ProCan™ - A new approach to cancer diagnosis and treatment options

Phil Robinson and Roger Reddel

The ACRF International Centre for the Proteome of Human Cancer was made possible by a $10 million Award from the Australian Cancer Research Foundation (ACRF) in Dec 2015.

Launched Sept 2016

Potentially the largest competitive medical research equipment grant in Australia!

http://www.cmri.org.au/ProCan
Cancer Affects Any Part of the Body – In Kids & Adults

Children generally develop different types of cancer to adults.

- **Leukaemia**
- **Lymphoma**
- **Brain**, other central nervous system and intracranial tumours (e.g. glioma)
- Other nervous system tumours (e.g. neuroblastoma)
- **Soft tissue sarcomas**
- Kidney tumours (e.g. Wilms tumour)
- Bone tumours
- Germ cell tumours
- Eye tumours
- Skin cancers
- Liver tumours
- Other
Two Challenges:
Define the cancer, find the treatment

Genomics:
• The ‘Genome’ is *all* our genes
• ‘Genomics’ is the study of all our genes *together*
• Very few drugs target genes
DNA Codes For Proteins: Proteins do the work in our cells

Proteomics:

- Genes code for making proteins
- The ‘Proteome’ is *all* the proteins from our genes
- ‘Proteomics’ is the study of *all* proteins together
- Most drugs target proteins

20,000 genes

Genes are *codes* to make proteins

A million proteins
Proteins Completely Fill Our Cells
Crowded beyond comprehension, billions of proteins moving

Nerve contacts (synapses)

Proteins in synapses
Most Drugs Work By Blocking Proteins

Drug (Pitstop)
Disease Changes The Proteome Unpredictably

Genome
- Mutation
- Deletion
- Rearrange

Proteome
- Environment (chemicals / UV)
- Infection (virus / bacteria)
- Inflammation / fever

There may already be a drug for this
Cancer Diagnosis Can Be Slow
Often the wrong treatments are used

The Current Way
One protein at a time
Drugs chosen by experience

Antibody stain

Our New Way
Most proteins at once
Drugs identified rationally

Proteome maps
The ProCan Concept

The problem
• Every cancer has different protein patterns (proteomes), makes treatment decisions difficult

The barrier
• Until now, only a small number of proteomes could be studied, and not reliably between labs

The ProCan plan
• Collect proteomes on an industrial scale, with universal, reliable outcomes
• Collect cancers from patients where their treatment outcomes are known
• Analyse the proteome of 70,000 cancers of all types, in 5-7 years

A simple plan – a huge project!
Why ProCan Can Succeed

Disruptive Technology

• Tiny biopsies liquefied by a Barocycler
• Proteomes collected by a new Mass Spectrometry technology – SWATH-MS
• New data analytics for treatment decisions

Custom-Built Factory

• Multiple instruments for high throughput
• Instruments work in harmony for consistent results over the years and for ISO accreditation
• Clear work flow and clear SOPs

A simple plan – a huge project!
ProCan Introduces Industrial-Scale Proteomics

Research-mode

Factory-mode

Digital proteome expression maps

World first industrial-scale cancer proteomics
How ProCan Industrialises Proteomics

Tumour sample → Proteins and peptides → SWATH-MS files → Data analysis

Tiny samples.. → ..allows high throughput

Meet the ‘Barry’ brothers (Barocyclers)

Rice grain

Grape
Collecting Proteomes on an Industrial Scale

Tumour sample → Proteins and peptides → SWATH-MS files → Data analysis

SWATH Mass Spectrometer

Harness the 6-pack
Collecting Proteomes on Industrial Scale

Huge computational power

OneOmics®
- Amazon cloud computing environment
- Enormous parallel computing power
- Data analysis and discovery
- Connects proteomics with genomics
- Community contributes new ‘apps’
Workflow Operation by **SOPs**

**Tumour sample**
- Tiny biopsies

**Proteins and peptides**
- Tumour liquefied

**SWATH-MS files**
- Microflow delivery to...
- SWATH mass spectrometers

**Data analysis**
- Data storage and discovery platforms

**Results**
- Treatment decision tool

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**Factory-mode data must be consistent between machines and across the years**

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[Image: OneOmics® CloudConnect BaseSpace® OpenSWATH by ETH Zürich]

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[Logo: ProCan™]

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[Logo: CHILDREN'S MEDICAL RESEARCH INSTITUTE: Jeans for Genes]
### Illustrative ProCan Clinical Report for Treating Oncologist

<table>
<thead>
<tr>
<th>Name:</th>
<th>Jamie Smith</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare No.:</td>
<td>12345678</td>
</tr>
<tr>
<td>Sample:</td>
<td>Brain tumour</td>
</tr>
<tr>
<td>Date of procedure:</td>
<td>16 Sept 2021</td>
</tr>
<tr>
<td>Date of report:</td>
<td>18 Sept 2021</td>
</tr>
<tr>
<td>Tissue classification:</td>
<td>a) Glioblastoma</td>
</tr>
<tr>
<td></td>
<td>b) De novo</td>
</tr>
<tr>
<td></td>
<td>c) Molecular category 4</td>
</tr>
<tr>
<td>Response markers:</td>
<td>MGMT – low (xxx Units)</td>
</tr>
<tr>
<td></td>
<td>EGFRvIII – high</td>
</tr>
<tr>
<td></td>
<td>VEGF - high</td>
</tr>
<tr>
<td></td>
<td>PDGF – high</td>
</tr>
<tr>
<td></td>
<td>PML - low</td>
</tr>
<tr>
<td></td>
<td>Protein XX – high</td>
</tr>
<tr>
<td></td>
<td>Protein YY – high</td>
</tr>
<tr>
<td>Likely response to:</td>
<td>1. Temozolomide</td>
</tr>
<tr>
<td></td>
<td>2. Tyrosine kinase inhibitor Dovitinib/TKI258</td>
</tr>
<tr>
<td></td>
<td>3. Oncolytic HSV-1 virus treatment</td>
</tr>
<tr>
<td></td>
<td>4. New treatment targeting protein XX or YY</td>
</tr>
</tbody>
</table>

### Prototype clinical report

- **Patient record**
- **Rapid report**
- **Improved diagnosis**
- **Greatly expands pathology**
- **Precise data provided**
- **New discoveries**
- **Futile treatments avoided**
- **Treatment decision tool for clinicians; Personalised for Jamie**
The collaboration of ProCan with the Cancer Moonshot announced by VP Joe Biden on 17 July 2016

The Moonshot goal is to bring forward cancer therapies: not 10-15 years away, but ~5 years....
ProCan Public Library of Digital Proteomes
Shared via the National Cancer Institute (Washington), last indefinitely

2-3 petabytes of data sharing for new data-mining
ProCan will provide new options

http://www.cmri.org.au/ProCan
ProCan Funding Support

AUSTRALIAN CANCER RESEARCH FOUNDATION

NSW GOVERNMENT

cancer institute NSW

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Jeans for Genes®