sebastián 1,2,3; Miguel Alcoceba 1,2,3; David Martín-García 4; Óscar Blanco 5; Mercedes Sanchez-Barba 6; Ana Balanzategui 1,2; Luis Marín 1,2; Santiago Montes-Moreno 3,7; Eva González-Barca 3; Emilia Pardal 3; Cristina Jiménez 1; María García-Álvarez 1; Guillem Clot 4; Ángel Carracedo 8,9; Norma C. Gutiérrez 1,2; M. Eugenia Sarasquete 1,2; Carmen Chilón 1,2; Rocio Corral1,2; M. Isabel Prieto-Conde 1; M. Dolores Caballero 1; 2,3; Iziar Salaverria 4; Ramón García-Sanz rgartcas@usal.es 1,10,2,3; Marcos González 1,10, 2
1. Molecular Biology & Histocompatibility Unit, Department of Hematology, IBSAL - University Hospital of Salamanca, Paseo de San Vicente, 58-182, 37007, Salamanca, Spain; 2. Institute of Biomedical Research of Salamanca (IBSAL), Salamanca, Spain; 3. Spanish Lymphoma/Autologous Bone Marrow Transplant Study Group (GELTAMO), Salamanca, Spain; 4. Hematopathology Unit, Hospital Clínic, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; 5. Dept of Pathology, University Hospital of Salamanca, Salamanca, Spain; 6. Dept of Statistics, University of Salamanca, Salamanca, Spain; 7. Department of Pathology, University Hospital of Marqués de Valdecilla/IFIMAV, Santander, Spain; 8. Fundación Pública Galega de Medicina Xénómica, IDIS, SERGAS, Santiago de Compostela, Spain; 9. Grupo de Medicina Xénómica, CIBERER, Universidad de Santiago de Compostela, Santiago de Compostela, Spain; 10. Center for Cancer Research (CIC, IIBMCC-USAL-CSIC), Salamanca, Spain
... Thirty-eight cases with available FFPE DNA were hybridized on the MIP assay using the Oncoscan FFPE Express custom service 2.0 (Affymetrix, Santa Clara, CA, USA), this version does not interrogate somatic mutations.

117- Meeting abstract
High-resolution copy number analysis using low input, degraded DNA from fine-needle aspirates and macrodissected archival Burkitt lymphoma material

Peixun Zhou1, Rachel Crossland1, Amy Erhorn1, Vikki Rand1
1Northern Institute for Cancer Research, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UK
British Journal of Haematology, October 2015, 171(S1): Abstract #121. [Special Issue: Fifth International Symposium on Childhood, Adolescent and Young Adult Non-Hodgkin Lymphoma Abstracts, 22 October 2015, Varese, Italy]
... Methods: 80 ng of DNA at concentrations of either 12 ng/μl (FNAs) or 4 ng/μl (FFPEm) were hybridised to the Affymetrix Oncoscan array. Data was analysed using Affymetrix Oncoscan Console and Nexus Express for Oncoscan. ... Conclusion: Affymetrix Oncoscan arrays provide a robust platform for high-resolution copy number analysis of degraded DNA at concentrations as low as 4 ng/μl. This opens up new opportunities to investigate the genomic landscape of patient material previously not possible.

118- Meeting abstract
Identification of a Subset of Peripheral T-Cell Lymphoma, Not Otherwise Specified, Characterized By FOXP3-Positive Regulatory T-Cell Phenotype, HTLV-1 Negativity and Poor Outcome

1Aarhus University Hospital, Aarhus, Denmark; 2Aarhus University Hospital, Aarhus, Denmark; 3Aarhus University Hospital, Aarhus C, Denmark; 4Copenhagen University Hospital Herlev, Herlev, Denmark; 5Odense University Hospital, Odense, Denmark; 6National Cancer Institute, Bethesda, MD; 7National Cancer Institute, Bethesda, MD; 8University Hospital Schleswig-Holstein Campus Kiel/Christian-Albrechts University, Kiel, Germany; 9City of Hope Medical Center, Duarte, CA.
Background: T-cell malignancies originating from regulatory T (Treg) cells are almost exclusively confined to human T-cell leukemia virus 1 (HTLV-1) associated adult T-cell leukemia/lymphoma (ATLL), although sporadic cases of other peripheral T-cell lymphomas (PTCLs) with hypothesized Treg derivation have been reported. Patients and methods: We investigated a series of 169 well characterized PTCLs for the expression of Treg-cell phenotypic markers FOXP3, CD25 and CD4 by immunohistochemistry (IHC) using tissue microarray on formalin-fixed paraffin
embedded tissue. Clinico-pathological data for patients enrolled were retrieved from the Danish Lymphoma Registry and medical records. Treg tumors were further investigated by Affymetrix Oncoscan analysis and Illumina Infinium HumanMethylation450 BeadChips. Results: Variable amounts of FOXP3-positive Treg cells were often (99% of the cases) found as part of the non-neoplastic cellular infiltrate. However, in five cases (3%) classified as PTCL, not otherwise specified (PTCL-NOS) the vast majority of what morphologically appeared to be the neoplastic cell population displayed a strong positivity for FOXP3, CD4, CD25 and CD3 suggesting a probable Treg origin of these cells. Cases were HTLV-1 negative and showed monoclonal rearrangements of the T-cell receptor genes. All cases were male older than 60 years and showed an aggressive clinical course with overall survival less than two years, despite all patients had low IPI-risk profile at the time of diagnosis. The PTCL with Treg phenotype showed a complex pattern of chromosomal imbalances. Moreover, as compared to normal T-cell subsets their DNA methylation profiles were mostly related to that of normal Treg cells but significantly differed from that. Conclusions: We suggest that FOXP3-positive PTCL, in the absence of HTLV-1 infection, constitute a distinct entity separated from PTCL-NOS, occurring predominantly in elderly male patients and characterized by a highly aggressive clinical behavior. Further genomic analyses are ongoing. The identification and characterization of these cases may be useful to guide upfront therapeutic strategies.

119- Independent development of lymphoid and histiocytic malignancies from a shared early precursor
E Waanders, K M Hebeda, E J Kamping, P J T A Groenen, A Simons, A Hoischen, M C J Jongmans, P M Hoogerbrugge, F N van Leeuwen, R P Kuiper and D M W M te Loo
Leukemia, 23 July 2015, doi:10.1038/leu.2015.193
... we isolated DNA from a formalin-fixed sample of the non-Langerhans cell histiocytosis in which the tumor cell percentage was >80% and repeated the copy number analysis on a lower-resolution formalin-fixed, paraffin-embedded (FFPE)-compatible Affymetrix Oncoscan array.

120- Integrated copy number and gene expression profiling analysis of epstein-barr virus-positive diffuse large b-cell lymphoma
Heejei Yoon1,2,†, Sanghui Park3, Hyunjong Ju1,2, Sang Yun Ha1, InSuk Sohn4, Jisuk Jo4, In-Gu Do1, Sookee Min5, Seok Jin Kim6, Won Seog Kim6, Hae Yong Yoo7,*, Young Hyeh Ko1,*
1Dept of Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; 2Samsung Biomedical Research Institute, Seoul, Korea; 3Dept of Pathology, Ewha Womans University School of Medicine, Seoul, Korea; 4Samsung Cancer Research Institute, Samsung Medical Center, Seoul, Korea; 5Dept of Pathology, Hallym University Sacred Heart Hospital, Pyongchon, Gyongido, Korea; 6Div of Hematology-Oncology, Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; 7Samsung Advanced Institute for Health Sciences & Technology, Sungkyunkwan University School of Medicine, Seoul, Korea
Viral oncogenes and host immunosonescence have been suggested as causes of Epstein-Barr virus-positive diffuse large B-cell lymphoma (EBV + DLBCL) of the elderly. To investigate the molecular genetic basis of immune evasion and tumor outgrowth, we analyzed copy number alterations (CNAs) and gene expression profiles in EBV + DLBCL samples compared with EBV − DLBCL ... The DNA copy number analysis was performed using the Oncoscan™ FFPE Express 2.0 Services of Affymetrix. The Oncoscan™ FFPE Express 330K MIP platform (Affymetrix ...
Non-leukemic pediatric mixed phenotype acute leukemia/lymphoma: genome-wide analysis and clinical outcome under treatment in a prospective clinical trial for lymphoblastic lymphoma

Itziar Salaverria1,2,*, Idoia Martin-Guerrero1,3,*, Birgit Burkhardt4, Catherine Chassagne-Clement5, Monika Szczepanowski6, Susanne Bans1, Wolfram Klapper6, Alfred Reiter7, Reiner Siebert1, Ilske Oschlies6
1Institute of Human Genetics, University Hospital Schleswig-Holstein, Campus Kiel/Christian-Albrechts University, Kiel, Germany; 2Hematopathology Unit, Hospital Clinic, Institut d’Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; 3Department of Genetics, Physical Anthropology and Animal Physiology, Faculty of Medicine, University of the Basque Country, UPV/EHU, Leioa, Spain; 4NHL-BFM Study Center and Department of Pediatric Hematology and Oncology, University Children’s Hospital, Munster, Germany; 5Department of Biopathology, Centre Leon Berard, Lyon, France; 6Department of Pathology, Hematopathology Section and Lymph Node Registry, University Hospital Schleswig-Holstein, Campus Kiel/ Christian-Albrechts University, Kiel, Germany; 7NHL-BFM Study Center and Department of Pediatric Hematology and Oncology, Justus-Liebig-University of Giessen, Giessen, Germany; *Two first authors contributed equally to the study.

British Journal of Haematology, October 2015, 171(S1): Abstract #135. [5th Intl Symp on Childhood, Adolescent and Young Adult Non-Hodgkin Lymphoma Abstracts, 22 October 2015, Varese, Italy]

Formalin-fixed paraffin-embedded samples from twelve pediatric non-leukemic MPAL (7 B-myeloid, 3 T-B, 2 T-myeloid), treated in the prospective trial Euro-LBL 02, were studied by fluorescence in situ hybridization for detection of breakpoints or gene fusions of IGH, MLL, BCR, ABL, TEL, AML1and RUNX1T1. Oncoscan (Affymetrix) was performed for detection of copy number (CN) and CN neutral-loss of heterozygosity (CNN-LOH) alterations. …

123-
**Recurrent loss of heterozygosity in 1p36 associated with TNFRSF14 mutations in IRF4 translocation negative pediatric follicular lymphomas**
Idoia Martin-Guerrero, Itziar Salaverria, Birgit Burkhardt, Monika Szczepanowski, Michael Baudis, Susanne Bans, Laurence de Leval, Africa Garcia-Orad, Heike Horn, Jasmin Lisfeld, Shoji Pellissery, Wolfram Klapper, Ilske Oschlies, Reiner Siebert
… DNAs from formalin-fixed paraffin-embedded material were hybridized on the MIP-assay using Oncoscan FFPE Express custom service (Affymetrix, Santa Clara, USA). Copy number determination of MIP-assay …

124-
**TP53 pathway analysis in paediatric Burkitt lymphoma reveals increased MDM4 expression as the only TP53 pathway abnormality detected in a subset of cases.**
… Thus, a total of 25 cases were analysed by qRT-PCR. Molecular inversion probe assay. Genomic DNA was submitted to Affymetrix for the Oncoscan FFPE Express™ molecular inversion probe (MIP) assay.

**Melanoma / Melanocytic Neoplasms**

125-
**Consistent copy number changes and recurrent PRKAR1A mutations distinguish Melanotic Schwannomas from Melanomas: SNP-array and next generation sequencing analysis**
Lu Wang1, Ahmet Zehir1, Justyna Sadowska1, Nengyi Zhou1, Marc Rosenblum1, Klaus Busam1, Narasimhan Agaram1, William Travis1, Maria Arcila1, Sijezana Dogan1, Michael F. Berger1,2, Donavan T. Cheng1, Marc Ladanyi1,2, Khedoudia Nafa1 andMeera Hameed1,*
1Dept of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY; 2Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, NY; Genes, Chromosomes and Cancer, August 2015, 54(8): 463-471.
…Genome-wide DNA CN alterations and AIs were analyzed by SNP-array using Affymetrix Oncoscan FFPE Assay

126-
**Differentiation of malignant melanoma from benign nevus using a novel genomic microarray with low specimen requirements.**
Chandler WM, Rowe LR, Florell SR, Jahromi MS, Schiffman JD, South ST.
… GMA used in this study was not optimized for melanoma, the modularity of the molecular inversion probe design means … In fact, the most recent version of the Oncoscan FFPE Express from Affymetrix (version 2.0
127- Genomic copy number analysis of a spectrum of blue nevi identifies recurrent aberrations of entire chromosomal arms in melanoma ex blue nevi
May P Chan1,2, Aleodor A Andea1,2, Paul W Harms1,2, Alison B Durham2, Rajiv M Patel1,2, Min Wang1, Patrick Robichaud2, Gary J Fisher2, Timothy M Johnson2 and Douglas R Fullen1,2
1Dept of Pathology, University of Michigan, Ann Arbor, MI, USA. 2Dept of Dermatology, University of Michigan, Ann Arbor, MI, USA
Modern Pathology, 8 January 2016 | doi:10.1038/modpathol.2015.153
Blue nevi may display significant atypia or undergo malignant transformation. Morphologic diagnosis of this spectrum of lesions is notoriously difficult, and molecular tools are increasingly used to improve diagnostic accuracy. We studied copy number aberrations in a cohort of cellular blue nevi, atypical cellular blue nevi, and melanomas ex blue nevi using Affymetrix's OncoScan platform ..........

