Translating medical innovation
introductory workshop
MRC Post Docs
10\textsuperscript{th} September 2014
Translating Medical Innovation

• Introductions & your ambitions for the session?
• Why translate?
• Examples of successful translation.
• Examples of in-progress translation.
• Translation considerations.
• Short break
  – Coffee and compose your own translation idea
• Highly interactive with your ideas!!!
• Careers in translation- discussion
• Evolution of academic translation -observations
Examples and Messages from the “Translators Journey”
Products and Services Pharma, Biotech, Start-ups and Academia

http://uk.linkedin.com/in/howardmarriage

Biotech Innovation & Future Health Ltd

GT Biologics
Chiravon
NeurocentRx

buldica
Dentherapy

* symbiosis
Pharmaceutical Services

R Roslin
Foundati

Reprofilix

FibromEd

CYCLACEL
UNIVERSITY OF
Southampton

Burroughs Wellcome & Co.
IDEAS THAT CHANGE LIVES

www.crick.ac.uk

The translators perspective
What is translation?

- Making impact beyond your immediate research area
  - Products and services aimed towards an unmet need – medical outcome or research enabling

- Translation is a long journey with many different people and skills
  - Concept to sale – research service 2-3 years & drug 12 years +

- Personal success is:
  - A quality hand over from your phase of the project
  - Increasing your knowledge about the opportunities and processes in translation.
Translation matters to The Crick and Society

- The Crick’s strategic priorities include:
  - Accelerate translation for health and wealth - This will focus on maximising the value that can be generated from the Crick's discovery science, measured in terms of improvements in the lives of people in the UK and internationally, and in new economic opportunities.
  - National benefits
    - Develop technologies and train scientists and technical staff to the highest standards, for the benefit of the wider UK biomedical science base
  - It will train the research leaders of the future
  - “and build a strong collaborative alumni”
Translation should matter to you

• It will be challenging but can be deeply rewarding!
• Research jobs in industry are translation
• Research in Universities looks for impact “is translation”
• Expose you to different professions and skills—
  • patent agents
  • regulatory
  • manufacturing
  • clinical
  • Media
  • Project management
25 public biotechs
$23 billion revenues
Translation is not new!

Professor Sir William Paton

Baird Macdonald Paton, pharmacologist: born Hendon, May 1917; staff, National Institute for Medical Research 1944-52; Reader in Pharmacology, University College London and UCH Medical School 1952-54; Professor of Pharmacology, Royal College of Surgeons 1954-59; Professor of Pharmacology, Oxford University, and Fellow of Balliol College 1959-84 (Emeritus); CBE 1968; Chairman, Committee for Doping 1970-71; Chairman, Research Defence Society 1972-84; Hon Director, Wellcome Institute for History of Medicine 1983-87; married 1942 Phoebe Rooke; died Oxford 17 October 1993.

THE FIRST effective treatment of high blood …

Heliox gas for diving ….

Research and legislation cannabis ….

HM joins in 1981 as MRC DPhil student to research into drug metabolism
Science to Product
Placenta to fermenter

Enzyme replacement therapy with modified sugar residues

First children treated with Cerazyme

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Glucose sensors

1996 $1.5Bn purchase of MediSense by Abbott
Sales of $1Bn + per year

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Autologous cartilage Therapy

Genzyme Tissue Repair Inc
Gene Therapy

Basic research St Marys and others
Genzyme developed enzymatic routes to phospholipids
Genzyme Translation team + St Marys clinical
Roslin Institute

• Dolly the Sheep
• Transgenic proteins
• Built PPL Ltd
How we work:

Client’s research needs

- UoE Investigators
- Models and Assays

Aquila R&D
- market interest
- Validation
- Commercial offering

Aquila BioMedical

Services
- In vitro
- In vivo
- Ex vivo

UoE Investigators
- Experimental design
- & Data interpretation

www.aquila-bm.com
Current Services

• **Multiple Sclerosis & Autoimmune Research**
  Exclusive in vitro and in vivo models → efficacy and MoA data
  
