

SPEAKER SPOTLIGHT:

The Future Of Peptides As Immune-Boosting Therapeutics

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Who is InterK Peptide Therapeutics Limited?

InterK Peptide Therapeutics Limited is an Australian unlisted public company with a small laboratory located in Sydney that operates as a late preclinical stage, virtual biotech, ie, a business model whereby personnel and operating overheads are minimized by outsourcing the majority of its R&D activity to selected contract research organisations along the eastern seaboard of Australia and overseas. This has enabled InterK to avoid the typically high infrastructure costs associated with traditional biopharmaceutical organisations whilst retaining all intellectual property rights. Since its inception the Company's R&D programme has pursued a combination of rational- and screen-based peptide design arising from synthetic modifications of naturally-occurring cell adhesion receptors.

What are some of the key accomplishments of InterK Peptide Therapeutics during the past few years?

InterK's small peptide-based compounds were initially screened against cancer cell lines with

the surprising finding that biochemical changes identified at nanomolar concentrations did not translate into growth inhibition. In order to resolve this conundrum the majority of protein kinases within the human genome were screened with the key discovery being activation of a specific kinase involved in the T cell receptor (TCR) immune response.

The kinase, called lymphocyte-specific protein tyrosine kinase (Lck), is critical in the early propagation and modulation of the TCR response against cancers and infectious agents. Lck is a member of the Src Family Kinases (SFKs) and, importantly, no selective activators of this kinase that do not also stimulate unwanted activity of other SFK members, have been identified to date.

The discovery has enabled InterK to identify an expanded repertoire of Th1-immune boosting effects *in vitro/in vivo* that has translated into tumour growth inhibition in animal models of melanoma and lung cancer in parallel with immune-boosting effects *in vivo*. A potential application for one of the peptides is also in anti-aging/skin care given that it inhibits UV-irradiation-induced DNA damage and collagen breakdown. In addition, related immune-boost-

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Dr Michael Agrez, MB,BS, MS, PhD, FRCS, FRACS, is Chief Executive Officer and Chief Scientific Officer of InterK Peptide Therapeutics Limited based in Sydney, Australia. InterK functions largely as a virtual biotech company with most of its R&D program being conducted as contract research undertaken by high-profile institutions along the eastern seaboard of Australia and overseas. The company's focus during the past ten years has been on development of peptides that boost the immune system. During his 30 year tenure with The University of Newcastle, Australia, Dr Agrez published numerous articles in international peer-reviewed journals that cover aspects of epidemiology, cancer screening, molecular biology and biochemistry whilst also being actively involved in healthcare administration and management. His academic contribution as a surgical scientist was acknowledged by the Royal Australasian College of Surgeons in the form of a national award in 2000 given to only one Australian surgeon that year.

ing peptides exhibit analgesic effects in animal models equivalent to morphine that has particular relevance to cancer patients given the immuno-suppressive effects of morphine.

Do peptide therapeutics have a promising future?

Peptides are short chains of amino acid monomers linked by amide bonds and are distinguished from proteins on the basis of size, ie, generally understood to contain approximately 50 amino acids or less. Notwithstanding the increasing cost of commercialisation and stringent regulatory controls the global peptide therapeutic market that was valued at US\$22 Billion in 2017 is expected to double by 2025.

Peptide therapeutics can offer advantages compared with small-molecule pharmaceutical ingredients that include selectivity with decreased off-target effects and, thereby, less toxicity combined with increased potency.

The current clinical pipeline is robust and is composed of approximately 130 peptide therapeutics with the top three therapeutic areas in Phase I- III studies being oncology, metabolic and infectious diseases. The cancer segment

is anticipated to dominate the application segment of the market in the next few years given the rise in death rate due to cancer and the increase in research activities for treating cancer patients.

What are InterK's main priorities in the immune-boosting space and current challenges?

Key global unmet needs in cancer treatment are to increase the responsiveness of immune cells to existing immunotherapy approaches and to identify reliable biomarkers that can predict responsiveness to checkpoint blockade immunotherapy. A priority for InterK's clinical study commencing early 2020, that involves patients who receive immunotherapy for advanced melanoma, is to determine from pre-and post-treatment blood samples whether immune cells isolated from non-responding patients can nevertheless be stimulated by InterK's peptides *ex vivo* and whether a "peptide signature" exists prior to treatment that can identify patients who are likely to respond.

Other priorities for InterK include formulation and clinical testing of the potential anti-aging/

skin care peptide and demonstration that the non-opiate analgesic peptides which inhibit kinase signalling known to be involved in drug addiction display efficacy against opioid addiction in a conditioned place preference behavioural animal model.

InterK also faces a number of challenges. For example, as a small, virtual biotech there are resource limitations and timely conclusion of contractual sponsored research is often delayed given competing priorities within academic institutions. In addition, enhancing both oral peptide absorption and half-life as well as targeting the tumour microenvironment remain on-going challenges.

Where is the peptide industry heading within the next few years?

Closing the gap between “market actual” and “market potential” remains a challenge during the next few years largely attributable to challenges with the route and method of delivery of peptide drugs.

Oral delivery whilst desirable needs to ensure achievement of therapeutically-relevant bioavailability with an inverse relationship existing between molecular weight and bioavailability. Notwithstanding that the parenteral route dominates the administration segment of the current peptide therapeutics market because of easy availability of peptide drugs in a form that can be administered parenterally, the oral segment of the market is anticipated to show the fastest growth rate in forthcoming years.

Improvements in oral bioavailability and targeting strategies that include peptide-antibody and peptide-nanopolymer conjugates as well as combinatorial approaches to simultaneously target ligands and their respective receptors and/or in combination with existing immunotherapy such as checkpoint blockade for the treatment of cancers will fuel the

demand for peptide therapeutics in forthcoming years. In addition, potential applications in nervous system, gastrointestinal, cardiovascular and respiratory disorders will further increase this demand.

What prompted InterK’s attendance at the Congress and what does InterK hope to gain from attending this type of conference?

Until now InterK has functioned somewhat below the radar in terms of advertising its immune-boosting peptides so as to constantly strengthen the scientific data underpinning its discoveries. The 7th Annual peptides & Oligonucleotides Congress offers a program of both breadth and depth within its Peptide-Focussed Streams presented by a field of international experts from industry and academia that has particular relevance to InterK’s R&D programme. In particular, the opportunity to learn more about the latest innovations in peptide synthesis is likely to benefit InterK in terms of market access for its peptides.

If the outcome of InterK’s clinical study indicates that for non-responding melanoma patients putatively “exhausted” immune cells can nevertheless be boosted by its peptides *ex vivo* just as has been demonstrated in a murine model of T cell exhaustion, then future human clinical trials are envisaged. Hence, InterK hopes that participation at the Congress will provide collaborative opportunities that can address formulation and delivery challenges for its suite of peptides that will facilitate their use not only in combinatorial cancer clinical trials but also in the areas of aged skin care, non-opiate analgesic administration and management of drug addiction.