128- Meeting abstract
Identification of NTRK3 Gene Rearrangement in Spitz Tumor Based on a Genome-Wide SNP-Array Analysis
Memorial Sloan Kettering Cancer Center, New York, NY.
...: We studied 119 Spitzoid tumor samples, a majority of which were histological diagnosed as atypical Spitz tumors. Genomic DNA was extracted from FFPE tumor material, and 80ng input DNA of each sample was used for genome-wide copy number and allelic imbalance analysis by SNP-array (OncoScan, Affymetrix). ...

129- Intratumoral genetic heterogeneity in metastatic melanoma is accompanied by variation in malignant behaviors
Matthew Anaka, Christopher Hudson, Pu-Han Lo, Hongdo Do, Otavia L Caballero, Ian D Davis, Alexander Dobrovic, Jonathan Cebron, Andreas Behren
BMC Medical Genomics, 11 Oct 2013, 6:40
... DNA extracted from cores taken from three separate FFPE tissue blocks was analyzed using the Affymetrix Oncoscan 2.0 platform.

130- Melanoma Mimic: A Case of Multiple Pagetoid Spitz Nevi
KaiLynne Harris, Scott R. Florell, Jason Papenfuss, Wendy Kohlmann, Mona Jahromi, Joshua D. Schiffman, John Quackenbush, Pamela Cassidy, and Sancy Leachman
... Three samples were run on OncoScan FFPE Express (Affymetrix, Santa Clara, California), which is a 330K single-nucleotide polymorphism microarray platform that uses...

131- This is an OncoScan reference
Mitotically Active Proliferative Nodule Arising in a Giant Congenital Melanocytic Nevus: A Diagnostic Pitfall
Nguyen, Thuy L. T. ; Theos, Amy; Kelly, David R.; Busam, Klaus; A. Andea, Aleodor
... In addition, analysis of DNA copy number changes using a single nucleotide polymorphism microarray (Affymetrix, Santa Clara, CA) showed no chromosomal aberrations. Excerpt not available.

132- Meeting abstract
Mutation and copy number analysis in melanoma biopsies from the phase 2 study of the oral MEK1/2 inhibitor trametinib—impact of BRAF amplification on response
C. H. Moy1, A. Santiago-Walker1, R. C. Gagnon1, B. Wubbenhorst2, K. D’Andrea2, O. Gardner1, D. DeMarini1, F. S. Wu1, K. Patel1, A.-M. Martin1, K. L. Nathanson2
1GlaxoSmithKline, Collegeville, PA, USA; 2Dept of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.
Genetic profiling was performed on archival biopsies (bx) used for BRAF mutation (mut) screening from 47 patients (pts) from the phase 2 study (NCT01037127) of trametinib (T) in pts with metastatic BRAF-mut melanoma (n = 97). Pts were previously treated with a BRAF inhibitor (cohort A, n = 19), or chemotherapy and/or immunotherapy (BRAF-inhibitor naïve; cohort B, n = 28). Mut profiling was performed using the Illumina TruSeq Amplicon Cancer Panel (NGS) (45 pts) and Sequenom MassARRAY. Copy number variation was determined using Affymetrix OncoScan (37 pts). BRAF V600E/K mut status was confirmed by NGS in 43/45 bx (96% concordance with screening PCR test); in the 2 discordant samples, an unusual BRAF change at the 600 position was observed (V600del and V600G).

Additional mut were identified in TP53, PTEN, NRAS, MYC, CDK4, CTNNB1, and there were 2 cases of IDH1 mut (R132H). Two pts with NRAS mut were both in cohort A. BRAF amplifications (amps) were found in 21 pts (cohort A, n = 6; cohort B, n = 15). Thirteen of 21 pts (cohort A, n = 1; cohort B, n = 12) with BRAF amps had no recorded therapies prior to bx, demonstrating that BRAF amps can arise in the absence of anticancer therapy. Pts with BRAF amps trended toward shorter progression-free survival (PFS) (HR = 2.21; P = 0.0587). Cohort B pts with V600K mut generally had less tumor reduction in response to T than did V600E pts. Overall, V600K pts exhibited a higher frequency of amps (5/6 amps, 83%) compared with V600E pts (14/29 amps, 48%). Cohort B pts with both BRAF amps and AKT3 gains (8/28 pts) exhibited the shortest PFS (median, 3 months) compared with those with a single amp (7.3 months), or no amp (7.4 months) in these genes (P = 0.0450). These data warrant further investigation into the impact of various BRAF genomic alterations on durable response with MAPK inhibition.

133-
The extent of whole-genome copy number alterations predicts aggressive features in primary melanomas

Greta Gandolfi1, Caterina Longo2, Elvira Moscarella2, Iris Zalaudek3, Valentina Sancisi1, Margherita Raucci2, Gloria Manzotti1, Mila Gugnoni1, Simonetta Piana4, Giuseppe Argenziano2,5,* and Alessia Ciarrocchi1,* 1Laboratory of Translational Research, Arcispedale S. Maria Nuova-IRCCS, Reggio Emilia, Italy; 2Skin Cancer Unit, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy; 3Dept of Dermatology and Venerology, Non-Melanoma Skin Cancer Unit, Medical University of Graz, Graz, Austria; 4Pathology Unit, Arcispedale S. Maria Nuova-IRCCS, Reggio Emilia, Italy; 5Dermatology Unit, Second Univ of Naples, Naples, Italy

Pigment Cell & Melanoma Research, Article first published online: 12 Jan 2016; doi: 10.1111/pcmr.12436

... Genomewide analysis of CNA and loss of heterozygosity (LOH) was performed using the Oncoscan FFPE Express Service (Affymetrix, Santa Clara, CA, USA).

134-
The Genomic Landscape of Childhood and Adolescent Melanoma

Charles Lu1,11, Jinghui Zhang2,11, Panduka Nagawahatte2, John Easton2, Seungjae Lee3, Zhifa Liu4, Li Ding1,5,6,7, Matthew A Wyczalkowski1, Marcus Valentine8, Fariba Navid9, Heather Mulder2, Ruth G Tatevosian3, James Dalton3, James Davenport3, Zhirong Yin3, Michael Edmonson2, Michael Rusc3h, Gang Wu2, Yongjin Li2, Matthew Parker2, Erin Hedlund2, Sheila Shurtleff3, Susana Raimondi3, Vadodaria Bhavin2, Yergeau Donald2, Elaine R Mardiss5,6,7, Richard K Wilson5,6,7, William E Evans10, David W Ellison3, Stanley Pound24, Michael Dyer2, James R Downing3, Alberto Pappo9, Armita Bahrami3 for St Jude Children's Research Hospital-Washington University Pediatric Cancer Genome Project 1The Genome Institute, Washington University School of Medicine in St Louis, St Louis, Missouri, USA; 2Dept of Computational Biology, St Jude Children’s Research Hospital, Memphis, Tennessee, USA; 3Dept of Pathology, St Jude Children’s Research Hospital, Memphis, Tennessee, USA; 4Dept of Biostatistics, St Jude Children’s Research Hospital, Memphis, Tennessee, USA; 5Dept of Genetics, Washington University School of Medicine in St Louis, St Louis, Missouri, USA; 6Dept of Medicine, Washington University School of Medicine in St Louis, St Louis, Missouri, USA; 7Siteman Cancer Center, Washington University School of Medicine in St Louis, St Louis, Missouri, USA; 8Dept of Cytogenetics, St Jude Children’s Research Hospital, Memphis, Tennessee, USA; 9Dept of Oncology, St Jude Children’s Research Hospital, Memphis, Tennessee, USA; 10Dept of Pharmaceutical Sciences, St Jude Children’s Research Hospital, Memphis, Tennessee, USA


Despite remarkable advances in the genomic characterization of adult melanoma, the molecular pathogenesis of pediatric melanoma remains largely unknown. We analyzed 15 conventional melanomas (CMs), 3 melanomas arising in congenital nevi (CNMs), and 5 spitzoid melanomas (SMs), using various platforms, including whole genome or exome sequencing, the molecular inversion probe assay, and/or targeted sequencing. ...Affymetrix OncoScan MIP assay--Genomic DNA was extracted from FFPE sections of 19 melanomas (Figure 1). ... A minimum quantity of 200 ng of genomic DNA was used as input per Affymetrix OncoScan guidelines.
Whole-genome copy-number analysis identifies new leads for chromosomal aberrations involved in the oncogenesis and metastatic behavior of uveal melanomas.

van Engen-van Grunsven, Adriana C.H.; Baar, Marjolein P.; Pfundt, Rolph; Rijntjes, Jos; Küsters-Vandevelde, Heidi V.N.; Delbecq, Ann-Laure; Keunen, Jan E.; Klevering, Jeroen B.; Wesseling, Pieter; Blox, Willeke A.M.; Groenen, Patricia J.T.A.


To further elucidate the genetic underpinnings of uveal melanoma (UM) and identify new markers that correlate with disease outcome, archival formalin-fixed, paraffin-embedded enucleation specimens from 25 patients with UM and a mean follow-up of 14 years were analyzed for whole-genome copy-number alterations using OncoScan analysis. Copy-number alterations of chromosomes 1, 3, 6, and 8 were also analyzed in these tumors using multiplex ligation-dependent probe-amplification, and mutations in GNAQ, GNA11, and BAP1 were searched for by Sanger sequencing. Our study confirms the previously reported GNAQ and GNA11 mutation frequencies in UM as well as the presence of monosomy 3 as a factor strongly indicating poor prognosis.----------

Multiple Cancer Types

An asbestos-exposed family with multiple cases of pleural malignant mesothelioma without inheritance of a predisposing BAP1 mutation

Mitchell Cheung a, Yuwaraj Kadariya a, Jianming Pei a, Jacqueline Talarchek a, Francesco Facciolo b, Paolo Visca c, Luisella Righi d, Ilaria Cozzi e, Joseph R. Testa a, Valeria Ascoli e

da Cancer Biology Program, Fox Chase Cancer Center, Philadelphia, PA, USA; b Dept of Oncologic Thoracic Surgery, Regina Elena Cancer Institute, Rome, Italy; c Dept of Pathology, Regina Elena Cancer Institute, Rome, Italy; d Dept of Oncology, San Luigi Hospital, University of Turin, Italy; e Dept of Radiological Sciences, Oncology and Pathology, Sapienza University of Rome, Italy.


We report a family with domestic exposure to asbestos and diagnosis of multiple cancers, including eight pleural malignant mesotheliomas and several other lung or pleural tumors. DNA sequence analysis revealed no evidence for an inherited mutation of BAP1. Sequence analysis of other potentially relevant genes, including TP53, CDKN2A, and BARD1, also revealed no mutation. DNA microarray analysis of tissue from two mesotheliomas revealed multiple genomic imbalances, including consistent losses of overlapping segments in 2q, 6q, 9p, 14q, 15q, and 22q, but no losses of chromosome 3 harboring the BAP1 locus. However, the results of immunohistochemical analysis demonstrated loss of nuclear BAP1 staining in three of six mesotheliomas tested, suggesting that somatic alterations of BAP1 occurred in a subset of tumors from this family. Since mesothelioma could be confirmed in only a single generation, domestic exposure to asbestos may be the predominant cause of mesothelioma in this family. Given the existence of unspecified malignant pleural tumors and lung cancers in a prior generation, we discuss the possibility that some other tumor susceptibility or modifier gene(s) may contribute to the high incidence of mesothelioma in this family. Because the incidence of mesothelioma in this family is higher than that expected even in workers heavily exposed to asbestos, we conclude that both asbestos exposure and genetic factors have played a role in the high rate of mesothelioma and potentially other pleural or lung cancers seen in this family.

Excerpt: ... CMA was performed using Affymetrix Oncoscan arrays.