  **Immunology:** Exclusive MBP-Tracker EAE → MoA data on T cell function
  
  **Remyelination:** Oligodendrocyte precursor cell (OPC) assays & Rodent CNS slice cultures

• **Inflammation:** advanced in vitro activation & differentiation of immune cells

• **Neuroscience:** Gold Standard Pain Models
Announcing: Aquila HistoPlex

Specialist and technically challenging histology for the commercial sector

Soon to be Scotland’s first accredited provider for ACDbio’s RNAscope
Detection of mRNA in cells and tissue sections
• First two products launched
  – Zestica* Fertility, a lubricant specifically formulated for couples trying to conceive (TTC)
  – Zestica* Moisture, for woman who are experiencing the menopause.

• 最初上市的两项产品
  – Zestica* 生育胶，专为试图怀孕的夫妻而开发的顺滑剂
  – Zestica* 润滑剂，专为更年期妇女开发
The Gene Race¹

- Gene therapy for Cystic Fibrosis
- Plasmid vs. virus
- Developed chemoenzymatic routes for phospholipids
- CF trials in St Marys Paddington
- 5000l fermenter of plasmid in Horizon
- $80M Neozyrne II

Nature News Blog

**Cystic-fibrosis gene-therapy trial rescued**
16 Mar 2012 | 16:23 BST | Posted by Heidi Ledford | Category: Biology & Biotechnology, Health and medicine

The UK government has awarded £3.1 million (US$4.9 million) to support a key gene-therapy trial for cystic fibrosis that was previously threatened by lack of funding. The trial, now scheduled for launch by the UK Cystic Fibrosis Gene Therapy Consortium this spring, is to be the largest of its kind.

¹BBC Horizon 1996
Press Release

1998-2005 - $120M latter

CYCCEL AND XCYTE THERAPIES COMBINE TO FORM INTERNATIONAL BIOPHARMACEUTICAL COMPANY

Dundee, Scotland, UK and Seattle, WA, USA – December 15, 2005 - Cyccel Group plc (Cyccel), a privately held corporation, and Xcyte Therapies, Inc. (Xcyte) (NASDAQ: XCYT, XCYTP) announced today that they have entered into a definitive agreement to combine the two companies. The transaction will create a publicly-traded international biopharmaceutical company with two clinical stage, mechanism-targeted, small molecule drug candidates in cancer, a third candidate expected to enter clinical trials in the second half of 2006 and a strong development pipeline.

The transaction is structured as an acquisition by Xcyte of all of the capital stock of Cyccel Limited, a wholly-owned subsidiary of Cyccel Group plc. The transaction is anticipated to close at the end of the first quarter of 2006 and is subject to satisfaction of certain customary closing conditions, including the approval of the shareholders of Cyccel and Xcyte.

The new company, to be called Cyccel Pharmaceuticals, Inc. (CPI), intends to build upon what it believes to be Cyccel's leading position in the area of cell cycle biology, with a portfolio of three orally-available, mechanism-targeted drugs that modulate the cancer cell cycle. Cyccel's drug pipeline includes seliciclib (CYC202), a cyclin dependent kinase (CDK) inhibitor in Phase II clinical trials for the treatment of non-small cell lung cancer; sapacitabine (CYC882), a nucleoside analog in Phase I trials; CYC116, an Aurora kinase inhibitor in IND-directed preclinical development; and early stage programs targeting important cell cycle mechanisms for the treatment of cancer, type 2 diabetes, inflammatory kidney diseases and viral infections.

Potential Milestones for 2006 for CPI include:
-- Initiation of a Phase Ib clinical trial of sapacitabine (CYC882) at a major U.S. cancer center in patients with advanced leukemias and myelodysplastic syndrome, expected in the first half of 2005.
-- Filing of an Investigational New Drug application with FDA to begin Phase I clinical trials with CYC116, an Aurora kinase inhibitor, expected in the second half of 2006.

