How can we incorporate proteomic and other 'omic data into clinical oncology?

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Fundamental problems with treating cancer

- Cancers are derived from own cells
- Cancer is caused by multiple mutations in DNA
  - Genetic instability → many changes, most random
    → heterogeneity within tumours
    → treatment resistance
  - Every cancer is different
    → need to "**personalise**" treatment

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The very long history of personalised cancer treatment

- **Tumour type**
  e.g., oophorectomy for breast cancer (Beatson, Lancet 1896)
- **Histopathology**
  e.g., testicular cancer
  - seminomas → respond to radiotherapy
  - non-seminomatous germ cell tumours
    → respond to platinum regimens (FDA approved 1978)
- **Molecular data**
  e.g., oestrogen receptor in breast cancer
  → predicts response to antioestrogens
  (Tamoxifen was approved for use in the UK in 1972)

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“Big” molecular data = ‘omics

- Genomics – DNA
- Epigenomics
- Transcriptomics – RNA
- Proteomics
- Glycomics
- Metabolomics

etc.

‘omics studies have transformed our understanding of cancer

but how can we incorporate 'omics into clinical oncology practice?

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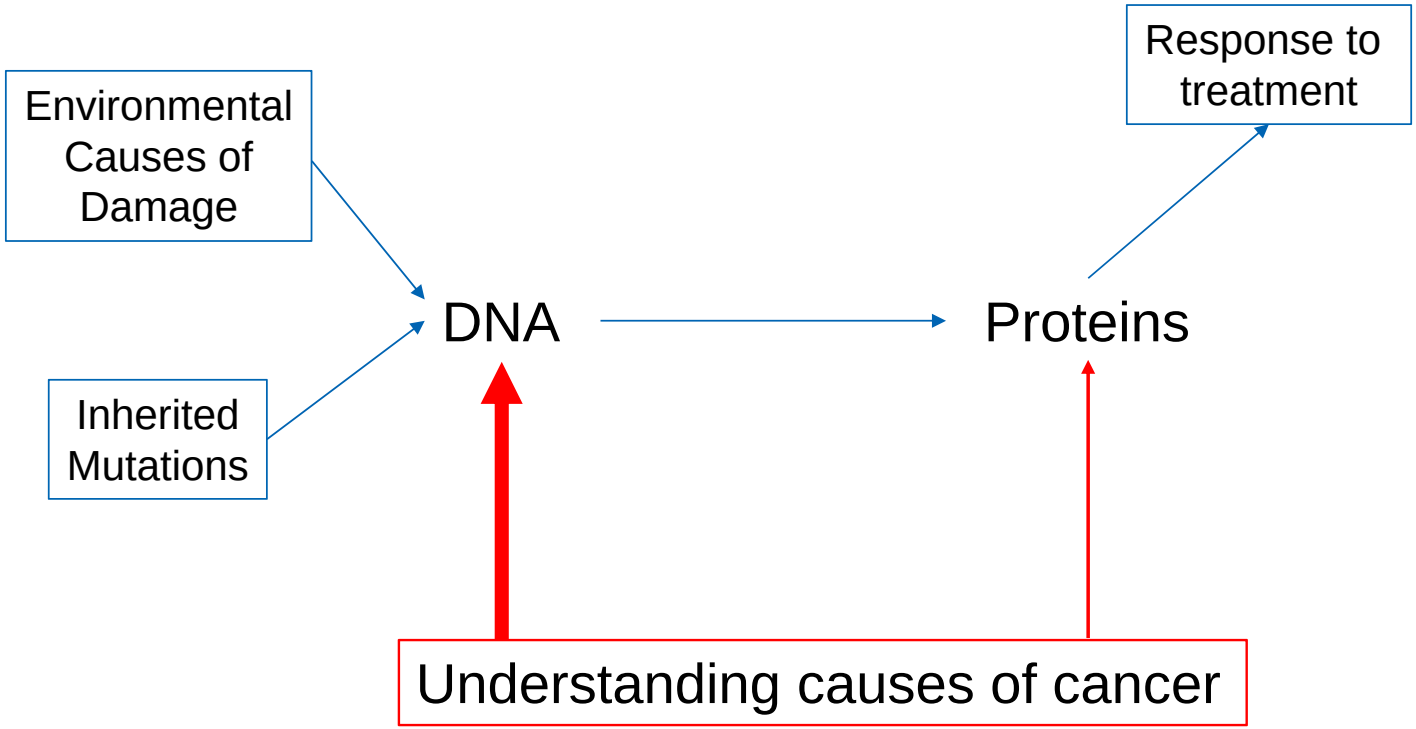
Genes and Proteins in Cancer