Clinical application of genomic profiling to find druggable targets for adolescent and young adult (AYA) cancer patients with metastasis

Soojin Cha, Jeongeun Lee, Jong-Yeon Shin, Ji-Yeon Kim, Sung Hoon Sim, Bhumsuk Keam, Tae Min Kim, Dong-Wan Kim, Dae Seog Heo, Se-Hoon Lee, Jong-II Kim


Background—Although adolescent and young adult (AYA) cancers are characterized by biological features and clinical outcomes distinct from those of other age groups, the molecular profile of AYA cancers has not been well defined. In this study, we analyzed cancer genomes from rare types of metastatic AYA cancers to identify driving and/or druggable genetic alterations. Methods—Prospectively collected AYA tumor samples from seven different patients were analyzed using three different genomics platforms (whole-exome sequencing, whole-transcriptome sequencing or OncoScan™). Using well-known bioinformatics tools (bwa, Picard, GATK, MuTect, and Somatic Indel Detector) and our annotation approach with open access databases (DAVID and DGIdb), we processed sequencing data and identified driving genetic alterations and their druggability. Results—The mutation frequencies of AYA cancers were lower than those of other adult cancers (median = 0.56), except for a germ cell tumor with hypermutation. We identified patient-specific genetic alterations in candidate driving genes: RASA2 and NF1 (prostate cancer), TP53 and CDKN2C (olfactory neuroblastoma), FAT1, NOTCH1, and SMAD4 (head and neck cancer), KRAS (urachal carcinoma), EML4-ALK (lung cancer), and MDM2 and PTEN (liposarcoma). We then
suggested potential drugs for each patient according to his or her altered genes and related pathways. By comparing candidate driving genes between AYA cancers and those from all age groups for the same type of cancer, we identified different driving genes in prostate cancer and a germ cell tumor in AYAs compared with all age groups, whereas three common alterations (TP53, FAT1, and NOTCH1) in head and neck cancer were identified in both groups. Conclusion—We identified the patient-specific genetic alterations and druggability of seven rare types of AYA cancers using three genomics platforms. Additionally, genetic alterations in cancers from AYA and those from all age groups varied by cancer type.

Excerpt: … We used the 330-k OncoScan™ FFPE platform (Affymetrix, Santa Clara, CA, USA) to identify candidate CNVs (amplification/deletion and loss-of-heterozygosity (LOH)). … A minimum of 80 ng of DNA from each sample was used for the OncoScan™ platform.

**Neuroblastoma**

<table>
<thead>
<tr>
<th>Meeting abstract</th>
<th>Multiple Segmental Chromosomal Aberrations in Low-Risk Neuroblastoma are Associated with Metastatic Relapse</th>
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... Formalin fixed, paraffin embedded (FFPE) diagnostic samples were used for whole-genome SNP and copy number analysis using OncoScan™ FFPE Express 2.0 (Affymetrix, Santa Clara, CA).

<table>
<thead>
<tr>
<th>Meeting abstract</th>
<th>Segmental Chromosomal Aberrations in Localized Neuroblastoma Can be Detected in Formalin-Fixed Paraffin-Embedded Tissue Samples and Are Associated With Recurrence</th>
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<tbody>
<tr>
<td>Navin Pinto MD1, Jodi R. Mayfield MD2, Gordana Raca MD, PhD3, Mark A. Applebaum MD4, Alexandre Chlenski PhD4, Madina Sukhanova PhD5, Rochelle Bagatell MD6, Meredith S. Irwin MD7, Anthony Little BS6, Jawhar Rawwas MD8, Yasmin Gosiengfiao MD9, Olivier Delattre MD, PhD10, Isabelle Janoueix-Lerosey PhD10, Eve Lapouble PhD11, Gudrun Schleiermacher MD, PhD10,11,12, Susan L. Cohn MD3*</td>
<td>... Patients with MYCN nonamplified International Neuroblastoma Staging System stage 1 and 2 disease who recurred were identified. CMA was performed with diagnostic FFPE samples using OncoScan™ FFPE Express 2.0. The prognostic significance of chromosomal pattern was validated in 105 patients with available CGH results.</td>
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**Ovary**

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<tr>
<th>Meeting abstract</th>
<th>Benign serous ovarian tumour: a redefining moment?</th>
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<tbody>
<tr>
<td>Sally Hunter1*, Kylie Gorringe1, Michael Anglesio2, AOCS1, Raghwa Sharma4, Blake Gilks3, Anna deFazio4, 5, David Huntsman2, Ian Campbell1</td>
<td>1Peter MacCallum Cancer Centre, Melbourne, VIC, Australia. 2The Center for Translational and Applied Genomics (CTAG) at the British Columbia (BC) Cancer Agency, Vancouver, BC, Canada. 3Dept of Pathology, Vancouver General Hospital, BC, Canada. 4Department of Gynaecological Oncology, Westmead Hospital, Westmead, NSW, Australia. 5Westmead Institute for Cancer Research, University of Sydney at Westmead Millennium Institute, Westmead Hospital, Westmead, VIC, Australia. Hered Cancer Clini Pract., online 12 Apr 2012; 10(Suppl 2): Abst # A83.</td>
</tr>
</tbody>
</table>
direct molecular evidence for the benign lesions as precursors is limited. This study aimed to perform high resolution copy number analysis using a series of benign serous ovarian tumours to identify any underlying genomic changes indicative of early events in tumorigenesis, which could assist in determining if these lesions represent precursors to some invasive serous ovarian carcinomas. This is the first ultra-high resolution copy number analysis of benign serous tumours of the ovary. High resolution copy number analysis was performed on tumour epithelial and fibroblast DNA using the Affymetrix OncoScan and SNP6.0 array platforms. Copy number aberrations (CNAs) were detected in the epithelium of only 5.6% (2/35) of serous cystadenomas and cystadenofibromas. Unexpectedly, CNAs were detected in the tumour fibroblasts in 36% (14/39) of cases, including gain of chromosome 12 in 10 cases. No KRAS or BRAF mutations were detectable in either component of the benign serous tumours. Chromosome 12 trisomy has been previously identified in pure fibromas, supporting the concept that a significant proportion of benign serous tumours are in fact primary fibromas with an associated cystic mass. This study therefore provides a novel perspective on the development of these tumours.

141- Copy Number Aberrations in Benign Serous Ovarian Tumors: A Case for Reclassification?
Sally M. Hunter, Michael S. Anglesio, Raghwa Sharma, C. Blake Gilks, Nataliya Melnyk, Yoke-Eng Chiew, Anna deFazio, for the Australian Ovarian Cancer Study Group, Teri A. Longacre, David G. Huntsman, Kylie L. Gorringe, and Ian G. Campbell
... High resolution CN analysis was conducted on DNA from the epithelial and fibroblast components of a cohort of benign (N = 39) and borderline (N = 24) serous tumors using the Affymetrix OncoScan assay and SNP6.0 arrays ..... 

142- FOXL2 mutation and large-scale genomic imbalances in adult granulosa cell tumors of the ovary
... We used a microarray platform designed for formalin-fixed, paraffin-embedded (FFPE) tissue specimens, the Affymetrix OncoScan FFPE Express 330K Molecular Inversion Probe (MIP) array, to explore the correlation between genomic imbalances detected by microarray and FOXL2 mutation status detected by pyrosequencing in a series of 21 archived AGCTs....

143- Loss-of-heterozygosity on chromosome 19q in early-stage serous ovarian cancer is associated with recurrent disease.
Skinnisdottir I, Mayrhofer M, Rydåker M, Akerud H, Isaksson A.
... Tumor samples from thirty-seven patients were analysed for allele-specific copy numbers using OncoScan single nucleotide polymorphism arrays from Affymetrix ... Genomic DNA was extracted from 51 FFPE Serous Ovarian cancer samples in compliance with the service provider's instructions for Affymetrix MIP_cn_330K/OncoScan™ FFPE Express Services and sent to Affymetrix Research Services Laboratory (ARSL) for processing [23].

144- Small cell carcinoma of the ovary, hypercalcemic type/ ovarian malignant rhabdoid tumor: report of a bilateral case in a teenager associated with SMARCA4 germline mutation.
Pierre-Marie Lavrut, François LE LOARER, Charline Normand, Céline Grosos, Rémi DUBOIS, Annie BUENERD, Cécile CONTER, Frédérique DIJOU, Jean-Yves Blay, and Sophie COLLARDEAU-FRACHON
Pediatric and Developmental Pathology, January/February 2016, 19(1): 56-60.
... Genomic profiling was performed on 80ng of FFPE gDNA with Oncoscan profiling (Affymetrix) according to the manufacturer's instructions.

145- Meeting abstract
Loss of heterozygosity as a molecular 'second hit' In familial pancreatic cancer
Zaheer S. Kanji, Stefano Serra, Spring Holter, Ayelet Borgida. Robert Grant, Steven Gallinger
AACR Annual Meeting 2013, Apr 09, 2013, Poster Board Number: 25, Abstract Number: 3157
BACKGROUND/HYPOTHESIS: Familial Pancreatic Cancer (FPC) has an autosomal dominant, variable penetrant mode of inheritance with >80% of its genetic cause yet to be discovered. We hypothesize that a high density DNA microarray analysis of Formalin-Fixed Paraffin Embedded (FFPE) FPC tumors will yield novel regions of genomic loss harboring disease causing FPC gene(s). METHODS: 156 FFPE FPC tumor specimens with matched normal tissue were reviewed by a pancreatic pathologist and tumors with <70% cellularity underwent laser capture microdissection. The samples with >70% cellularity were microdissected directly from marked unstained slides. A total of 74 samples were DNA extracted, whole genome amplified and processed on the Affymetrix 660K Oncoscan Microarray. Copy number analysis was performed using Nexus Copy Number Variation Version 6.1 software employing the SNP-FASST2 segmentation and Allele Specific Copy Number Analysis of Tumors (ASCAT) algorithms. PRELIMINARY RESULTS: A pair-wise analysis of 55 FPC samples with matched normal tissue was performed. Recurrent regions of loss of heterozygosity (LOH) were known loci of importance in pancreatic tumorigenesis, including CDKN2A, p53 and SMAD4. Copy neutral/gain LOH was observed throughout the genome and may account for >35% of chromosomal loss. Recurrent novel genetic loci displaying LOH was observed on chromosomes: 3p(25%), 5q(18%), 6p(22%), 12q(18%) and Xq (42%). Examination of 2 FPC siblings elucidates shared loss regions spanning the 3p22.2-3p22.3 and 17p13.3 loci. Candidate tumor suppressor genes (TSGs) of interest include DCLK3, SERPINF1, SERPINF2 and SMYD4. CONCLUSION: We have described for the first time the presence of copy neutral/gain LOH in FPC highlighting previously unknown regions displaying genetic loss. Further confirmation with quantitative PCR, integrating with germline exome sequencing data, and validation of putative TSGs shared by members of high risk FPC kindreds will help uncover novel genes associated with this disease.

**Pineal Tumors**

146-

Papillary tumor of the pineal region: A distinct molecular entity

Stephanie Heim1, Martin Sill2, David T. W. Jones3, Alexandre Vasiljevic4,5, Anne Jouvët4,5, Michelle Fèvre-Montange5, Pieter Wesseling6,7, Rudi Beschorner8, Michel Mittelbronn9, Patricia Kohlhof10, Volker Hovestadt11, Pascal Johann3,12, Marcel Kool3,12, Kristian W. Pałtler3, Andrey Korshunov13,14,15, Vincent Ruland1, Jan Sperveslage16, Christian Thomas1, Hendrik Witt3,12, Andreas von Deimling3,14,15, Werner Paulus1, Stefan M. Pfister3,12,15, David Capper13,14,15,†, Martin Hasselblatt1,†,*

1Institute of Neuropathology, University Hospital Münster, Münster, Germany; 2Division of Biostatistics, German Cancer Research Center (DKFZ), Heidelberg, Germany; 3Division of Pediatric Neurooncology, German Cancer Research Center (DKFZ), Heidelberg, Germany; 4Centre de Pathologie et Neuropathologie Est, Centre de Biologie et Pathologie Est, Groupement Hospitalier Est, Hospices Civils de Lyon, Bron Cedex, France; 5CRNL, INSERM U1028, CNRS UMR 5292, Equipe Neuro-oncologie et Neuro-inflammation, Université de Lyon, Lyon Cedex 08, France; 6Dept of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands; 7Dept of Pathology, VU University Medical Center, Amsterdam, The Netherlands; 8Institute for Pathology and Neuropathology, Department of Neuropathology, University of Tübingen, Tübingen, Germany; 9Institute of Neurology (Edinger Institute), Goethe University, Frankfurt, Germany; 10Dept of Pathology, Klinikum Stuttgart, Stuttgart, Germany; 11Division of Molecular Genetics, German Cancer Research Center (DKFZ), Heidelberg, Germany; 12Dept of Pediatric Oncology and Hematology, University Hospital Heidelberg, Germany; 13Dept of Neuropathology, University Hospital Heidelberg, Heidelberg, Germany; 14Clinical Cooperation Unit Neuropathology, German Cancer Research Center (DKFZ), Heidelberg, Germany; 15German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany; 16Gerhard-Domagk-Institute of Pathology, University Hospital Münster, Münster, Germany

Brain Pathology, Accepted manuscript online: 25 JUN 2015

... DNA methylation profiling using Illumina 450k arrays reliably distinguished PTPR from ependymomas and pineal parenchymal tumors of intermediate differentiation .....A total of 75ng DNA was submitted to OncoScan FFPE Express analysis (Affymetrix, Santa Clara CA). The MIP SNP ... Methylation data (450k Array) 22/24 (91%) CNV data (OncoScan) 13/24 (60%) ...
... Each of these 28 foci were subjected to whole-genome sequencing (WGS) and OncoScan SNP arrays to yield comprehensive genetic profiles. Following independent pathology reviews and manual macro-dissection of tumour areas of ≥70% cellularity, WGS (≥50x tumour, ≥30x germline) was performed on as little as 50 ng genomic DNA, and OncoScan arrays were performed using as little as 30 ng DNA using either amplified or innate genomic DNA.