Sir John Banham, Chairman of Cyccel, stated, "The transaction will create an international public company with approximately $30 million in cash, a franchise in one of the most exciting fields of biology and a development-stage portfolio of targeted oncology drug candidates affecting the cancer cell cycle. We believe that cell cycle targeted drugs will become increasingly important in the modern treatment of cancer as a chronic disease. Cyccel is well positioned to benefit from the increasing adoption of orally-active therapeutics for the long-term management of cancer patients. Our drug discovery capabilities are complemented by research into cancer disease pathways in the laboratories of our founding scientists Professors David Lane and David Glover. Our combined insights into cancer biology have resulted in innovative biomarker technology that may help us identify subgroups of patients that are more likely to benefit from our treatments."
GT BIOLOGICS

Anti-inflammatories inspired by nature
Novel applications for gut bacteria drugs, nutraceutical human and veterinary

From Bugs to Drugs
Inflammatory Bowel Diseases
Imbalance and Disruption of Gut Bacteria

Crohn’s Disease

Ulcerative Colitis/Cancer

IBD

Loss of Good Bacteria
Human Liver Models for Toxicity

1981 HM white board in lab
“no reliable method for predicting toxic metabolites in humans - works fine in mice”

1981-2013

Pharmacogenetic Predisposition to Adverse Drug Reactions - patient selection not best solution

- US 2008 - 1.5 to 3 million annual hospitalizations, 80 to 140 thousand annual deaths, $30-50B
- 1/3 of all drugs withdrawn post-launch due to problems with safety
- Pharmacogenetic Predisposition to Adverse Drug Reactions
- Attrition due to liver toxicity is high – 40% in preclinical; 31% in clinical trials
- Drug discovery screening relies on ineffective human & animal model technology
- Current standard for liver tox testing is liver cells from cadavers and resections: poor quality, limited supply, different sources

Stem cell technology + novel 3D supports + phenomenal expertise
GSK Discovery Partnerships with Academia (DPAc)

1st DPAc - Acute Pancreatitis Project:
Mr Damian Mole & Dr Scott Webster

- Druggable target validated in Edinburgh
- Assays and screening sequence
- Active compounds
- Access to animal models of disease
- Access to patients

Collaboration Established in October 2011
Research & Clinical Milestones, Royalties on sales
3rd research event milestone achieved
Complex pain, Simple solutions.

- Oral drug formulation and new indication
- Optimised topical formulation
- Supported by clinical data “launched” as specials
- Using clinical data obtain approval
The Relay Race of Translation!
Think of a translation proposition?

• Knowledge (your) of the market gaps*
  – The product/service that you wish was there
  – The product/service that could be better
    • Devices
    • Diagnostics
    • Reagents
    • Research enabling tools
    • Computer app
    • Medical informatics
    • Enzymatic transformation
    • Cell therapy
    • New medicines
    • Ag Bio
    • Green Biotech

Your imagination tested and converted to investor propositions

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Product/Service Concept

- what is it?
- who will buy it?
- what will they pay?
- how many potential customers?
- when will it be available?
Market Pull

- why will the customer want your product/service?
- is it an incremental or disruptive?
- what will it displace, replace, complement?
- what advantage does it give the customer?
- what is its USPs (unique selling points)?
Legal/Patent

- how will you generate exclusivity?
- is the concept novel and inventive (patentability)?
- will you require a licence/permission (freedom to operate) from others?
Collaborators/Partners

- Who could you work with to reach your market quicker or reduce technical/commercial risks?
Financial

• How much money might be required for the likely phases of research, prototype development, and manufacture, distribution?
• Where might this be available?
Comparables/Competitors

Suggest 2-3 companies who are closest to your product/market. Identify some key features of your business such as size, maturity, product range and location.
Translational Ideas

• Coffee fuelled 10 minutes of focussed thinking – small groups are fine

• Suggestions for at least 5 unmet needs
  – what is it?
  – who will buy it?
  – what will they pay?
  – how many potential customers?
  – when will it be available?

• All participate in discussions
  – How will we make it happen?

Jan 2014
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Careers in Translation

• Discussion
  – What jobs are translation?
  – How do you get one?
  – Where does it take you?
Evolution of academic translation

• Changes in commercial environment
  – increased need for academic input
  – More financial support for translation
  – Outcome over early income
  – Models
    – Edinburgh BioQuarter
    – Francis Crick Institute