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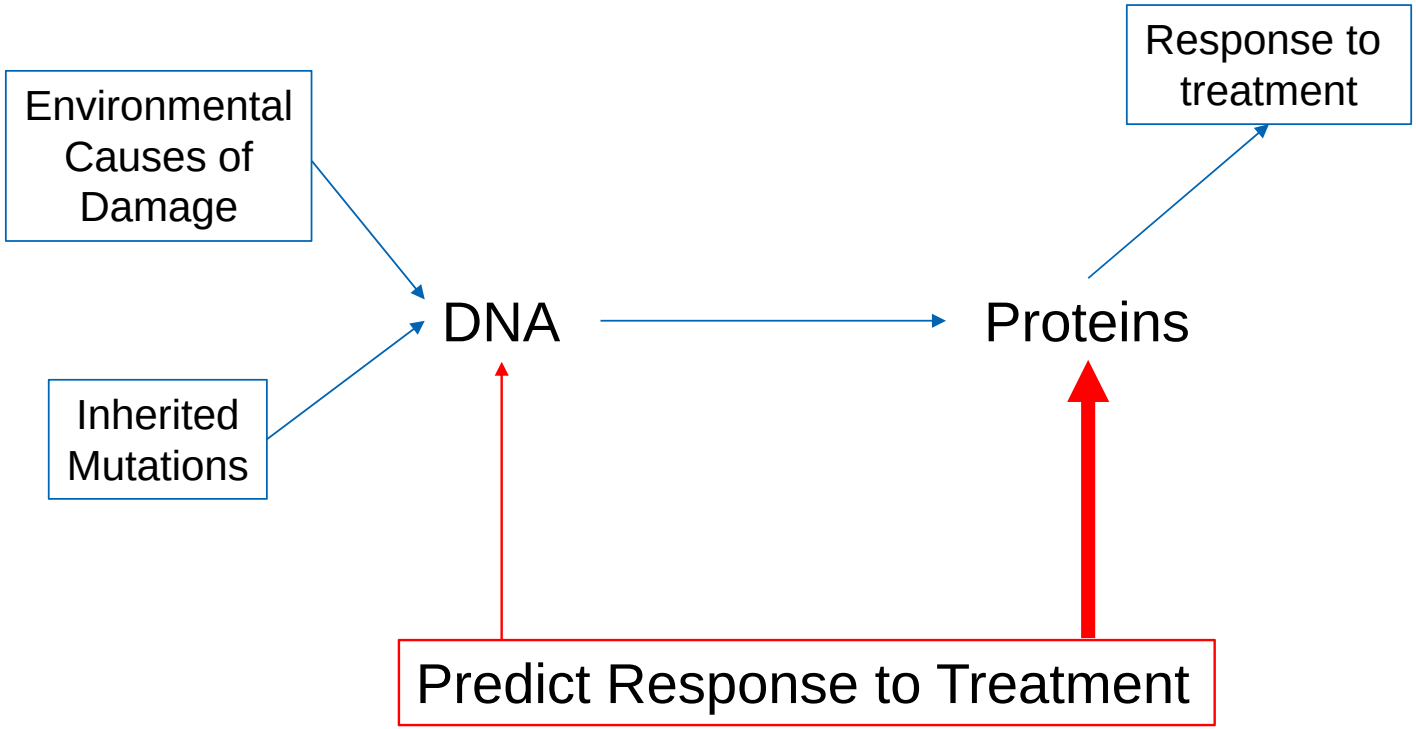

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The ACRF International Centre for the **Pro**teome of Human **Can**cer

Professor
Phil Robinson

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ProCan's Very Simple Concept

Response to treatment

The Problem: Every cancer has a different pattern of 'omics (esp. proteins)

Proteins (+other 'omics?)