149- **Oncoscan not mentioned; authors acknowledge using Oncoscan in BioArray News, 23 Oct 2012, “Team Uses Affy's OncoScan to Develop Prostate Cancer Prognostic Diagnosis, Envisions Clinical Use”**

**Clustering-Based Method for Developing a Genomic Copy Number Alteration Signature for Predicting the Metastatic Potential of Prostate Cancer**

Alexander Pearlman, Christopher Campbell, Eric Brooks, Alex Genshaft, Shahin Shajahan, Michael Ittman, G. Steven Bova, Jonathan Melamed, Iliana Holcomb, Robert J. Schneider, Harry Ostrer


150- **Combined Tumor Suppressor Defects Characterize Clinically Defined Aggressive Variant Prostate Cancers**

Ana M. Aparicio1,*, Li Shen2, Elsa M Li Ning Tapia3, Jing-Fang Lu3, Hsiang-Chun Chen4, Jiexin Zhang5, Guanglin Wu6, Xuemei Wang7, Patricia Troncoso8, Paul Corr9, Timothy C. Thompson10, Bradley Broom11, Keith A. Baggerly11, Sankar N. Maity6, and Christopher Logothetis6

1Genitourinary Medical Oncology, UT MD Anderson Cancer Center; 2Bioinformatics & Comp Biology, UT MD Anderson Cancer Center; 3Dept of Genitourinary Medical Oncology and David H. Koch Center for Applied Research of Genitourinary Cancers, University of Texas M. D. Anderson Cancer Center; 4Biostatistics, MD Anderson Cancer Center; 5Bioinformatics and Computational Biology, University of Texas, MD Anderson Cancer Centre; 6Genitourinary Medical Oncology, University of Texas MD Anderson Cancer Center; 7Biostatistics, University of Texas M. D. Anderson Cancer Center; 8Pathology, MD Anderson Cancer Center; 9GenitoUinary Medical Oncology, Unit 1374, MD Anderson; 10Dept of Genitourinary Medical Oncology - Research, UT MD Anderson Cancer Center; 11Dept of Bioinformatics Computer Biology, University of Texas M.D. Anderson Cancer Center.

Clinical Cancer Research, Online First November 6, 2015; doi: 10.1158/1078-0432.CCR-15-1259

... DNA from 36 and 8 PDX was analyzed by Oncoscan® for copy number gains (CNG) and losses (CNL) ... Gene expression of 6 PDX profiled using the U133A2.0 Plus array ... copy number estimates from Affymetrix SNP6 arrays

151- **Meeting abstract**

**Genetic Heterogeneity of Gleason Score 7 Prostate Cancer: A Pilot Study of the Canadian Prostate Cancer Genome Network (CPC-GENE)**


... The Canadian Prostate Cancer Genome Network (CPC-GENE) has undertaken a pilot study to provide an evaluation of the heterogeneity in Gleason score 7 PCa using a robust genomic approach. Gleason score (GS) 4+3 and 3+4 tumors from 5 frozen radical prostatectomies were analyzed using whole-genome sequencing (WGS) and Affymetrix OncoScan SNP arrays to determine differential genetic signatures ... Across multiple specimens, single nucleotide variants (SNVs) and copy number variations (CNVs) identified using WGS were validated with ~98% accuracy against the OncoScan platform....................................................

152- **Meeting abstract**

**GENOMIC PROFILING OF KCONFAB MEN WITH A BRCA MUTATION STATUS AND PROSTATE CANCER**

Ania Sliwinski, Heather Thorne, Damien Bolton, Gail Risbridger, Renea Taylor, David Clouston
The Journal of Urology, April 2015, 193(4 Sup): e748, Abstract #MP61-04 [AUA Annual Meeting] ... Areas of normal prostate, PIN, adenocarcinoma and IDC were marked by a pathologist and microdissected from archival FFPE blocks. Genome-wide copy number data was generated using the Affymetrix OncoScan™ array and interpreted using Nexus Copy Number™ software for areas of copy number gain or loss. …

153- Meeting abstract
Identifying high risk features and genomic instability in men with familial prostate cancer
G. Risbridger, R. Sliwinski, H. Thorne, T. Taylor, M. Papargiris, S. Hunter, I. Campbell, H. Thorne, J. Li, G. Mitchell, D. Clouston, R. Bristow, D. Murphy, M. Frydenberg, D. Bolton. 1Monash University, Anatomy & Developmental Biology, Melbourne, Australia; 2University of Melbourne, Austin Hospital, kConFab, Research Dept & Department of Urology, Melbourne, Australia; 3kConFab & Sir Peter MacCallum Cancer Centre, University of Melbourne, Dept of Oncology & kConFab, Research Dept, Melbourne, Australia; 4Monash University, Dept of Physiology, Melbourne, Australia; 5Cancer Genetics Laboratory, Cancer Genetics Laboratory, Melbourne, Australia; 6kConFab & Familial Cancer Centre, Research Dept, Melbourne, Australia; 7 Bioinformatics & gSir Peter MacCallum Cancer Centre, University of Melbourne, Research & Dept of Oncology, Melbourne, Australia; 8kConFab & Familial Cancer Centre & Sir Peter MacCallum Cancer Centre, University of Melbourne, Research Dept & Dept of Oncology, Melbourne, Australia; 9Tissupath, Melbourne, Australia; 10Princess Margaret Cancer Centre, Toronto, Canada; 11Peter MacCallum Cancer Centre & Epworth HealthCare, Division of Cancer Surgery & Epworth Research Centre, Melbourne, Australia; 12Sir Peter MacCallum Cancer Centre, University of Melbourne & Monash Medical Centre, Monash University, Dept of Oncology & Dept of Urology, Melbourne, Australia; 13University of Melbourne, Austin Hospital, Dept of Urology, Melbourne, Australia
European Journal of Cancer, Sep 2015, 51(3): Abst #2569. [European Cancer Congress 2015] …. Genome-wide copy number data was generated using the Affymetrix OncoScan™ array and interpreted using Nexus Copy Number™ software. …

154- Patient-derived Xenografts Reveal that Intraductal Carcinoma of the Prostate Is a Prominent Pathology in BRCA2 Mutation Carriers with Prostate Cancer and Correlates with Poor Prognosis
Gail P. Risbridger, Renea A. Taylor, David Clouston, Ania Sliwinski, Heather Thorne, Sally Hunter, Jason Li, Gillian Mitchy, Declan Murphy, Mark Frydenberg, David Pook, John Pedersen, Roxanne Toivanen, Hong Wang, Melissa Papargiris, Mitchell G. Lawrence, Damien M. Bolton
Background—Intraductal carcinoma of the prostate (IDC-P) is a distinct clinicopathologic entity associated with aggressive prostate cancer (PCa). PCa patients carrying a breast cancer 2, early onset (BRCA2) germline mutation exhibit highly aggressive tumours with poor prognosis. Objective—To investigate the presence and implications of IDC-P in men with a strong family history of PCa who either carry a BRCA2 pathogenic mutation or do not carry the mutation (BRCAX). … Samples were screened on Affymetrix (Santa Clara, CA, USA) OncoScan platform v.2 and v.3.

155- Spatial genomic heterogeneity within localized, multifocal prostate cancer
Nature Genetics, online 25 May 2015, 47:736-745. doi:10.1038/ng.3315
… whole genome-amplified (iGRT biopsy) or genomic (radical prostatectomy) DNA on Affymetrix OncoScan FFPE Express 2.0 SNP arrays … assayed using the HuGene 2.0 Affymetrix array … (batch 2) were assayed using the Human Transcriptome Array (HTA) …

156- Meeting abstract
Validation of a prostate cancer metastasis signature in a FFPE cohort of primary tumors.
A. Pearlman, C. Campbell, J. Loke, S. Freedland, Y. Shao, H. Ostrer
... The material was sent to Affymetrix Service Center in Santa Clara, CA and run on the OncoscanTM V2 SNP array developed specifically for gDNA samples extracted from ffpe archived tissue.

157- **Meeting abstract**

**Whole genome sequencing of low-input fresh frozen prostate cancer biopsies**

... we compared our results to genotyping-array results generated using the Affymetrix OncoScan platform. Single-nucleotide variants detected using arrays were validated >99% of the time by sequence data, confirming that the use of a low-input library did not hinder mutation detection.

158- **Renal / Kidney**

**Balanced Translocations Disrupting SMARCB1 Are Hallmark Recurrent Genetic Alterations in Renal Medullary Carcinomas**
Julien Calderaro a, b, c, Julien Masliah-Planchon d, e, Wilfrid Richer e, f, Laetitia Maillot d, Pascale Maille a, Ludovic Mansuy g, Claire Bastien h, Alexandre de la Taille b, c, i, Hélène Bousson j, Cécile Charpy a, Anne Jourdain k, Claire Bléchet l, Gaelle Pierron d, David Gentien m, Laurence Choudat n, Christophe Tournigand c, j, Olivier Delattre d, e, Yves Allory a, b, c, Franck Bourdeaut e, f, o

a APHP, Groupe Hospitalier Henri Mondor, Département de Pathologie, Créteil, France; b INSERM, U955, Institut Mondor de Recherche Biomédicale, Créteil, France; c Université Paris-Est Créteil, Créteil, France; d Institut Curie, Unité de Génétique Somatique, Paris, France; e INSERM U830, Génétique et Biologie des Cancers, Institut Curie, Paris, France; f Siric Institut Curie, Recherche Translationnelle en Oncologie Pédiatrique, Paris, France; g CHU Nancy, Hôpital d’enfants, Service d’Hématologie-oncologie pédiatrique, Vandoeuvre les Nancy, France; h CHU Nancy, Hôpital Brabois, Service d’Anatomie pathologique, Vandoeuvre les Nancy, France; i APHP, Groupe Hospitalier Henri Mondor, Service d’Urologie, Créteil, France; j APHP, Groupe Hospitalier Henri Mondor, Service d’Oncologie médicale, Créteil, France; k CHU Tours, Hôpital Clocheville, Service d’oncologie et d’hématologie pédiatrique, Tours, France; l CHU Tours, Service d’Anatomie et de cytologie pathologiques, Tours, France; m Plateforme de Biologie Moléculaire, Département de Recherche Translationnelle, Institut Curie, Centre de Recherche, Paris, France; n APHP, Hôpital Bichat, Département de Pathologie, Paris, France; o Institut Curie, Département d’Oncologie Pédiatrique -Adolescents Jeunes Adultes, Paris, France

European Urology, Available online 1 October 2015, In Press, Corrected Proof
... DNA extracted from a formalin-fixed paraffin-embedded (FFPE) sample (INI137) was analyzed with an Oncoscan microarray (Affymetrix, ... Expression profiling on Affymetrix U133Plus v.2.0 ...

159- **Clear cell papillary renal cell carcinoma: A chromosomal microarray analysis of two cases using a novel Molecular Inversion Probe (MIP) technology**
Borislav A. Alexiev, Ying S. Zou
Chromosomal microarray analysis using novel Molecular Inversion Probe (MIP) technology demonstrated 2,570 kb copy neutral LOH of 10q11.22 in two clear cell papillary renal cell carcinomas ... this is the first study demonstrating copy neutral LOH of 10q11.22 in clear cell papillary renal cell carcinomas using the new MIP SNP Oncoscan FFPE Assay Kit on formalin-fixed paraffin-embedded tumor samples.

160- **Meeting abstract**

**Correlation of chromosome (Chr) 14 loss and 5q gain with outcomes of pazopanib treatment in patients (pts) with metastatic clear cell renal cell carcinoma (mRCC).**
Gary R. Hudes, Jianming Pei, Yuan Liu, Robert C. Gagnon, Christopher Carpenter, Lini Pandite, Joseph Testa
... Pts DNA samples from the Phase II (VEG102616) pazopanib trial were analyzed by using Affymetrix Oncoscan.
Eosinophilic, Solid, and Cystic Renal Cell Carcinoma: Clinicopathologic Study of 16 Unique, Sporadic Neoplasms Occurring in Women

Trpkov, Kiril; Hes, Ondrej; Bonert, Michael; Lopez, Jose I.; Bonsib, Stephen M.; Nesi, Gabriella; Comperat, Eva; Sibony, Mathilde; Berney, Daniel M.; Martinek, Petr; Bulimbasic, Stela; Suster, Saul; Sangoi, Ankur; Yilmaz, Asli; Higgins, John P.; Zhou, Ming; Gill, Anthony J.; Przybycin, Christopher G.; Magi-Galluzzi, Cristina; McKenney, Jesse K.

A unique renal neoplasm characterized by eosinophilic cytoplasm and solid and cystic growth was recently reported in patients with tuberous sclerosis complex (TSC). We searched multiple institutional archives and consult files in an attempt to identify a sporadic counterpart ... Although similar to a subset of renal cell carcinomas (RCCs) seen in TSC, we propose that sporadic “eosinophilic, solid, and cystic RCC,” which occurs predominantly in female individuals and is characterized by distinct morphologic features, predominant CK20-positive/CK7-negative immunophenotype, and indolent behavior, represents a novel subtype of RCC ... OncoScan molecular karyotyping was supported by Affymetrix Inc. and was performed at ARUP Laboratories.

