Congress Highlights
Basic science and Translational research
(with a focus on Biomarkers)

Carlos Caldas
Biomarkers (genomic!)

• Molecular stratification
• Molecular monitoring
Cancers are heterogeneous

Box 2 | Stratification of non-small-cell lung cancers on the basis of activating mutations

The pie chart (see the figure) shows the distribution of various reported activating oncogenic mutations in a survey of 139 non-small-cell lung cancer (NSCLC)-derived cell lines. Also shown for all the activating mutations (except KRAS) are inhibitors that selectively target the activated oncoproteins, yielding growth inhibition and/or apoptosis of cancer cell lines with the corresponding mutated oncogenes. There are currently no inhibitors that target oncogenic KRAS.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Oncogenic activation</th>
<th>Frequency</th>
<th>Refs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Patients</td>
<td>Cell lines</td>
</tr>
<tr>
<td>EGFR</td>
<td>Deletion (ΔE746-A750), point mutation (L858R) and amplification</td>
<td>10–40%</td>
<td>5%</td>
</tr>
<tr>
<td>ALK</td>
<td>Translocation (EML4–ALK)</td>
<td>3–7%</td>
<td>2%</td>
</tr>
<tr>
<td>MET</td>
<td>Amplification</td>
<td>11%</td>
<td>2%</td>
</tr>
<tr>
<td>PDGFR</td>
<td>Amplification</td>
<td>13%</td>
<td>1%</td>
</tr>
<tr>
<td>ROS</td>
<td>Translocation (CD74–ROS)</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>ERBB2</td>
<td>Insertion</td>
<td>2–4%</td>
<td>1%</td>
</tr>
<tr>
<td>BRAF</td>
<td>Point mutation (exon 11)</td>
<td>3%</td>
<td>6%</td>
</tr>
<tr>
<td>PIK3CA</td>
<td>Point mutation</td>
<td>2%</td>
<td>10%</td>
</tr>
<tr>
<td>MEK1</td>
<td>Point mutation</td>
<td>0.50%</td>
<td>1%</td>
</tr>
</tbody>
</table>

EGFR, epidermal growth factor receptor; PDGFR, platelet-derived growth factor.
Cancer genomes within reach

2000: first human genome:
cost $ 2,700,000,000

2010: many cancer genomes
cost: $ 10,000

Extrapolate to 2020: cost $ 0.04 per genome
THE IMPACT OF THE CANCER GENOME PROJECT AND HIGH-THROUGHPUT ANALYSES ON PERSONALISED ONCOLOGY: TODAY AND TOMORROW
Invited abstract

Abstract: 9IN

THE MOLECULAR HETEROGENEITY OF BREAST TUMORS
A. Berresen-Dale
Genetics, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, and the K.G. Jebsen Center for BC Research, University of Oslo, Norway, Oslo, NORWAY

INITIAL SEQUENCING OF BREAST CANCER GENOMES
M. Stratton
Cancer Genome Projects, The Wellcome Trust Sanger Institute, Hinxton, UNITED KINGDOM

TOWARDS DECIPHERING THE GENETIC LANDSCAPE IN MELANOMA
Y. Samuels\(^1\), T.D. Prickett\(^1\), X. Wei\(^1\), J.C. Lin\(^2\), J.K. Teer\(^1\), S.A. Rosenberg\(^3\)
\(^1\) National Institutes of Health, NHGRI, Bethesda, MD, UNITED STATES OF AMERICA
\(^2\) Washington University School of Medicine, St Louis, MO, UNITED STATES OF AMERICA
\(^3\) National Institutes of Health, NCI, Bethesda, MD, UNITED STATES OF AMERICA

MUTATIONAL AND CHROMOSOMAL SURVEYS OF PANCREATIC TUMORS
A. Scarpa
ARC-NET Research Centre and Department of Pathology and Diagnostic, University of Verona, Verona, ITALY
Abstract: 170O

PROGNOSTIC AND PREDICTIVE VALUES OF KRAS IN EGFR-BASED SUBGROUPS AND COMBINED WITH P53 IN COMPLETELY RESECTED NON-SMALL CELL LUNG CANCER (NSCLC): A LACE-BIO STUDY

P.A. Janne¹, F.A. Shepherd², C. Domerg³, G. Le Teuff³, R. Kratzke⁴, P. Hainaut⁵, J. Pignon⁶, R. Rosell⁶, J. Soria⁷, M. Tsao⁸

Abstract: 1670

PREVALENCE AND CLINICAL OUTCOMES FOR PATIENTS WITH ALK GENE REARRANGEMENT IN EUROPE: PRELIMINARY RESULTS FROM THE EUROPEAN THORACIC ONCOLOGY PLATFORM LUNGSCAPE PROJECT

