CHILDREN'S MEDICAL RESEARCH INSTITUTE
Jeans for Genes®

ProCan®

ProCan®

Proteomic Patient Selection Tools for Oncology Clinical Trials

ProCan® is a global first cancer research program and facility producing high-throughput, cancer proteomic data from a single platform across all types of human cancer. Our programs are clinician-led, our focus is oncology and we have established an in-house database containing the proteomic analysis of many thousands of tumor samples together with clinical outcome data regarding the patients' subsequent treatment.

Patient Selection Tools • Oncology focus • Clinician-led • In-house data sets

Previous Limitations

The biology of each individual cancer is primarily driven by its protein content. Proteins play key roles in cellular processes and most effective cancer treatments target proteins rather than genes.

Cancers continue to mutate randomly after they form and those which look similar by microscopic examination may differ markedly in their molecular composition. This accounts for differences in their response to treatment. Consequently, personalised treatment is essential to achieve optimal outcomes, but accomplishing this task in a clinically-relevant time frame and cost-effective manner remains a major challenge.

Currently, the molecular data available to cancer clinicians is primarily in the form of information concerning a small number of proteins via immunohistochemical (IHC) staining of tissue sections or, in some cases, genomic data. While helpful in identifying driver mutations, genomic and transcriptomic data are incapable of predicting the proteome sufficiently accurately. The limited amount of protein data available by IHC is a major impediment to personalised cancer treatment.

Oncology clinical trials, like all clinical trials, often fail due to suboptimal patient selection. Consequently, there are many oncology drugs with very good efficacy in a small number of patients that have been shelved due to an inadequate overall response rate. Given the time and expense involved in conducting clinical trials, improving patient selection methods through the identification of proteomic signatures in responsive patients would greatly increase the efficiency and outcomes of such trials. In some cases, it may also present the opportunity to resurrect some previously failed drugs.

Current Technology

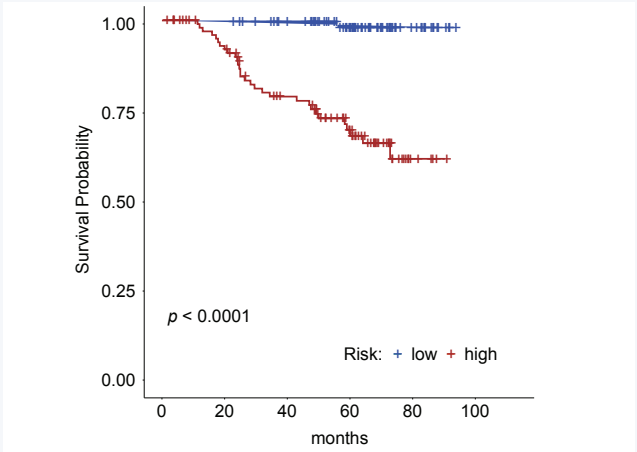
Until recently methods for reliably analysing all proteins in a tissue (the proteome) in a clinically-relevant manner have not been available. This started to change with the advent of the technology combiningPressure Cycling Technology (PCT) with SWATH mass spectrometry (MS), a Data-Independent Acquisition (DIA) MS approach, in 2015. This technology npw generates high quality, large scale, proteomic data rapidly (within 24-36 hours), from small cancer samples.

Installation of six SWATH-MS mass spectrometers alongside multiple PCT machines in the purpose-built ProCan® facility, created the potential for large-scale, high-throughput analysis of the human cancer proteome. Extensive further development of the technology has resulted in a highly reliable analytic pipeline that produces reproducible proteomic data across the suite of mass spectrometers and over long time periods.