162- **High-resolution genomic analysis suggests the absence of recurrent genomic alterations other than SMARCB1 aberrations in atypical teratoid/rhabdoid tumors.**
Genes Chromosomes Cancer. 2013 Feb, 52(2) : 185-90.
... To identify potential additional genetic alterations, high-resolution genome-wide analysis was performed using a molecular inversion probe single-nucleotide polymorphism (MIP SNP) assay (Affymetrix OncoScan formalin-fixed paraffin-embedded express) on DNA isolated from 18 formalin-fixed paraffin-embedded archival samples ... On MIP SNP screening for somatic mutations, the presence of a SMARCB1 mutation (c.472C>T p.R158X) was confirmed, but no recurrent mutations of other cancer relevant genes could be identified.

163- **Meeting abstract**
Molecular Inversion Probes for Detection of Copy Number Alterations and Loss of Heterozygosity in Renal Cell Carcinoma
Vaidehi Jobanputra, Odelia Nahum, Lesley E. Northop , Federico A. Monzon, Brynn Levy, CCMC QC committee
Cancer Genetics, May 2013, 206(5) : 212. [Abstracts, Cancer Cytogenomics Microarray Consortium / CA gdb meeting, Chicago, IL, August 5-7, 2013]
... The DNA specimens were processed with 250K Nsp SNP arrays and OncoScanTM FFPE Express platform (Affymetrix). Concordance for the CN and LOH for each sample was evaluated between arrays and the OncoScan calls. This pilot study validated the findings of the cytogenomic arrays and demonstrates the feasibility of using this technology to analyze RCC.

164- **Retrospective analysis of FFPE based Wilms’ Tumor samples through Copy Number and Somatic Mutation related Molecular Inversion Probe Based Array**
Neetu Singh, Dinesh K. Sahu, Madhumati Goel, Ravi Kant, Devendra K. Gupta
In this report, retrospectively, we analyzed fifteen histo-pathologically characterized FFPE based Wilms’ Tumor (WT) samples following an integrative approach of copy number (CN) and loss of heterozygosity (LOH) imbalances. The isolated-DNA was tested on CN and somatic-mutation related Molecular-Inversion-Probe based-Oncoscan Array™ and was analyzed through Nexus-Express OncoScan-3.0 and 7.0 software.........

165- **Meeting abstract**
THE THERAPEUTIC CHANGES OF ATYPICAL TERATOID/RHABDOID TUMOR IN MOLECULAR CHARACTERS
Mario Suzuki1, Akihide Kondo1, Ikuko Ogino1, Junya Fujimura2, Sachi Sakaguchi2, Masakazu Miyajima1 and Hajime Arai1
1Dept of Neurosurgery, Juntendo University School of Medicine, Tokyo, Japan ; 2Dept of Pediatrics, Hematology and Oncology, Juntendo University School of Medicine, Tokyo, Japan

Rhabdoid Tumor
BACKGROUND: Atypical teratoid/rhabdoid tumor (AT/RT) is a highly malignant tumor in early childhood. Though it is widely known that over 90% of tumors show loss of INI1 nuclear staining histologically, at this point comprehended molecular analysis of this tumor has not been done. In this report, we investigate the differences between primary tumor, recurrent tumor post induction chemotherapy, and the tumor post radiation therapy in the profiling of expression genes.

MATERIALS AND METHODS: We had 3 cases of AT/RT patients who had several surgical interventions. Using these tumor tissues, we investigated the changes between primary and recurrent tumors, histological and molecular biologically with a commercially utilized SNP array system. (OncoScan Assay Kit, Affymetrix) The data were analyzed with a commercially utilized software (Nexus Express Software).

RESULTS: We have made copy number analysis and mutation study in cancer specific genes. Several common changes in molecular sense can be seen after interventions, such as specific drug treatments and radiation therapy.

CONCLUSION: Our study may show how this tumor acquires the resistance to conventional therapies. Further study is needed to identify the malignant characters of this tumor.

Skeletal Muscle / Rhabdomyosarcoma

166- A recurrent neomorphic mutation in MYOD1 defines a clinically aggressive subset of embryonal rhabdomyosarcoma associated with PI3K-AKT pathway mutations

Shinji Kohsaka, Neerav Shukla, Nabahet Ameur, Tatsuuo Ito, Charlotte K Y Ng, Lu Wang, Diana Lim, Angela Marchetti, Agnes Viale, Mono Pirun, Nicholas D Socci, Li-Xuan Qin, Raf Sciort, Julia Bridge, Samuel Singer, Paul Meyers, Leonard H Wexler, Frederic G Barr, Snjezana Dogan, Jonathan A Fletcher, Jorge S Reis-Filho & Marc Ladanyi


... expression microarray analysis, RNA was processed at the Memorial Sloan Kettering Cancer Center ... Affymetrix GeneChip Human Genome U133 Plus 2.0 Array ... approximately 39,000 of the best-characterized human genes. The GeneChip Mouse Genome 430A 2.0 Array ... For OncoScan FFPE Assays, DNA was extracted ...

167- Preliminary analysis of the mutational landscape of non-rhabdomyosarcoma soft tissue sarcoma: A Children's Oncology Group study.

Raphael Asher Wilson, James Robert Anderson, Julie M Gastier-Foster, Douglas S. Hawkins, Sheri L. Spunt and Stephen Skapek

The University of Texas Southwestern Medical Center, Dallas, TX; College of Public Health, University of Nebraska Medical Center, Omaha, NE; Nationwide Children's Hospital, Columbus, OH; Seattle Children's Hospital, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA; St. Jude Children's Research Hospital, Memphis, TN

Journal of Clinical Oncology, 20 May 2014, 32(Suppl 15) : Abstr# 10510. [ASCO Annual Meeting]

Background: Pediatric non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) represent a histologically diverse group of more than 20 tumor subtypes, including synovial sarcoma, liposarcoma, and malignant peripheral nerve sheath tumors. Unlike children with rhabdomyosarcoma, systemic chemotherapy has failed to improve survival for those with NRSTS. Of the nearly 50% with intermediate or high-risk disease, only 50% and 15%, respectively, are expected to survive. Methods: To determine more effective, targeted therapies, we analyzed 55 archived formalin-fixed paraffin-embedded (FFPE) cases of NRSTS using Sequenom's MassARRAY system to interrogate 296 unique “actionable” mutations (mutations that can be targeted by currently available drugs) in 33 oncogenes and tumor suppressor genes. We also analyzed 15 of the samples for copy-number variation and 74 additional “actionable” mutations in 9 cancer-associated genes using the Affymetrix OncoScan platform. Results: Using MassARRAY, we found 11 mutations in 8 NRSTS subtypes. Interestingly, about half of these mutations are in genes involved in the Ras signaling pathway. We found an additional 33 potential mutations in 15 NRSTS subtypes, 28 of which are involved in Ras signaling; these mutations were detected at around 10% of the alleles present in a sample, the detection limit for MassARRAY, so they cannot be distinguished from background with certainty. Using OncoScan, we found that 67% and 73% of the samples contained mutations in EGFR and TP53, respectively, and 53% contained mutations in NRAS. 6 of the 15 samples contained between 1 and 5 large chromosomal gains or losses, while 2 of the samples had more than 10 large gains or losses. 3 recurrent gains were found in several of the samples, while 10 of the samples contained gains or losses in at least one gene. Conclusions: The rarity of the individual NRSTS subtypes has made it nearly impossible to determine the mutational profiles and optimal treatment for this group of tumors. With the ability to extract information from FFPE material using new genomic platforms, we have successfully grouped tumor subtypes and have identified actionable mutations guiding future directions.
Skin

Cutaneous basal cell carcinomas: evidence of clonality and recurrent chromosomal losses

... To our knowledge, copy number variations (CNVs) and copy-neutral loss of heterozygosity (CN-LOH) have not been investigated in cutaneous carcinomas. We analyzed four carcinomas with basal cell carcinoma (BCC) and osteosarcomatous components for CNVs/CN-LOH by comparative genomic hybridization/single-nucleotide polymorphism array, TP53 hotspot mutations by polymerase chain reaction and Sanger sequencing, and TP53 genomic rearrangements by fluorescence in situ hybridization ... For each tissue sample 80 ng of DNA was processed for analysis using the Oncoscan™ FFPE V3 kit (Affymetrix, Santa Clara, California) and hybridized on two GeneChip OncoScan Arrays ... our study is the first to examine copy number changes and clonality in basal cell carcinomas with osteosarcomatous differentiation.

169-

Human skin carcinoma arising from kidney transplant-derived tumor cells
Laurence Verneuil, Mariana Varna, Philippe Ratajczak, Christophe Leboeuf, Louis-François Plassa, Morad Elbouchtaoui, Pierre Schneider, Wissam Sandid, Celeste Lebbé, Marie-Noelle Peraldi, François Sigaux, Hugues de Thé, Anne Janin
Journal of Clinical Investigation, 3 Sep 2013, 123(9): 3797-3801.
... DNA from laser-microdissected p53+ tumor cells in skin SCC was studied using the molecular inversion probe-based genotyping system OncoScan Express (Affymetrix), which determines genotype of 330,000 SNPs.

Spleen

Well-differentiated angiosarcoma of spleen: a teaching case mimicking hemangioma and cytogenetic analysis with array comparative genomic hybridization
Lichen Xu†, Yimin Zhang†, Hong Zhao, Qingxiao Chen, Weihang Ma and Lanjuan Li
... this is the first time analyzed cytogenetic alteration in a well-differentiated primary splenic angiosarcoma ... we applied Affymetrix Onco-Scan™ FFPE Express molecular inversion probe microarray platform to analyze the chromosome abnormal ...

Squamous Cell Carcinoma

Recurrent point mutations in the kinetochore gene KNSTRN in cutaneous squamous cell carcinoma
... Affymetrix OncoScan arrays were used to interrogate genomic DNA and identify chromosomal gains and losses in each sample ... Genomic DNA purified from ten fresh primary SCCs was interrogated using Affymetrix OncoScan arrays (v3) ...

Synovial Sarcoma

Next generation sequencing in synovial sarcoma reveals novel gene mutations.
Oncotarget, 22 September 2015, 6(33): 34680-34690.
... Copy number variation was assessed in six tumors using the Oncoscan array (Affymetrix, USA).
Thoracic Neoplasms

SMARCA4 inactivation defines a group of undifferentiated thoracic malignancies transcriptionally related to BAF-deficient sarcomas


Nature Genetics, online 7 Sep 2015, 47:1200–1205 doi:10.1038/ng.3399

... OncoScan SNP profiling. Molecular inversion probes were hybridized to 80 ng of genomic DNA from formalin-fixed, paraffin-embedded samples ...

Thyroid

Germline ESR2 Mutation Predisposes to Medullary Thyroid Carcinoma and Causes Up-Regulation of RET Expression


1Centre for Rare Diseases and Personalised Medicine, University of Birmingham, Birmingham B15 2TT, UK; 2School of Clinical and Experimental Medicine, University of Birmingham, B15 2TT, UK; 3West Midlands Regional Genetics Service, Birmingham Women's Hospital, Birmingham B15 2TG, UK; 4Queen Elizabeth Hospital, Queen Elizabeth Medical Centre, Birmingham B15 2TH, UK; 5West Midlands Regional Genetics Laboratory, Birmingham Women's Hospital, Birmingham B15 2TG, UK; 6Human Biomaterials Resource Centre, College of Medical and Dental Sciences, University of Birmingham, Birmingham B15 2TT, UK; 7School of Endocrine Surgery, Belfast Health and Social Care Trust, Royal Victoria Hospital, Belfast, Northern Ireland, UK; 8Cancer Genetics, Level 9, Kolling Building and Endocrine Surgical Unit, Royal North Shore Hospital, University of Sydney, Pacific Highway, St. Leonards, NSW, 2065, Australia; 9Division of Cancer Biology and Genetics, Cancer Research Institute, Queen's University, Canada; 10Centre for Cancer Research and Cell Biology, Queen's University of Belfast, 97 Lisburn Road, Belfast BT9 7AE; 11Hereditary Endocrine Cancer Group, Spanish National Cancer Research Centre (CNIO), Madrid, Spain and Centro de Investigación Biomédica en Red de Enfermedades Raras, Madrid, Spain; 12Division of Genetics and Molecular Medicine, King's College London School of Medicine, Guy's Hospital, London, UK; 13Queen Mary University of London, Barts and The London School of Medicine and Dentistry, London, UK; 14Dept of Medical Genetics, University of Cambridge and NIHR Cambridge Biomedical Research Centre, Cambridge, UK; 15Manchester Centre for Genomic Medicine, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Sciences Centre (MAHSC), Manchester M13 9WL, UK.