F. Blackhall¹, S. Peters², K.M. Kerr³, K. O'Byrne⁴, H. Hager⁵, A. Sejda⁶, A. Soltermann⁷, C. Dooms⁸, E. Felip⁹, A. Marchetti¹⁰, E-J.M. Speel¹¹, N. Price¹², S. Savic¹³, J. de Jong¹⁴, M. Martorell¹⁵, E. Thunnissen¹⁶, L. Bubendorf¹⁷, O. Dafni¹⁸, R. Rosell¹⁹, R.A. Stahel²⁰
It’s Diagnostics, Stupid

René Bernards

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DOI 10.1016/j.cell.2010.03.018

To stem the spiraling cost of cancer treatment, a concerted effort is urgently needed to develop molecular diagnostics to better identify the patients that respond to expensive targeted therapies. Opportunities and obstacles in the development of such drug response biomarkers are discussed here.
ARRAY CGH AND DNA SEQUENCING TO PERSONALIZE THERAPY FOR METASTATIC BREAST CANCER: A PROSPECTIVE NATIONAL TRIAL (UNICANCER SAFIR-01)

F. ANDRÉ¹, T. BACHELOT², M. CAMPONE³, M. ARNEDOS¹, F. COMMO¹, A. GONÇALVES⁴, C. LEVY⁵, J.-M. FERRERO⁶, L. LACROIX¹, V. DIÉRAS⁷, F. DALENÇ⁸, D. GENTIEN⁷, M. LACROIX TRIKI⁸, Q. WANG², J. ADELAIDE⁴, M. JIMENEZ⁷, H. BONNEFOI¹⁰

ESMO 2012, Vienna 1st October 2012
MOSCATO trial

Difficult-to-treat cancers
Biopsy of metastatic sites
Frozen sample
CGH/hot spot mutations (96 amplicons by NGS)
N=600

Targeted therapies

Algorithm:
Gene Amplification
Gene mutation on therapeutic target

120 patients included until now

PI: JC Soria
Molecular monitoring

Abstract: 255PD

CORRELATION BETWEEN CIRCULATING TUMOR CELLS (CTCS), PET/CT RESPONSE AND PATHOLOGICAL COMPLETE RESPONSE (PCR) IN PRIMARY HER2-POSITIVE (HER2+) BREAST CANCER PATIENTS: A SUB-STUDY FROM THE NEOALTTO TRIAL

H.A. Azim¹, F. Rothe¹, C.M. Aura², M. Bavington³, M. Maetens¹, G. Rouas¹, E. De Azambuja⁴, C. Sotinou¹, S. Di Cosmo⁵, M. Ignatiadis¹

¹ Breast Cancer Translational Research Laboratory, Institute Jules Bordet, Brussels, BELGIUM
² Molecular Pathology Laboratory, VHIO, Barcelona, SPAIN
³ Programming, Frontier Science, Kintraig, UNITED KINGDOM
⁴ Breast Data Centre, Institute Jules Bordet, Brussels, BELGIUM
⁵ Medical Oncology, Istituto Nazionale Tumor, Milan, ITALY

Abstract: 168O

QUANTIFICATION OF CELL FREE DNA AS A PROGNOSTIC FACTOR IN ADVANCED NSCLC

A. Dowler Nygaard¹, K. Spindler¹, R. Andersen², N. Pallisgaard², A. Jakobsen¹

¹ Department of Oncology, Vejle Hospital, Vejle, DENMARK
² Department of Clinical Biochemistry, Vejle Hospital Sygehus Lillebaelt, Vejle Sygehus, Vejle, DENMARK
Monitoring metastatic breast cancer using circulating tumour DNA

Dr Sarah-Jane Dawson MBBS, FRACP, PhD
Department of Oncology, University of Cambridge
Cancer Research UK, Cambridge Research Institute
Cambridge University Hospitals NHS Foundation Trust

Total vs. Tumour specific circulating DNA

- Tumour specific circulating DNA shows more dynamic change

Changes in ctDNA levels often predate changes on imaging

- Rising ctDNA levels predated progressive disease on imaging in 59% cases
- Average lead time in ctDNA changes prior to changes on imaging was 5 months
Cancer sequencing unravels clonal evolution

Carlos Caldas
Conventional cancer treatment:

Diagnosis
- Stage, Grade, IHC

Treatment
- Chemotherapy
Personalized cancer treatment:

Diagnosis:
Which pathways are active?

Treatment:
Pathway targeted therapy
Thank you!