Blood-based Cancer Diagnostic Signature

A signature of Nuclear Transport Proteins expressed in serum of patients has the potential for non-specifically detecting early-stage cancer

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Background

Cancer disease is frequently only diagnosed at a late stage when treatment options are limited. The challenge is that not all cancers behave the same, and the gold standard diagnostic test thus remains an invasive biopsy of the tumor once it is found.

Consequently there remains a need for a simple and quick “rule-in rule-out” blood test capable of non-specifically identifying cancer, which can then initiate a more thorough assessment to diagnose the specific cancer. Such test could increase the likelihood of an early diagnosis, ensure early treatment is initiated, and improve survival rate.

Technology Overview

The nucleus of a cell is central to the wellbeing of any living organism. It stores and organises information from other cellular components and protects this information. It communicates with the rest of the cell, exchanges RNA and facilitates several important processes.

The nuclear envelope is a double membrane surrounding the nucleus and contains pores forming part of large complex of proteins known as the Nuclear Pore Complex (NPC). Any material entering or exiting the nucleus must past through the NPC.

Nuclear transport proteins (NTPs) are proteins that assist with the transport (import or export) of large molecules, such as RNA, across the nuclear membranes of cells and through the NPC. Examples of nuclear transport proteins are the Karyopherins.

Early research at UCT by Prof Virna Leaner and Dr Pauline van der Watt showed that Crm1 and Karyopherin β1 (Kpnβ1), also known as Importin β, are overexpressed in cervical cancer and are critical for cancer cell survival and proliferation.[1] Others have also identified that some nuclear transport proteins are elevated in various cancer cell types. However, the inventors were the first to have identified a signature of nuclear transport proteins in the serum of patients that is indicative of cancer versus no-cancer.

More specifically, the inventors have identified a total of 7 nuclear transport proteins (Kpnβ1, CRM1, Kpnα2, CAS, Ran, Ipo5 and Tnpo1) that are secreted by cancer cells as a family and detectable in serum. These 7 proteins, identified following a screening process of about 26 related NTPs, together provide exceptional predictive ability for non-specifically detecting cancer, even early-stage cancer. The results are highly promising and patent applications haven filed. This indicates strong potential utility as a cancer diagnostic.

The ability to discriminate between cancer and no-cancer was evaluated for different combinations of the seven proteins, including each one individually. As an example, the combination of all seven candidate biomarkers gave an Area-under-Curve (AUC) of 0.944 with a sensitivity of 92.5 % at 86.8 % specificity, which is exceptional ability to discriminate between cervical cancer cases and non-cancer controls. The same combination gave an AUC of 0.963 with a sensitivity of 95.3 % at 87.5% specificity, which indicates exceptional ability to discriminate between oesophageal cancer cases and non-cancer controls.

[1] P.J. van der Watt, C.P. Maske, D.T. Hendricks, M.I. Parker, L. Denny, D. Govender, M.J. Birrer, V.D. Leaner, "The karyopherin proteins, Crm1 and karyopherin beta1, are overexpressed in cervical cancer and are critical for cancer cell survival and proliferation", Int. J. Cancer 124 (2009) 1829–1840. https://cansa.org.za/files/2012/05/Karyopherin-proteins-Crm1-and-Karyopherin-b1.pdf).

Benefits

The main benefit is the potential ability to non-specifically detect cancer, even early stage cancer, through a simple blood test. This will ensure patients are diagnosed early and are put on anti-cancer treatment earlier, which could reduce the total cost of treatment and increase the survival rate. The technology can also potentially be used to track efficacy of anti-cancer treatment, and therefore serve as a companion diagnostic to anti-cancer therapies.

Applications

- A blood-based early-stage cancer diagnostic.
- Prognosis tracker for cancer therapeutics.
- Companion diagnostic alongside cancer therapeutics such as nuclear transport protein inhibitors.

Opportunity

UCT is looking for a partner to further test this technology and develop this into a commercial diagnostic test through regulatory approvals. The ideal commercialisation modality is a license.

Patents

- PCT patent application number PCT/IB2021/061690
- UK patent application number 2019682.0

IP Status

- Patent application submitted
- Provisional patent

Seeking

- Development partner
- Commercial partner
- Licensing