Human Molecular Genetics, online 3 Mrch 2016; doi: 10.1038/hmg/ddw057

Familial medullary thyroid cancer (MTC) and its precursor, C cell hyperplasia (CCH), is associated with germline RET mutations causing multiple endocrine neoplasia type 2. However, some rare families with apparent MTC/CCH predisposition do not have a detectable RET mutation. To identify novel MTC/CCH predisposition genes we undertook exome resequencing studies in a family with apparent predisposition to MTC/CCH and no identifiable RET mutation. We identified a novel ESR2 frameshift mutation, c.948delT, which segregated with histological diagnosis following thyroid surgery in family members and demonstrated loss of ESR2 encoded ERβ expression in the MTC tumour. ERα and ERβ form heterodimers binding DNA at specific estrogen response elements (ERE) to regulate gene transcription. ERβ represses ERα mediated activation of the ERE and the RET promoter contains three ERE. In vivo, immunostaining of CCH and MTC using an anti-RET antibody demonstrated increased RET expression. Together these findings identify germline ESR2 mutation as a novel cause of familial MTC/CCH and provide important insights into a novel mechanism causing increased RET expression in tumourigenesis.

Excerpt: ... The OncoScan® FFPE assay kit platform was utilized to identify whole-genome copy number ...

Uterus / Endometrial

Genomic Aberrations of BRCA1-Mutated Fallopian Tube Carcinomas
Sally M. Hunter, Georgina L. Ryland, Phillip Moss, kConFab Investigators, Kylie L. Gorringe, Ian G. Campbell


... Copy number data were generated using the OncoScan 2.0 service (Affymetrix Inc.), ... that allows the detection of genome-wide, allele-specific copy number and also provides mutation-specific probe information ...

176- **Molecular characteristics of endometrial cancer coexisting with peritoneal malignant mesothelioma in Li-Fraumeni-like syndrome**

Angel Chao1, Chyong-Huey Lai1, Yun-Shien Lee2,3, Shir-Hwa Ueng4, Chiao-Yun Lin1, Tzu-Hao Wang1,2*

1 Dept of Obstetrics and Gynecology, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan; 2 Genomic Medicine Research Core Laboratory, Chang Gung Memorial Hospital, Taoyuan, Taiwan; 3 Dept of Biotechnology, Ming-Chuan University, Taoyuan, Taiwan; 4 Dept of Pathology, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan

BMC Cancer, 15 January 2015, 15:8

Background Endometrial cancer that occurs concurrently with peritoneal malignant mesothelioma (PMM) is difficult to diagnose preoperatively. Case presentation A postmenopausal woman had endometrial cancer extending to the cervix, vagina and pelvic lymph nodes, and PMM in bilateral ovaries, cul-de-sac, and multiple peritoneal sites. Adjuvant therapies included chemotherapy and radiotherapy. Targeted, massively parallel DNA sequencing and molecular inversion probe microarray analysis revealed a germline TP53 mutation compatible with Li-Fraumeni-like syndrome, somatic mutations of PIK3CA in the endometrial cancer, and a somatic mutation of GNA11 and JAK3 in the PMM...

Genomic profiling of tumor tissues was done with MIP-based microarray analysis (Oncoscan, Affymetrix).

177- **Poster presentation**

**Monosomy 14 in a subgroup of primary uterine leiomyosarcomas**

Carsten Holzmann, Dominique Markowski, Dirk Koczan, Thomas Löning and Jörn Bullerdiek

Institute for Medical Genetics, University Rostock Medical Center


... A total of nine tumors were investigated by copy number variation arrays. In all cases, histology examination had revealed a smooth muscle origin of the lesions different from ordinary leiomyomas. DNA from FFPE samples was isolated using the QIAamp DNA Mini Kit and the amount of double stranded DNA was measured using the Qubit dsDNA HS Assay Kit. For the OncoScan FFPE Assay based on Molecular Inversion Probe (MIP) technology, 80 ng dsDNA was labelled and hybridized using a GeneChip Fluidics Station 450 .............

178- **Patterns of Chromosomal Abnormalities that Can Improve Diagnosis of Uterine Smooth Muscle Tumors**

CARSTEN HOLZMANN1, DOMINIQUE NADINE MARKOWSKI2, INGO VON LEFFERN3, THOMAS LÖNING4 and JÖRN BULLERDIEK1,2

1 Institute of Medical Genetics, University Rostock Medical Center, Rostock, Germany; 2 Center of Human Genetics, University of Bremen, Bremen, Germany; 3 Albertinen-Hospital, Gynecological Clinics, Gynecology and Obstetrics Department, Hamburg, Germany; 4 Albertinen-Hospital, Institute of Pathology, Hamburg, Germany


Background/Aim: Compared to leiomyomas, smooth muscle tumors of uncertain malignant potential (STUMP), and leiomyosarcomas (LMS) originating from the Muellerian duct are very rare. Their molecular pathogenesis remains poorly understood. The present article aims at performing genetic analyses of these tumors that may help assist histopathological examination. Materials and Methods: Ten tumors (four STUMP and six LMS) were investigated by copy number arrays ......The OncoScan FFPE Assay (Affymetrix, ...) offers the detection of genome-wide copy number and copy-neutral LOH.

179- **Hyperhaploid uterine mesenchymal tumors - a novel genetic subgroup?**

Carsten Holzmann a, Thomas Löning b, Jörn Bullerdiek a, c, *

a Institute of Medical Genetics, University Rostock Medical Center, Rostock, Germany; b Pathology Dept, Albertinen-Hospital, Hamburg, Germany; c Center of Human Genetics, University of Bremen, Bremen, Germany.

Cancer Genetics, Available online 8 March 2016, In Press, Accepted Manuscript
Hyperhaploid karyotypes have been described to occur in subsets of various solid tumors and leukemias. In these cases, monosomy is noted for most of the chromosomes while a few chromosomes still remain disomic. Evidence has emerged that at least in some tumor entities these remaining chromosomes are non-randomly selected. In addition, structural alterations can accompany the reduced chromosome number and secondary duplication of the chromosome complement is also a frequent finding. In this report, we describe hyperhaploidy in a case of an endometrial stromal nodule of a 50 year old woman who underwent hysterectomy because of symptomatic uterine fibroids. In addition, we review two other recently described cases of uterine mesenchymal tumors with that type of genetic alteration. Despite some histologic differences, striking similarities between these three cases exist with respect to the chromosomes were retained as disomic. Thus, the question arises if hyperhaploidy defines a novel genetic subgroup of uterine mesenchymal tumors.

Excerpt: … The OncoScan FFPE Assay (Affymetrix, Santa Clara, CA) results in a 300-kb genome-wide copy number resolution and an enhanced copy number resolution of 50-100 kb in ~900 cancer genes.

180- 
**Burkitt Lymphoma**

*Genome wide copy number analysis of paediatric Burkitt lymphoma using formalin-fixed tissues reveals a subset with gain of chromosome 13q and corresponding miRNA over expression.*


… DNA was quantitated with PicoGreen (Invitrogen, Carlsbad, CA, USA) and submitted for OncoScan FFPE Express (Affymetrix, Santa Clara, CA, USA), a MIP SNP assay, performed at Affymetrix (Wang et al, 2005, 2007; Schiffman et al, 2009, 2010). …

181- 
**TP53 pathway analysis in paediatric Burkitt lymphoma reveals increased MDM4 expression as the only TP53 pathway abnormality detected in a subset of cases.**


… Thus, a total of 25 cases were analysed by qRT-PCR. Molecular inversion probe assay. Genomic DNA was submitted to Affymetrix for the Oncoscan FFPE Express™ molecular inversion probe (MIP) assay.

182- 
**High-resolution genomic analysis suggests the absence of recurrent genomic alterations other than SMARCB1 aberrations in atypical teratoid/rhabdoid tumors.**


… To identify potential additional genetic alterations, high-resolution genome-wide analysis was performed using a molecular inversion probe single-nucleotide polymorphism (MIP SNP) assay (Affymetrix OncoScan formalin-fixed paraffin-embedded express) on DNA isolated from 18 formalin-fixed paraffin-embedded archival samples … On MIP SNP screening for somatic mutations, the presence of a SMARCB1 mutation (c.472C>T p.R158X) was confirmed, but no recurrent mutations of other cancer relevant genes could be identified.
**Methods / Evaluation / Validation**

183- **Meeting abstract**

A high-throughput allelic copy-number and somatic mutation platform utilizing a 75-ng DNA input in a 330,000 Molecular Inversion Probes (MIP) assay with FFPE samples

Yuker Wang, Ron Sapolsky, Sumathi Venkatapathy, Farooq Siddiqui, Fan Shen.

AACR 2011, Apr 06, 2011, Abstr #4868.

... Using only 75 ng of genomic DNA input, we have obtained both good genotyping and CN data, which is offered as a service-only product under the name “Oncoscan FFPE Express” by Affymetrix. For FFPE samples, good concordance between normal and tumor sample pairs is also observed.

184- **Meeting abstract**

A New Method for High Fidelity Copy Number Analysis in Solid Tumor Samples and its implementation in the OncoScan™ FFPE Assay Kit.


Copy number analysis in tumors is rapidly gaining importance in cancer therapy as a tool for differential diagnosis with impact on potential treatment, [1]. Although formalin fixed paraffin embedded (FFPE) blocks are common sources of material for both research and clinical diagnostics, DNA degradation in FFPE presents a major challenge for accurate measurement of copy number. We address this challenge using molecular inversion probes, which capture the alleles of over 220,000 SNPs at carefully selected genomic locations, evenly distributed across the genome and with increased density within ~900 cancer-related genes. Additionally, we created a reference that establishes the baseline response for a normal copy number state at each locus. This reference was generated by assessing the probe-by-probe response in 400 normal FFPE samples from over 20 sources covering a broad range of geographic locations, block ages, gender and tissue of origin. Another challenge of FFPE samples is the presence of normal cells in most biopsy samples, which affects copy number estimates. To address this problem of variable tumor burden, we developed TuScan™, an algorithm inspired by ASCAT [2], to estimate the integer copy number in the tumor at each locus. When a major clone is responsible for the majority of copy number changes, the algorithm estimates the tumor burden in the sample and reports the integer copy number in the cancer portion only, effectively subtracting the normal component, thereby enabling a comparison between samples with different tumor burden. For highly heterogeneous samples or very low tumor burden, the algorithm reports the fractional (average) copy number of all cells within the sample. To validate the method, 28 FFPE tumors which included copy number events previously determined by FISH were titrated at various percentages (80%, 70%, 60%, 40%) with their matched normal and were analyzed for copy number changes using the TuScan™ algorithm. Given that the algorithm computes copy number states in the tumor portion, the same copy number state should be reported at each locus for each of the titration levels. Over 90% of aberrant markers had concordant copy number states across titration points for 26/28 samples. For two tumor samples the algorithms were not able to determine a tumor burden for the lower titration levels.

185- **Meeting abstract**

A New Molecular Inversion Probe (MIP) Based and Cancer-focused Whole-genome Copy Number Platform Requires Only 75 Ng of Input DNA From FFPE Samples

Y. Wang, R. Sapolsky, S. Venkatapathy, G. Stengel, A. Estabrook, A. Shukla, P. Weaver, W. Wu, V. Huynh, L. Greenfield

EACR-22, Abst #559. [22nd Biennial Congress, Eur Assoc Cancer Res, 7-10 July 2012, Barcelona, Spain]

... The OncoScan™ FFPE Express 2.0 deliver three types of data (SNP, CN, and somatic mutation) from just 75 ng non-amplified genomic DNA .. The content of the OncoScan™ platform was expanded to include 200genes of high value in cancer research and diagnosis. The platform was shown to work well on both frozen and archival FFPE samples. SNP, CN, and somatic mutations can be interrogated by the same assay, offering an unprecedented opportunity for both retrospective studies where only FFPE samples are available and for ongoing clinical research where only tiny amounts of biopsy are accessible.
Analytical Validation of Chromosomal Microarray Analysis with Solid Tumor FFPE Specimens
Joel A. Lefferts, Scott A. Turner, Emmeline Z. Liu, Elizabeth I. Reader, Konstantinos Linos, Laura J. Tafe, Gregory J. Tsongalis
Pathology Dept, Geisel School of Medicine, Hanover, NH; Dartmouth Hitchcock Medical Center and Norris Cotton Cancer Center, Lebanon, NH.

Chromosomal microarray analysis (CMA) is widely used in the constitutional setting, making samples for validation studies readily available. Validation of solid tumor CMA using formalin fixed, paraffin-embedded (FFPE) tissue derived DNA presents unique challenges. Validation samples can be difficult to obtain due to limited numbers of laboratories performing this type of testing and lower DNA yields from FFPE tissue. Additionally, use of DNA or tissue samples from other laboratories may not be ideal because of inter-laboratory differences in FFPE DNA extraction methods and tissue processing. Focusing on gliomas and dermatology specimens, we describe a strategy used in our laboratory to validate the OncoScan FFPE Assay Kit (Affymetrix) using specimens from our internal tissue archive. DNA was extracted from 16 glioma and 7 melanocytic lesions using modified protocols of the Gentra Puregene Tissue kit (QIAGEN) or QIAamp FFPE Tissue kit (QIAGEN). Select tissue specimens were extracted using both methods. DNA was subjected to CMA analysis using the OncoScan FFPE Assay kit (Affymetrix) according to the manufacturer’s protocol. CMA results were compared with previous 1p/19q FISH results (gliomas) or a combination of traditional histopathology, immunohistochemistry, and CMA testing in a reference laboratory (dermatopathology). CMA results from all 16 glioma samples were concordant with respect to 1p/19q co-deletion status (6 positive, 10 negative for the co-deletion) with additional concordance for other gains and losses involving chromosomes 1 and 19. All 7 melanocytic lesions were concordant with previous CMA (n = 2), BAP-1 immunohistochemistry (3p loss; n = 2), or histopathology (n = 3).

