Liverpool Lung Project Biobank

Dr. Mike Davies
(on behalf of Prof. John Field)
• Lung Cancer is the biggest cause of cancer death in the UK.
• Late presentation of the disease is a major factor in high mortality.
• Early detection, based on risk profiling, imaging (CT) or novel biomarkers aim to reduce this.
• Better targeted therapies required.

http://www.cancerresearchuk.org/cancer-info/cancerstats/mortality/cancerdeaths/#Twenty
LLP Biobank facilitates Excellence in RESEARCH

- A cancer biobank
- A hospital cohort biobank (diagnostic samples from suspected cancer patients)
- A population cohort biobank (minimally invasive samples from at-risk LLP cohort)
- Samples + DATA
- Research through local & international collaborations (academia & industry)
Tissues, tumours, data

Epidemiology + Outcome data = Risk prediction

**LLP Risk Model** (% risk of lung cancer within 5 years)

UK Lung Cancer Screening Trial

www.mylungrisk.co.uk
Tissues, tumours, data

Epidemiology + Outcome data = Risk prediction

Population cohort DNA = GWAS = Cancer predisposition

Blood, sputum, buccal scrapes, breath = screening

Blood, bronchial lavage, sputum = screening/diagnosis

Biopsy/resection = diagnosis/prognosis/treatment
**Infrastructure**

**Data Systems**
- Outcome data: MCCR, ONS, HES
- Clinical data
- Epidemiology data
- Risk model data

**Recruit**
- Surgical: LHCH
- Rapid Access Clinics: LHCH, AUH, WH
- COPD: RLBUH
- LLP: CRC
- LLP: GP clinics

**Biomaterial**
- Tissue
- Protein
- DNA
- RNA
- microRNA
- VOCs

**Biomaterials and associated clinical information:**
local, national and international collaboration or independent research

**LIMS**

**Provision**

**LLP Biobank**
## Cohort Timelines

<table>
<thead>
<tr>
<th>Study</th>
<th>Collection</th>
<th>Data (subjects)</th>
<th>Biobanked Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population cohort</td>
<td>Population controls</td>
<td>6942</td>
<td>121195</td>
</tr>
<tr>
<td>Population cohort</td>
<td>Hospital cohort controls</td>
<td>1276</td>
<td>10675</td>
</tr>
<tr>
<td>Primary care patients</td>
<td>Lung Cancer Cases</td>
<td>2491</td>
<td>19235</td>
</tr>
<tr>
<td>Hospital cohort</td>
<td>Total</td>
<td>10709</td>
<td>147119</td>
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<tr>
<td>Hospital cohort- COPD</td>
<td></td>
<td></td>
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<tr>
<td>Hospital cohort- ENT</td>
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<tr>
<td>Surgical - LHCH</td>
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<tr>
<td>Sample</td>
<td>Study (grant funding)</td>
<td>Example Output</td>
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<tr>
<td>-------------------------</td>
<td>--------------------------------------------</td>
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<tr>
<td>Bronchial Lavage</td>
<td>Diagnostic DNA methylation (CRUK)</td>
<td>Nikolaidis <em>Can Res</em> (2012)</td>
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<tr>
<td>Tumour &amp; Normal DNA</td>
<td>DNA methylation (CURELUNG)</td>
<td>Sandoval <em>JCO</em> (2013)</td>
<td></td>
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</tbody>
</table>
A susceptibility locus for lung cancer maps to nicotinic acetylcholine receptor subunit genes on 15q25
Molecular diagnosis in bronchial washings

Clinical Studies

DNA Methylation Biomarkers Offer Improved Diagnostic Efficiency in Lung Cancer

Georgios Nikolaidis¹, Olaide Y. Raji¹, Soultana Markopoulou¹ ², John R. Gosney¹, Julie Bryan¹, Chris Warburton², Martin Walshaw³, John Sheard², John K. Field¹, and Triantafillos Liloglou¹

Table 4. Validation of the best subset logit model in the bronchial washings validation set. Comparative efficiency of the models including DNA methylation (p16, RASSF1, WT1, TERT) only and DNA methylation with incorporated cytology versus cytology only.