The ProCan Concept: For every newly diagnosed cancer,
search a global database for the cancers with the most similar 'omics pattern,
and find out what treatments worked,
and which treatments didn't work

Simple concept – complex project

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ProCan's Very Simple Concept

Proteomics is not new (the word was coined in Australia in 1994)
so why hasn't this been done before?

The Barrier: Up until now, it has only been possible to study the proteome of small numbers of cancers, using relatively large samples, and the results were not always reproducible from one lab to another

Project plan:
analyse the proteome of 70,000 cancers of all types
with known outcomes of treatment
over the next 5-7 years

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ProCan's technology

1. New "disruptive" technology
2. Purpose-built data factory

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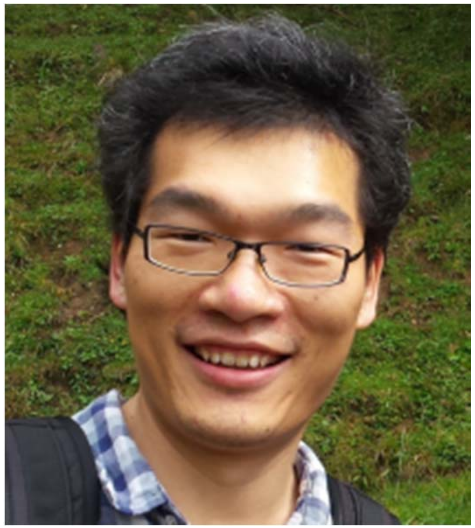
ProCan's technology

1. **New "disruptive" technology**
2. **Purpose-built data factory**

Professor Rüdi Aebersold
(ETH Zurich)



Dr Tiannan Guo

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Guo T, et al. ***Nature Medicine***. 2015. 21, 407–413

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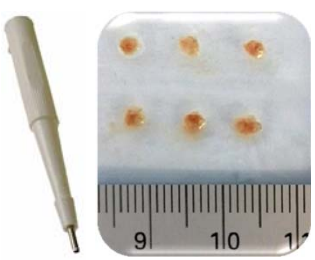
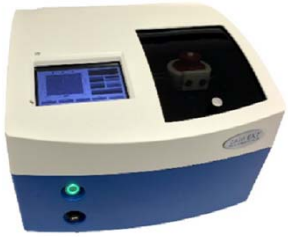
ProCan's technology

1. New "disruptive" technology
2. Purpose-built data factory

- Very small samples
- Highly reproducible
- Fast
- Complete record of all proteins