Biomarker evaluation in phase I clinical trials of selective PI3K and PI3K/mTOR inhibitors
Jill Spoerke, Carol O’Brien, Yibing Yan, Mark R. Lackner.
AACR Annual Meeting 2012, Tuesday, Apr 03, 2012, Abst #4821.

... Select samples were analyzed for an expanded mutation panel and genome-wide copy number alterations using the Oncoscan platform (Affymetrix).

Cell-free DNA derived from ascites: Detection of copy number and somatic mutations using OncoScan FFPE® Assay
Hatim Husain1, Sumathi Venkatapathy2, German Gomez1, Brian Woodward1, Suzanna Lee1, Lubena Khambay1, Lily Chen2, Radha Duttanga2, Eric T. Fung2, and Razelle Kurzrock1
1Center for Personalized Cancer Therapy, Univ of California San Diego, Moores Cancer Center, La Jolla, CA; 2Affymetrix, Santa Clara, CA.

... Eleven ascites samples from patients with metastatic epithelial neoplasms (gastric, N = 3; pancreas, N = 3; ovarian, N = 2; breast, N = 2; and lung cancer, N = 1) were investigated. Cell-free DNA was isolated from supernatant of ascites fluid (50 ml) after centrifugation using commercially available DNA purification kits (Norgen Biotek Corp and Qiagen), and analyzed using the OncoScan FFPE Assay kit. ...

CGH arrays compared for DNA isolated from formalin-fixed, paraffin-embedded material
Oscar Krijgsman, Danielle Israeli, Josien C. Haan, Hendrik F. van Essen, Serge J. Smeets, Paul P. Eijk, Renske D. M. Steenbergen, Klaas Kok, Sabine Teijpar, Gerrit A. Meijer, Bauke Ylstra

... in situ synthesized oligonucleotides evenly distributed over the genome (space ~17 kb) and 4,548 additional unique oligonucleotides, covering 238 of the Cancer Census genes (4x180k array, Agilent Technologies, Palo Alto, CA); and (C) Affymetrix OncoScan FFPE chip ...
Clinical massively parallel next-generation sequencing analysis of 409 cancer-related genes for mutations and copy number variations in solid tumours


... Gene copy number variations ... confirmed by molecular inversion probe (MIP) array ... using the OncoScan FFPE assay kit (Affymetrix ...}

Meeting abstract

Clinical translation pathway to Precision Medicine in GBM through simulation and repurposing.

Sandeep C. Pingle, Pengfei Jiang, Rajesh Mukhavaram, Natsuko Nomura, Prashant Nair, Ansu Kumar, Neeraj Singh, Taher Abbasi, Shireen Vali and Santosh Kesari

UC San Diego Moores Cancer Center, La Jolla, CA; UC San Diego, La Jolla, CA; Cellworks Research India Ltd, Bangalore, India; Cellworks Research India Ltd., Bangalore, India; CellWorks Group, Bangalore, India; CellWorks Group Inc., San Jose, CA; Cellworks Group, San Jose, CA


To create simulation avatars of patient-derived GBM tumors, we used copy number, expression, and mutation data (OncoScan, Human Transcripome Array - Affymetrix) ............

Comparative Genomic Hybridization and Array Based CGH in Cancer [Chapter 3]

Roland Hubaux Ph.D., Victor D. Martinez Ph.D., David Rowbotham B.SC., Wan L. Lam Ph.D.

Molecular Testing in Cancer, editors George M. Yousef, Serge Jothy. Springer, NY, 2014. Pages 27-37. ...

Cross-laboratory validation of the OncoScan® FFPE Assay, a multiplex tool for whole genome tumour profiling

Joseph M Foster1*, Assa Oumie1, Fiona S Togneri4, Fabiana Ramos Vasques4, Debra Hau4, Morag Taylor2, Emma Tinkler-Hundal2, Katie Southward2, Paul Medlow3, Keith McGreeghan-Crosby3, Iris Halfpenny3, Dominic J McMullan4, Phil Quirke2, Katherine E Keating3, Mike Griffiths4, Karen G Spink1 and Fiona Brew1

1 Affymetrix UK Ltd, High Wycombe, UK; 2 Leeds Institute of Cancer and Pathology, Section of Tumour Biology and Pathology, Leeds University, Leeds, UK; 3 Almac Diagnostics, Craigavon, Northern Ireland, UK; 4 West Midlands Regional Genetics Laboratory, Birmingham, UK


Background--Adoption of new technology in both basic research and clinical settings requires rigorous validation of analytical performance. The OncoScan® FFPE Assay is a multiplexing tool that offers genome-wide copy number and loss of heterozygosity detection, as well as identification of frequently tested somatic mutations. Methods--In this study, 162 formalin fixed paraffin embedded samples, representing six different tumour types, were profiled in triplicate across three independent laboratories. OncoScan® formalin fixed paraffin embedded assay data was then analysed for reproducibility of genome-wide copy number, loss of heterozygosity and somatic mutations. Where available, somatic mutation data was compared to data from orthogonal technologies (pyro/sanger sequencing).

Results--Cross site comparisons of genome-wide copy number and loss of heterozygosity profiles showed greater than 95% average agreement between sites. Somatic mutations pre-validated by orthogonal technologies showed greater than 90% agreement with OncoScan® somatic mutation calls and somatic mutation concordance between sites averaged 97%. Conclusions--Reproducibility of whole-genome copy number, loss of heterozygosity and somatic mutation data using the OncoScan® assay has been demonstrated with comparatively low DNA inputs from a range of highly degraded formalin fixed paraffin embedded samples. In addition, our data shows examples of clinically-relevant aberrations that demonstrate the potential utility of the OncoScan® assay as a robust clinical tool for guiding tumour therapy.
194- Meeting abstract
Cross-site reproducibility and orthogonal validation of copy number and somatic mutation calls of OncoScan® FFPE Assay Kit in solid tumors
Joseph M. Foster1, Assa Oumie1, Fiona S. Togneri2, Morag Taylor3, Sofia Alyas2, Paula Wojtowicz2, Henry Wood3, Emma Tinker-Hundal3, Katie Southward3, Dominic McMullan2, Phil Quirke3, Katherine E. Keating4, Mike Griffiths2, Karen G. Spink1, Fiona Brew1, Eric Fung5, and Jeanette Schmidt5
1Affymetrix UK Ltd, Wooburn Green, UK; 2West Midlands Regional Genetics Laboratory, Birmingham, UK; 3Leeds Institute of Cancer and Pathology, Leeds, uk; 4Almac Diagnostics, Craigavon, UK; 5Affymetrix, Santa Clara, CA.
Cancer Res 2015;75(15 Suppl):Abstract # 626. [AACR 106th Annual Mtg 2015; Apr 18-22, 2015]
Objectives--Copy number (CN) and somatic mutation (SM) analysis in tumors is rapidly gaining importance in cancer management as a tool for differential diagnosis, determination of prognosis, and selection of therapeutic. Genome-wide copy number and LOH detection as well as a panel of frequently tested somatic mutations can be detected with OncoScan® FFPE Assay Kit. We report on a validation study of OncoScan FFPE Assay Kit CN and SM data by orthogonal technologies (FISH and NGS, respectively) to estimate the sensitivity and specificity parameters of the platform. … Conclusion--In this study we validated both CN and SM calls using OncoScan FFPE Assay Kit and demonstrated a high degree of agreement with orthogonal methods in all aspects. Reproducibility of whole-genome CN, LOH, and SM data using OncoScan Assay Kit has also been demonstrated for a range of FFPE samples, including highly degraded samples. This study is a step forward in evaluating the potential clinical utility of a platform combining genome-wide copy number and somatic mutation calls within the national health service of the UK.

195- Evaluating the repair of DNA derived from formalin-fixed paraffin-embedded tissues prior to genomic profiling by SNP-CGH analysis
Abdel Nasser Hosein, Sarah Song, Amy E McCart Reed, Janani Jayanthan, Lynne E Reid, Jamie R Kutascovic, Margaret C Cummings, Nic Waddell, Sunil R Lakhani, Georgia Chenevix-Trench, Peter T Simpson
Laboratory Investigation, June 2013, 93:701-710.
… The recently developed Oncoscan FFPE platform (Affymetrix), a high-resolution SNP array based on molecular inversion probes, appears to perform well in comparison with aCGH platforms and so might prove to be a successful method for studying FFPE samples for CNAs.23,24

196- Meeting abstract
Evaluation of the Affymetrix OncoScan Genome-Wide SNP-Array Analysis Platform for Solid Tumor Molecular Diagnosis
Memorial Sloan Kettering Cancer Center, New York, NY.
… We present here our experience with OncoScan SNP-array analysis of DNA copy number changes and copy neutral loss of heterozygosity (CN-LOH) in solid tumors, which performs well in comparison to array CGH (aCGH) platforms but requires less input DNA and is less sensitive to DNA quality. …Our study also revealed highly consistent findings between Agilent aCGH and Affymetrix OncoScan analysis but the latter demonstrated higher sensitivity in the detection of minor abnormal clones as verified by FISH analysis (Technical sensitivity of OncoScan=25% established empirically) ……………………………………………………….We demonstrated that high-quality SNP-array data can be generated on the Affymetrix OncoScan platform from both FF- and FFPE DNAs with an input of only 80ng. OncoScan analysis provides a fast turnaround time and robust data analysis for genome-wide CN and CN-LOH analyses in clinical diagnosis.
197- **FACETS: Fraction and Allele-Specific Copy Number Estimates from Tumor Sequencing**  
Ronglai Shen1, Venkatraman Seshan1  
1Memorial Sloan-Kettering Cancer Center  
Follow  
Memorial Sloan-Kettering Cancer Center, Dept. of Epidemiology & Biostatistics Working Paper Series.  
http://biostats.bepress.com/mskccbiostat/paper29  
... To facilitate intratumor heterogeneity analysis, we developed a unified analysis pipeline called FACETS for DNA sequencing of tumor-normal pairs (including whole-exome, whole-genome, and targeted capture sequencing), to 1) perform joint segmentation of total and allelic copy ratio, and to 2) estimate tumor purity, ploidy, allele-specific copy number and associated cell fraction profile ... The most representative analysis workflow used in many intratumor heterogeneity studies involves first obtaining tumor sample purity estimate (eg, ABSOLUTE (8) or similar algorithm), copy number states (estimated from SNP6 or OncoScan platform using ASCAT (13) ...  

198- **FYI, brief comment only**  
**Genomic Aberrations in Myeloid Sarcoma without Blood or Bone Marrow Involvement: Characterization of Formalin-Fixed Paraffin-Embedded Samples by Chromosomal Microarrays**  
Leukemia Research, Sep 2014, 38(9) :1091-1096.  
... However, a specialized array technology has recently been developed for FFPE samples (OncoScan™, Affymetrix, Santa Clara, CA) [13]. Further study will be required to determine its utility in the evaluation of MS samples....  

199- **Massively parallel DNA sequencing from routinely processed cytological smears**  
Laure Piqueret-Stephan MSc1,2, Charles Marcailou MSc3, Cécile Reyes MSc4, Aurélie Honoré MSc5, Mélanie Letexier MSc3, David Gentien MSc4, Nathalie Droin PhD1,6, Ludovic Lacroix PharmD5,7, Jean-Yves Scoazec MD, PhD5,7 and Philippe Vielh MD, PhD1,2,5,7,*  
1Gustave Roussy, Villejuif, France; 2Unité Mixte de Recherche 981, INSERM, Villejuif, France; 3Genopole Campus 1, IntegraGen SA, Evry, France; 4Genomic Platform, Translational Research Dept, Institut Curie, Paris, France; 5Analyse Moléculaire, Modélisation et Imagerie de la maladie Cancéreuse (AMMICa) CNRS Unité Mixte de Service 3655, INSERM US23, Paris Sud University), Translational Research Laboratory, Gustave Roussy, Villejuif, France; 6Unit 1009, INSERM, Villejuif, France; 7Dept of Biopathology, Gustave Roussy, Villejuif, France  
Cancer Cytopathology, Article first published online: 27 October 2015  
... Genomic profiling (copy number, gains, loss, and loss of heterozygosity) was performed by means of the Affymetrix OncoScan assay according to the supplier's recommendations (Affymetrix FFPE assay kit, reference 902293).  

