SickKids
Industry Partnerships & Commercialization

TECHNOLOGY BRIEF

DIAGNOSTICS & RESEARCH TOOLS

Machine learning-driven NGS-based diagnostic tests to optimize clinical response in oncology

BACKGROUND

Tumour cells circumvent normal DNA repair safeguards which allow for the accumulation of genetic mutations that drive tumour growth. Tumour Mutational Burden (TMB) is increasingly recognized as a potential prognostic biomarker for response to precision therapeutics such as immune checkpoint inhibitors (ICI). Existing methods (based on a universal TMB cut-off point of 10 mutations per megabase (hyperTMB)) to assess candidacy for, and relative response to, ICIs have improved treatment for some types of cancers, but are an imperfect indicator and fail to accurately identify the ideal target patient population across all cancers.

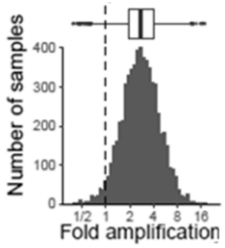

Fig 1: Histogram showing the transcriptional output of 6,095 cancers

RNA (transcriptional) content of rapidly proliferating tumour cells is greater than that in normal cells and suggests that cells which globally increase transcription have a growth advantage over those that cannot. Increased transcriptional output measured using RNA amplification by our researchers was determined to be an independent prognostic marker for disease outcomes across over 6,000 patient samples and 22 cancer types.

DESCRIPTION OF THE INVENTION

The Tabori and Shlien labs have developed the first direct method to quantify RNA output in tumour samples. Amplified RNA output detected and analyzed by their proprietary machine learning algorithm "RNAmp" determined that RNA amplification (hyperTX) measured by RNAmp is a precise, prognostic indicator of patient survival; patient groups with increased RNA levels have significantly worse survival.

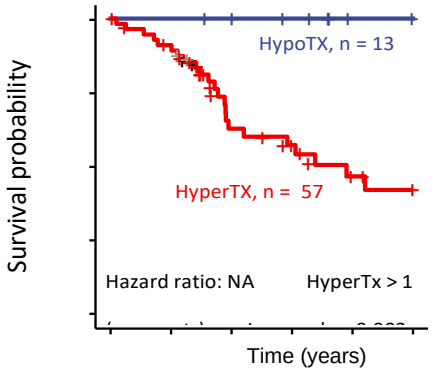

Fig 2: Survival differences based on RNAmp

Non-hyperTMB tumours, identified as hypoTX by this invention, express more mutations and were as responsive to immune checkpoint inhibitor (ICI) as hyperTMB patients (62% vs 68% respectively). As these non-hyper TMB patients are not regularly selected for ICI therapy, RNAmp biomarker analysis

KEYWORDS
Cancer, tumor, biomarker, diagnostic, prognostic, hypermutant, amplification

reveals a new segment of the tumour patient population for ICI therapy and improved patient outcomes.

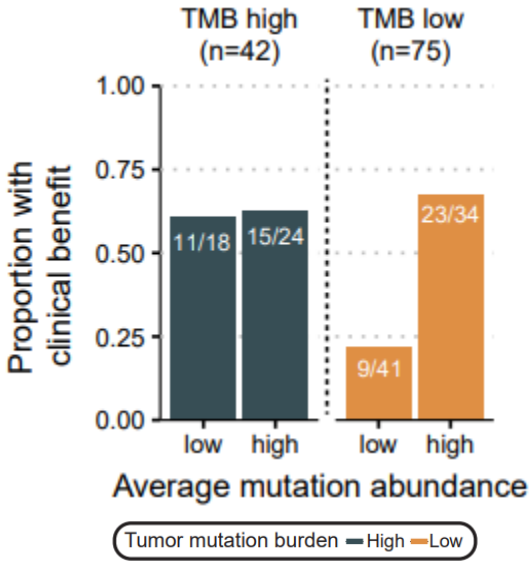

Fig 3: Clinical benefits differ for patients with different TMBs

COMMERCIAL APPLICATIONS & ADVANTAGES

While many companies and institutions perform cancer gene testing, the utility of these tests has limitations. In addition, the introduction of hyperTMB as a complex biomarker for tumour treatment has illustrated the need for more accurate methods within specific tumour types and subclasses. There remains a large unmet need to reliably determine patient responsiveness to treatments, as a large segment of cancer patients exhibit resistance toward immunotherapies. Our invention addresses this need and accurately identifies immune checkpoint inhibitor responders within low TMB tumour patient populations.

This first-in-class Tumour Profiling Test based on amplified RNA signatures developed by the Tabori and Shlien labs is unparalleled in the industry.

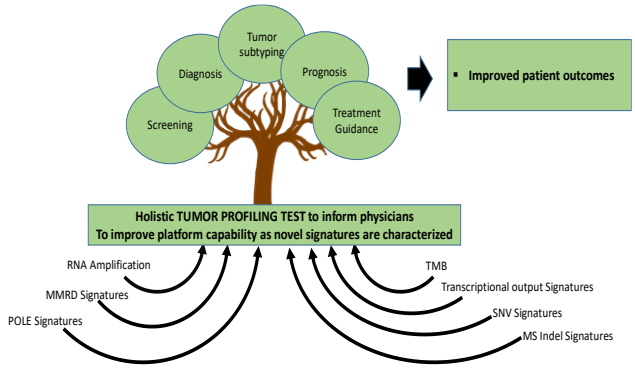

Fig 4: Clinical utility of RNAmp biomarker

Combining the lead asset of RNAmp with numerous diagnostic tests developed at SickKids, such as genomic hyper mutant analysis, MSI, SNV, MMRD and POLE signatures, provides a company creation/investment opportunity with a unique position in the industry providing:

- Novel assays for tumour subtyping and diagnosis
- Unparalleled prognostic biomarker accuracy
- Predictive patient responsiveness to cancer treatments

With a $400M diagnostic market for ICI therapy alone, this opportunity represents a chance to enter at the forefront of precision, complex biomarker analysis.

DEVELOPMENT STAGE

Prototypes developed.

PATENT STATUS

PCT and provisional patent applications filed.

IP&C is seeking partners to advance this technology.

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