<table>
<thead>
<tr>
<th></th>
<th>Cytology</th>
<th>Negative</th>
<th>Positive</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td><strong>Methylation panel model</strong></td>
<td>Lung cancer</td>
<td>19</td>
<td>57</td>
<td>75%</td>
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<td></td>
<td>Controls</td>
<td>98</td>
<td>10</td>
<td>91%</td>
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<tr>
<td><strong>Methylation panel + cytology model</strong></td>
<td>Lung cancer</td>
<td>25</td>
<td>114</td>
<td>82%</td>
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<tr>
<td></td>
<td>Controls</td>
<td>100</td>
<td>9</td>
<td>92%</td>
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<tr>
<td><strong>Cytology only</strong></td>
<td>Lung cancer</td>
<td>76</td>
<td>63</td>
<td>45%</td>
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<tr>
<td></td>
<td>Controls</td>
<td>108</td>
<td>1</td>
<td>99%</td>
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</tbody>
</table>
A microRNA-based prediction algorithm for diagnosis of non-small lung cell carcinoma in minimal biopsy material

N G Bediaga, M P A Davies, A Acha-Sagredo, R Hyde, O Y Raji, R Page, M Walshaw, J Gosney, A Alfrevic, J K Field and T Lloglou
Progressive lung cancer determined by expression profiling and transcriptional regulation

NAMSHIK HAN\textsuperscript{1,2}, ZULKIFLI DOL\textsuperscript{1}, OLGA VASIEVA\textsuperscript{3}, RUSSELL HYDE\textsuperscript{3,4}, TRIANTAFILLOS LILOGLOU\textsuperscript{4}, OLAIDE RAJI\textsuperscript{4}, ELISABETH BRAMBILLA\textsuperscript{5}, CHRISTIAN BRAMBILLA\textsuperscript{5}, YVES MARTINET\textsuperscript{6}, GABRIELLA SOZZI\textsuperscript{7}, ANGELA RISCH\textsuperscript{8}, LUIS M. MONTUENGA\textsuperscript{9}, THE EUELC CONSORTIUM, ANDY BRASS\textsuperscript{1,2} and JOHN K. FIELD\textsuperscript{4}

\textsuperscript{1}School of Computer Science, The University of Manchester, Kilburn Building, Oxford Road; \textsuperscript{2}Faculty of Life Sciences, The University of Manchester, Michael Smith Building, Dover Street, Manchester; \textsuperscript{3}Institute of Integrative Biology, University of Liverpool; \textsuperscript{4}Roy Castle Lung Cancer Research Programme, University of Liverpool Cancer Research Centre, Department of Clinical and Molecular Cancer Medicine, Liverpool, \textsuperscript{5}Inserm, U1251, CHU Besançon, France; \textsuperscript{6}Centre Hospitalier Universitaire de Bordeaux, France; \textsuperscript{7}German Cancer Research Center (DKFZ), Heidelberg, Germany; \textsuperscript{8}CIMA, University of Navarra, Spain; \textsuperscript{9}University of Manchester, Manchester, UK.

Tumour progression—Tumour mRNA
A Prognostic DNA Methylation Signature for Stage I Non–Small-Cell Lung Cancer

Juan Sandoval, Jesus Mendez-Gonzalez, Ernest Nadal, Guoan Chen, F. Javier Carmona, Sergi Sayols, Sebastian Moran, Holger Heyn, Miguel Vizoso, Antonio Gomez, Montse Sanchez-Cespedes, Yassen Assenov, Fabian Müller, Christoph Bock, Miquel Taron, Josefina Mora, Lucia A. Muscarella, Triantafillos Liloglou, Michael Davies, Marina Pollan, Maria J. Pajares, Wenceslao Torre, Luis M. Montuenga, Elisabeth Brambilla, John K. Field, Luca Roz, Marco Lo Iacono, Giorgio V. Scagliotti, Rafael Rosell, David G. Beer, and Manel Esteller
Integrative genome analyses identify key somatic driver mutations of small-cell lung cancer