Pressure Cycling Technology

SWATH-MS

Permanent
Digital record

Data Analysis

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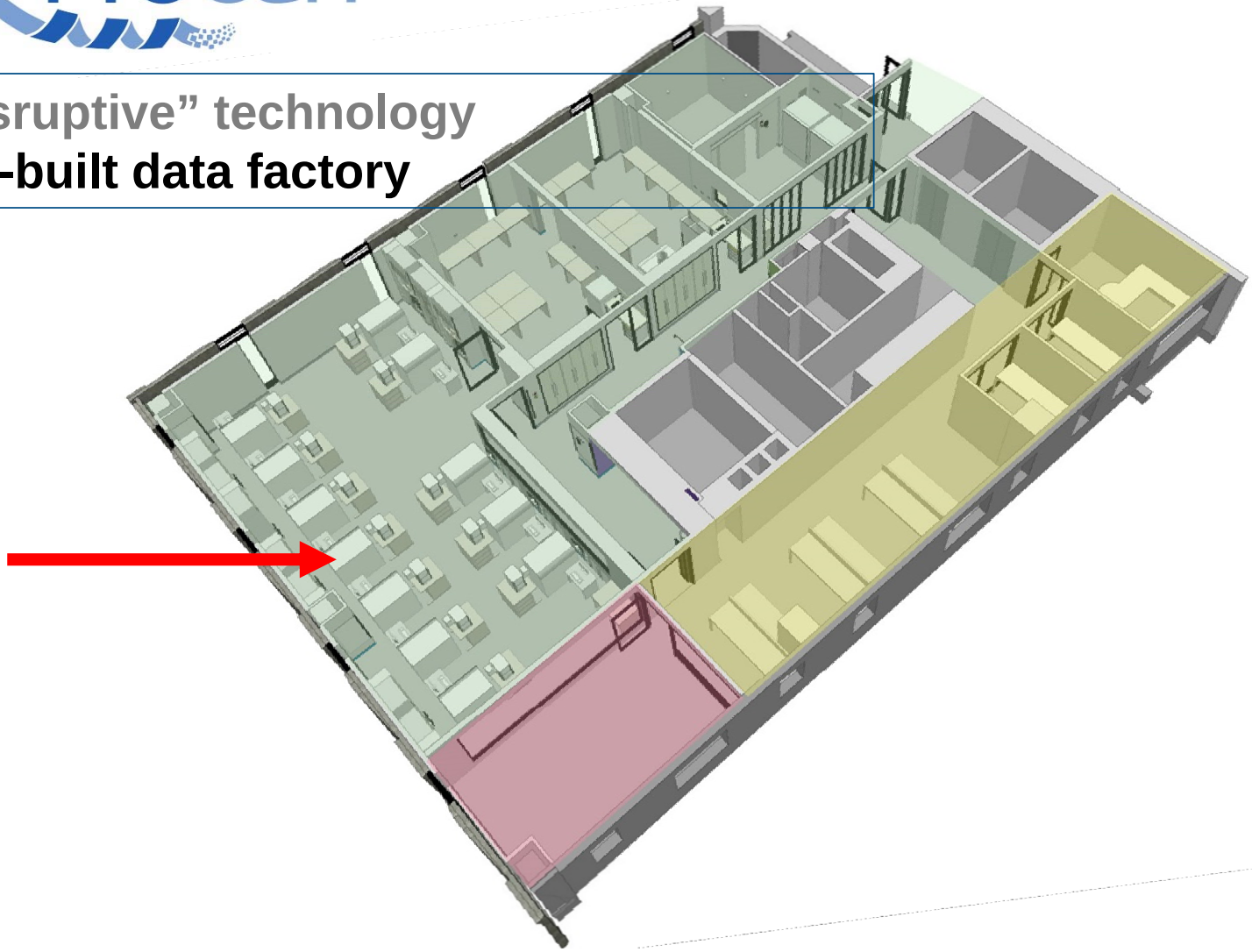

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ProCan's technology

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"Industrial" scale

One of only two "industrialised" proteomics centres globally and the only one focused on cancers

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ProCan's timeline

-10 years: PCT

-5 years: SWATH-MS

PCT-SWATH MS

2015: Proof of principle (kidney cancer)

Dec 2015: $10 million ACRF Award to ProCan

Sept 2016: ProCan launch

Feb 2017: First project

5-7 years: 70,000 cancers analysed

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Outcomes

Year 2-3: replace most or all existing cancer diagnostics

Year 5: computation-based diagnosis and individualised treatment-decision report

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Outcomes

Name:	Jane Citizen
Med Rec No.:	12345678
Sample:	1 mg lower medial quadrant L. breast
Procedure date:	26 August 2022
Report date:	28 August 2022
Classification:	Adenocarcinoma breast Luminal-B “Metastatic Risk-3”
Proteins:	Estrogen Receptor – positive (xxx Units) Progesterone Receptor – positive HER-2 – negative BRCA1 – low “Protein YY – high”
Responds to:	Antiestrogen – 95% PARP inhibitor – 78% “New drug XX” – 88%

DNA data also?
Other ‘omics?

Outcomes

- Replace most or all existing cancer diagnostics
- Faster
- More objective – same quality for patient in rural Australia as in major city hospital
- Cheaper?
- Enhanced ability to predict best treatment for individual patient
- Discovery of new cancer treatment targets?