200- **Microarrays-Based Molecular Profiling to Identify Genomic Alterations** [Chapter 4]  
David Gentien, Cecile Reyes  
Pan-cancer Integrative Molecular Portrait Towards a New Paradigm in Precision Medicine, editors Christophe Le Tournneau and Maud Kamal, Springer Intl Publishing, Switzerland : 2015. pp 31-45. ...  
Description of the MIP Affymetrix assay used to hybridize OncoScan arrays.  

201- **Molecular Genetics Methods in Discovery of Chromosome Structure** [Chapter 2]  
Donna G. Albertson  
A variety of molecular and cytogenetic techniques, differing in resolution and capabilities for high throughput or single cell analysis, for example, have been used to investigate the altered state of tumour genomes. Some of these methods have become the mainstay of clinical cancer diagnosis and patient management ... Available as the Oncoscans FFPE Assay from Affymetrix, Inc., the technology can be used to detect selected cancer relevant single nucleotide mutations and measures copy number and LOH with 300 kb resolution from small amounts of DNA extracted from frozen or FFPE ...
202- Meeting abstract
OncoScan™ FFPE Express 2.0: a cancer-focused whole-genome copy number platform requiring only 75 ng of input DNA from FFPE samples
Yuker Wang, Ron Sapolsky, Sumathi Venkatapathy, Farooq Siddiqui, Fan Shen, Rong Jiang.

... The OncoScan™ FFPE Express 2.0 platform is able to deliver three types of high-quality data (SNP, CN, and somatic mutation calls) from just 75 ng non-amplified genomic DNA ... We have developed a powerful new version of the OncoScan™ platform that works well on both frozen and archival FFPE samples. All three types of mutation analysis (SNP, CN, and somatic mutations) can be interrogated by the same assay, offering an unprecedented opportunity for both retrospective studies where only FFPE samples are available and for ongoing clinical research where only small amounts of biopsy sample are accessible.

203- Resistance to HSP90 inhibition involving loss of MCL1 addiction
S Busacca1, E W P Law1, I R Powley2, D A Proia3, M Sequeira3, J Le Quesne1,2, A Klabatsa4, J M Edwards2, K B Matchett5, J L Luo1, J H Pringle1, M El-Tanani6, M MacFarlane2 and D A Fennell1
1Dept of Cancer Studies, Cancer Research UK Leicester Centre, University of Leicester, Leicester, UK; 2MRC Toxicology Unit, Leicester, UK; 3Synta Pharmaceuticals Corp., Lexington, MA, USA; 4Div of Cancer Studies, King’s College London, London, UK; 5Centre for Cancer Research and Cell Biology, Queen’s Univ Belfast, Belfast, UK; 6Institute of Cancer Therapeutics, School of Life Sciences, Univ of Bradford, Bradford, UK.
Oncogene advance online publication 22 June 2015; doi: 10.1038/onc.2015.213

... 80 ng of gDNA was analysed using the OncoScan FFPE Assay Kit (Affymetrix, Wooburn Green High Wycombe, UK).

204- SeqControl: process control for DNA sequencing
Lauren C Chong, Marco A Albuquerque, Nicholas J Harding, Cristian Caloian, Michelle Chan-Seng-Yue, Richard de Borja, Michael Fraser, Robert E Denroche, Timothy A Beck, Theodorus van der Kwast, Robert G Bristow, John D McPherson & Paul C Boutros

... tumor samples, we hybridized an aliquot of DNA from each sample to an OncoScan Affymetrix microarray.

205- Meeting abstract
Somatic Copy Number Assessment in Tumors Based on Amplicon Coverage in a Targeted NGS Panel
J.A. Lefferts1,2, J.D. Peterson1,2, S.A. Turner1, F.B. de Abreu1, L.J. Tafe1, G.J. Tsongalis1
1Dartmouth-Hitchcock Medical Center, Lebanon, NH; 2Geisel School of Medicine at Dartmouth, Hanover, NH.

... Samples with predicted copy number changes were subjected to OncoScan FFPE Assay (Affymetrix) and/or FISH for confirmation. Results: Copy number gains (gene amplifications) and/or losses (likely homozygous deletions) of genes included in the 50 gene NGS panel were predicted in 10/50 (20%) of samples included in this analysis. Six of these samples with DNA isolated from tissue with >50% tumor content and at least 80 ng available were selected for confirmation with OncoScan. ... Conclusions: Amplicon-based NGS panels such as CHPv2 that are designed to detect point mutations and small insertions and deletions may also be used to detect larger somatic copy number changes such as amplifications and homozygous deletions spanning one or several genes. Additional validation would be required before introducing this type of analysis in routine clinical testing.

206- Streamlining the OncoScan® Array Procedure for Use in a Clinical Laboratory.
Paxton CN1, Rowe LR1, South ST1.
1ARUP Institute for Clinical and Experimental Pathology®, Salt Lake City, UT.

... The objective of this study was to identify steps in the OncoScan procedure that could be modified to make the process more efficient and technician-friendly in the clinical laboratory setting. Eighteen samples ... were reprocessed using a modified protocol. The two primary modifications to the protocol included the elimination of a brief "chill and spin" step and an adjustment to the overnight hybridization temperature to allow for simultaneous hybridization of OncoScan and CytoScan® arrays.
This chapter will focus on important considerations and parameters of capture-based targeting methods, describe the most widely used target capture-based strategies in clinical testing, compare target-based capture to amplification-based capture, and illustrate general clinical applications. The OncoScan FFPE Express 2.0 Service launched in the spring of 2011 interrogates greater than 335,000 loci over the entire genome for somatic changes, copy number changes, and LOH. Affymetrix also provides the DMET (Drug Metabolizing Enzymes and Transport) Plus Assay.

Telomeric Allelic Imbalance Indicates Defective DNA Repair and Sensitivity to DNA-Damaging Agents

Nicolai J. Birkbak, Zhigang C. Wang, Ji-Young Kim, Aron C. Eklund, Qiyuan Li, Ruiyang Tian, Christian Bowman-Colin, Yang Li, April Greene-Colozzi, J. Dirk Iglehart, Nadine Tung, Paula D. Ryan, Judy E. Garber, Daniel P. Silver, Zoltan Szallasi, Andrea L. Richardson

Cancer Discovery, April 2012, 2: 366

DNA was sent to Affymetrix, Inc. for determination of genotypes via use of the molecular inversion probe-based genotyping system, OncoScan FFPE Express (43).

The Clinical Validation of Chromosomal Genomic Array Testing in Formalin-Fixed, Paraffin-Embedded Solid Tumor Tissues (FFPE-CGAT)

X. Qu, P.S. Laurent, M.S. Tretiakova, T. Antic, S. Tykodi, M. Fang


FFPE-CGAT was performed using the OncoScan FFPE assay kit (Affymetrix, CA), which utilizes the molecular inversion probe (MIP) technology.

Universal probe amplification: Multiplex screening technologies for genetic variations [open access]

Jung Hun Park, Ki Soo Park, Kyungmee Lee, Hyowon Jang and Hyun Gyu Park*

Biotechnology Journal [Special Issue: Biotech Methods and Advances], January 2015, 10(1): 45-55.

DNA microarray-based MIP assay was the basis for the high-throughput SNP genotyping of the human genome. Hardenbol et al. first described the genotyping of 1, 121 SNP sites using the MIP method on human chromosome 6 for IgA nephropathy [10]. The Affymetrix Company have commercialized a DNA microarray platform for MIP assays known as Genechip tag arrays. Furthermore, Affymetrix successfully developed ‘OncoScan FFPE Express Service’ to analyze genetic variations from degraded or low concentrations of target genomic DNAs based on MIP technology [70].

Use of Affymetrix Arrays in the Diagnosis of Gene Copy-Number Variation

Farah R. Zahir, Marco A. Marra

Current Protocols in Human Genetics, 1 April 2015, UNIT 8.13

Here we discuss the application of the CytoScan high-density (HD) platform for the detection of genomic imbalance. We provide an overview of the sequence of computational analyses involved in identifying pathogenic CNVs and highlight important parameters for consideration in assessing the pathogenicity of a detected CNV. Among them, OncoScan FFPE (formalin-fixed paraffin-embedded) is designed to screen FFPE samples.

Validation of a Modified OncoScan Protocol for Use in a Clinical Laboratory

Christian N. Paxton, Leslie R. Rowe, Sarah T. South

ARUP Institute for Clinical and Experimental Pathology, Salt Lake City, UT, USA

Cancer Genetics, June 2015, 208(6): 361.
Introduction of new procedures into the clinical laboratory always poses potential challenges to the established workflow. In recent years microarray analysis has gained acceptance as a first tier test for detection of copy number changes (CNCs) and loss of heterozygosity (LOH) in the clinical laboratory. Affymetrix recently introduced the OncoScan array for the testing of formalin-fixed paraffin embedded samples. The primary challenge to adopting the OncoScan array into our lab was a difference in hybridization temperatures between the OncoScan and CytoScan arrays, preventing simultaneous hybridization.

213- Meeting abstract
Validation of Molecular Inversion Probe-based Array for Detection of Copy Number Variations in Solid Organ Cancers using Formalin-Fixed, Paraffin Embedded Tissue

... Here, in a clinical laboratory setup, we describe validation of OncoScan (Affymetrix, CA), a molecular inversion probe (MIP)-based array for detection of CNVs with a focus on 900 cancer-related genes using low quantity of FFPE DNA for simultaneous analysis of CNVs, loss-of-heterozygosity (LOH), and tumor mosaicism in solid tumors... OncoScan proved to be a robust platform to detect CNVs with low quantities of FFPE DNA.
214-
**Chromosomal rearrangements in cancer: Detection and potential causal mechanisms**
Paul Hasty, Cristina Montagna
... This review describes technological advances in methods used to detect simple and complex chromosomal rearrangements, cancers that exhibit these rearrangements, potential mechanisms for rearrangement of chromosomes, and intervention strategies designed specifically against fusion gene products and causal DNA repair/synthesis pathways ... Several array designs are available for the cancer genome (eg, Agilent 400K CGH/SNP and Affymetrix CytoScan and OncoScan FFPE arrays). Such arrays are used in cancer ...

215-
**Chromothripsis in cancer cells: An update**
Agata Rode, Kendra Korinna Maass, Karolin Viktoria Willmund, Peter Lichter and Aurélie Ernst
International Journal of Cancer, Article first published online: 30 October 2015
... Malignant melanoma, 20, aCGH, 10, [20]. Uveal melanoma, 25, OncoScan assay, 8, [21]. Hepatocellular carcinoma, 88, WGS, 5.7, [22]. Glioblastoma. 18, WGS, 38.9, [17]. Grade IV glioma, IDH mutant, 24, OncoScan assay, 37.5, [24]. Grade II-III glioma, 45, OncoScan assay, 11.1, ...

216-
**Molecular inversion probes: a novel microarray technology and its application in cancer research**
Yuker Wang, MariEllen Cottman, Joshua D. Schiffman
... This review describes the initial history of MIP technology, details of the MIP assay, its current analysis techniques, and recent publications related to this novel platform ... The new OncoScan FFPE Express 2.0 was designed in collaboration with members of the cancer research teams formed by the American Association of Cancer Research (AACR) Stand Up to Cancer (SU2C) initiative, with further input from international clinical and basic scientists in the field of cancer research.

217- **Review**
**Not All Next Generation Sequencing Diagnostics are Created Equal: Understanding the Nuances of Solid Tumor Assay Design for Somatic Mutation Detection**
Phillip N. Gray *, Charles L.M. Dunlop and Aaron M. Elliott
Cancers, 17 July 2015, 7(3), 1313-1332
... In addition, CNV analysis was performed using OncoScan®, a MIP-based microarray platform for CNV analysis from Affymetrix [82].... The CNV results from OncoScan include a genome-wide karyotype, log-ratio and B-allele frequency plots (Figure 7) .... using an NGS based approach for CNV analysis in polyploidy samples is flawed .... the FoundationOne report lists a loss of EGFR, which agrees with the OncoScan result. However, the OncoScan result shows a homozygous loss and the FoundationOne report does not specify whether it is homozygous or hemizygous.

218- **Meeting summary**
**OECI-EACR precision medicine for cancer: Conference report 1-4 March 2015, Luxembourg**
Anna Golebiowska,1 Sabrina Fritah,1 and Maria Romina Girotti2
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Eccancermedicalscience, online 3 April 2015, 9: 519.
The ‘Precision Medicine for Cancer’ was the first meeting of a new series of conferences organised biannually by the European Association for Cancer Research (EACR) and the Organisation for European Cancer Institutes (OECI). The main objective of the meeting was to focus on novel topics in precision medicine by allowing strong interactions between participants and to access the speakers easily.... This OECI-EACR 2015 report will highlight the major findings of this outstanding meeting.... The conference accommodated two satellite symposia presented by NanoString and Affymetrix. Both companies presented their novel technologies in personalised medicine. NanoString nCounter technology promises a high multiplex amplification-free system for detection of hundreds of targets simultaneously via digital detection. Affymetrix highlighted their new OncoScan FFPE Assay for the high resolution whole-genome copy number analysis of as little as 80ng DNA. Both technologies can be applied to challenging samples (FFPE).