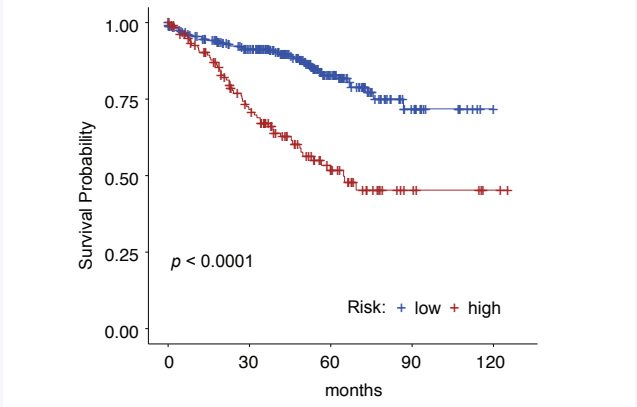
ProCan® Capabilities

ProCan® has a multidisciplinary team that includes board-certified medical oncologists, histopathologists, proteomicists, data scientists, software engineers and an operations group. After several years of development and optimisation, ProCan® is now operating in a high throughput manner. Collaborations are ongoing with many cancer research groups in Australia, Europe, UK, USA, Canada and Japan, to analyse cohorts of pre-treatment cancer tissue samples which are annotated with clinical information including treatment outcomes an wherever available, the proteomic data are compared with other 'omic' data. Procan® is reliably identifying proteomic signatures that define, for example, a tumor's site of origin, and proteomic-based risk scores that can categorize patients into high- and low-risk groups in terms of prognosis and/or chance of responding to a specific treatment. Figure 1 provides three examples of prognostic signatures for prostate cancer, colorectal cancer and advanced melanoma.

A: Prostate Cancer Prognostic Proteomic Signature



B: Colorectal Cancer Prognostic Proteomic Signature



C: Advanced Melanoma Prognostic Proteomic Signature

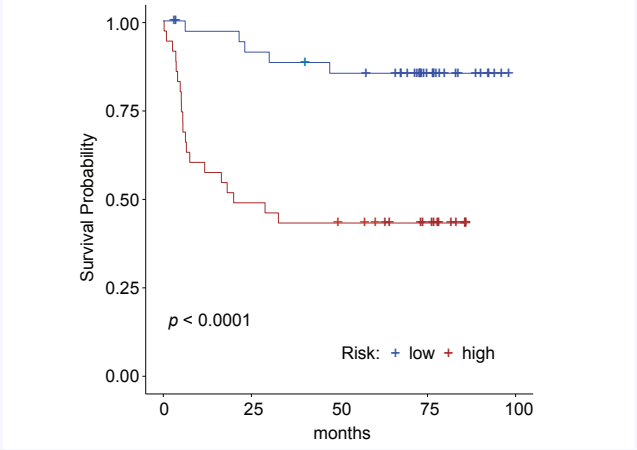


Figure 1: Examples of prognostic proteomic signatures

Personalised Treatment

ProCan® aims to improve cancer treatment decisions through the use of proteomic data that is interpreted by computational analysis of a database of proteomic and associated clinical data, together with other 'omic data, for tens of thousands of tumor samples. The research program is identifying molecular signatures (biomarkers) within the proteomic data that can be used to predict the response of individual cancers to specific treatments. This will enhance the ability of oncologists to identify the most suitable cancer treatment for each patient, improving the treatment outcome and avoiding the side-effects of treatments that would be ineffective for that patient.

Improved Clinical Trials and Drug Development

ProCan® has the ability to identify biomarker signatures for particular drugs (new or abandoned) thereby assisting with clinical trial design and cohort selection. This may reduce costs and time involved in conducting clinical trials as well as optimising the success of the trials.

By identifying proteomic signatures of response during early-stage clinical trials, investigators will have a tool to select patients for later-phase clinical trials, whose cancers exhibit the previously identified signatures.

It is also expected that the large cancer proteomic database being generated by ProCan® will underpin the identification of new treatment targets and new indications for existing drugs.

Partnering

Seeking companies in early phase oncology trials looking to develop effective patient selection tools for later-stage clinical trials.

Worldwide, ProCan® is a unique centre, exclusively focused on cancer.

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