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ProCan Collaborations

Every aspect of the ProCan project is designed to be collaborative on a national and international scale

The 70,000 tumours will be supplied by ~100 different collaborating research groups

Data will be made available to other researchers and clinicians globally

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ProCan Collaborations

CANCER MOONSHOT

ProCan collaboration with Cancer Moonshot announced by Vice-President Joe Biden on 17 July 2016

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ProCan Collaborations

Ideal collaborations:

- **Clinical expertise!**
- **Retrospective collection of tumours with <u>treatment outcomes already known</u> (or prospective collection where outcomes will be known within a few years)**
- **Cohort has been collected for the purpose of addressing an important clinical question (e.g., as part of a clinical trial)**
- **Other 'omic data already available (e.g. whole genome sequencing)**
- **Tumours contribute to a balanced representation of all cancer types within ProCan's 70,000 tumour capacity**

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Data Platform

Future routine testing (also clinical trials)

- ‘Omics data pre-treatment
- Outcome data captured routinely (with appropriate consent)

ProCan “data factory”

- Proteomics
- Other ‘omics capacity to be added if justified

Other data sources

- Clinical
- Other ‘omics
- Other high-throughput proteomics facilities in future?

Global Data and Computational Platform

- ‘Omics data
- Clinical data esp. treatment outcomes
- Algorithm-driven individualised treatment recommendations

(self-learning system)

ProCan Personnel

Skills of core facility team include:
- **proteomics**
- **anatomical pathology**
- **laboratory management**
- **software engineering**
- **bioinformatics**
- **health economics**

Many opportunities for involvement of PhD students and clinical trainees, especially :
- **medical oncology**
- **radiation oncology**
- **surgical oncology**
- **anatomical pathology**
- **biochemical pathology**
- **clinical bioinformatics**

Team leaders
Proteomics (Scientific Director): Tiannan Guo
Anatomical Pathology: Rosemary Balleine
Software Engineering: Brett Tully
Bioinformatics: to be appointed soon

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Funding model

It is our intention to source all of the funds needed to provide the proteomics data to our collaborators “in exchange” for everything that they bring to the collaboration (clinical expertise, tumour sets and associated data).

We will also be very happy to submit joint grant applications to help obtain operating expenses for proteomics.

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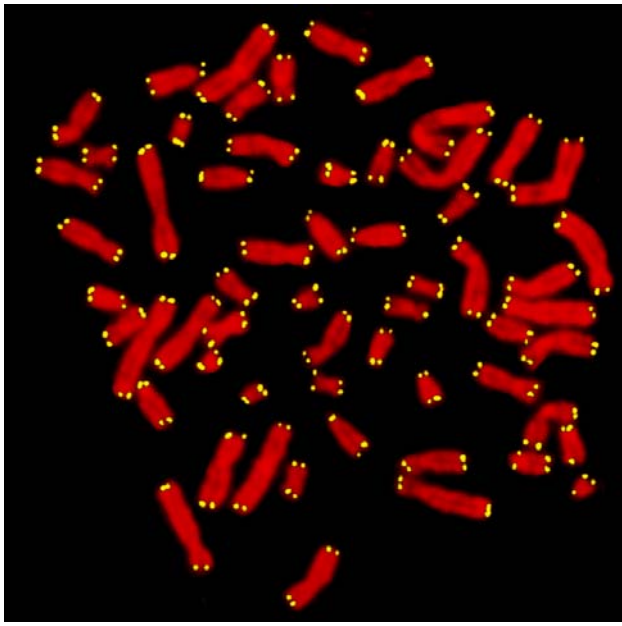
Finally ……



CMRI has substantial expertise in telomere research and DNA repair.

Telomere length, telomere length maintenance mechanisms, and DNA repair processes are very likely to contribute to outcomes of cytotoxic chemotherapy and radiation treatment.

All of these parameters will be explicitly measured as part of the ProCan project.

Outcomes

Name: Jamie Smith
Medicare No.: 12345678

Sample: Brain tumour

Date of procedure: 16 Sept 2021

Date of report: 18 Sept 2021

Tissue classification: Glioblastoma
De novo
Molecular category 4

Response markers: MGMT – low (xxx Units)
EGFRvIII – high
VEGF - high
PDGFR – high
PML - low
Protein XX – high

Likely response to: 1. Temozolomide
2. Tyrosine kinase inhibitor
3. Cancer-killing virus treatment
4. New treatment targeting protein XX

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NSW GOVERNMENT | cancer institute NSW

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