Martin Peifer1,2,57, Lynnette Fernández-Cuesta1,2,57, Martin L Sos1-4, Julie George1,2, Danila Seidel1,2,5, Lawryn H Kasper6, Dennis Plenker1,2, Frauke Leenders1,2,5, Ruping Sun7, Thomas Zander1-4, Roopika Menon8, Mirjam Koker1,2, Ilona Dahmen1,2, Christian Müller1,2, Vincenzo Di Cerbo9, Hans-Ulrich Schildhaus10, Janine Altmüller11, Ingelore Baessmann11, Christian Becker11, Bram de Wilde12, Jo Vandesompele12, Diana Böhm8, Sascha Ansén3,4, Franziska Gabler2, Ines Wilkening2, Stefanie Heynck2, Johannes M Heuckmann1,2, Xin Lu12, Scott L Carter13, Kristian Cibulskis13, Shantanu Banerji13, Gad Getz13, Kwon-Sik Park14,15,

Nature Genetics
Cancer Genomics: NGS on Tumour & Normal DNA

A Genomics-Based Classification of Human Lung Tumors
The Clinical Lung Cancer Genome Project (CLCGP) and Network Genomic Medicine (NGM),
Sci Transl Med 5, 209ra153 (2013);
DOI: 10.1126/scitranslmed.3006802
Early Detection – breath analysis
EU Framework7 – LCAOS
European multicentre collaboration led by Prof Hossam Haick, Technion, Israel

- A Lung Cancer artificial olfactory sensor
- A nanotechnology-based electronic nose for detecting Volatile Organic Compounds (VOCs).
- Analyses the exhaled breath for screening, diagnosing and monitoring lung cancer.
- Detects cancer and discriminates between the different stages of the disease, or different mutations.
At Risk population → Lung cancer patients → Clinical Trials MCCRN

- Early Detection CT screening (UKLS)
- Risk Stratification
  - LLP Risk Prediction Model Annals Int Med 2012
  - GWAS Hung Nature 2008
  - International Lung Cancer Consortium (ILCCO)
- Data sources: MCCR, ONS, HES

Lung cancer patients:
- Non-resectable tumours
  - Plasma
  - Sputum
- Resectable tumours
  - Biopsies
  - Tumour tissue

Samples:
- Early detection: DNA methylation in biological fluids
- Early detection: microRNA in biological fluids
- Early detection: breath test
- Biomarkers of therapeutic stratification

Molecular Epidemiology:
- Genome and methylome analysis by NGS.
- Prognostic biomarkers
- Gene networks: redefining the molecular pathology of NSCLC

Biobank:
- Biobank Development & validation

Clinical Diagnostics Molecular profiling
ACKNOWLEDGEMENTS

University of Liverpool
Roy Castle Lung Cancer Research Programme

Prof John Field
Lakis Liloglou

Research Nurses
Peris Widdows
Angela Tobin
Sarah Feeney
Angela Kenny

Clinical Resources
Julie Bryan
Stephanie Unsworth
Derek Pye
Jennie Goggins

Epidemiology
Michael Marcus
Adrian Cassidy
Olaide Raji
Ying Chen

IT
Asaf Niaz
Nail Hodge

RLBUH
John Gosney
Tom Giles

LHCH
Martin Walshaw
Martin Ledson
Colin Smyth
Richard Page
John Holemans

Sefton NHS
Primary Care Trust

Knowsley NHS
Primary Care Trust

Liverpool NHS
Primary Care Trust

Scientists, students, international collaborators, funding bodies....
The Roy Castle Lung Cancer Foundation for generous support over many years.

All those patients and population cohort members who have so generously given their samples, data and time to helping lung cancer research and the LLP Biobank.

Scientists, students, international collaborators, funding bodies....
Thank-you