

>>>RAGE PROJECT - an opportunity for novel anti- inflammatory drug development

>>>market opportunity

The Inflammatory Diseases market is the largest in the world with a value in excess of US\$30 billion per annum. Rheumatoid arthritis, sepsis, atopic dermatitis and multiple sclerosis are some of the most common inflammatory related diseases. The value of anti-inflammatory drug development is set to explode over the next 5 years.

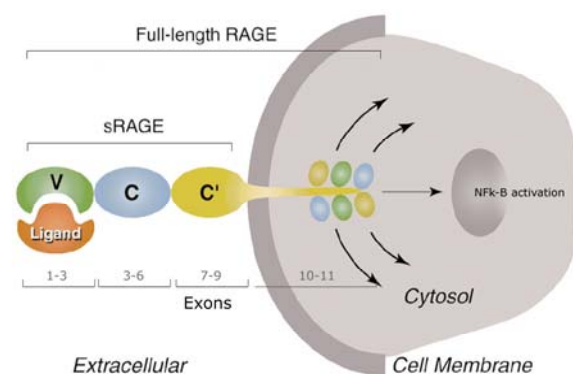
>>>competition

The increased longevity of the population has seen greater demand for anti-inflammatory products due to the association between ageing and these disorders. A number of anti-inflammatory products are in development and competition is expected to increase dramatically in the future. The opportunity for new discoveries and drug development in this ever growing and competitive marketplace is therefore vast

An increasing number of research groups are presently working on RAGE as a target for anti-inflammatory drug discovery. However, the unique approach taken in this project provides a competitive advantage.

>>> project description

The Receptor for Advanced Glycation End products (RAGE) is a member of the immunoglobulin super family and has been implicated in inflammatory diseases diabetes, amyloidoses and tumour metastasis. The receptor was first identified in 1992 as a binding target for advanced glycation end products (AGEs). RAGE binds a variety of seemingly unrelated ligands that includes amphoterin, calgranulins, AGEs and sheet fibrils characteristic of amyloids. As the activation of RAGE by these various ligands contributes to the progression of the various pathologies, it represents an excellent target for pharmacological intervention.



Soluble forms of RAGE (sRAGE) are naturally secreted and prevent the adverse effects of RAGE signalling by acting as a decoy. Furthermore, the administration of sRAGE or anti-RAGE antibodies reduce the symptoms and progression of its associated disease states. Limitations of sRAGE as a therapeutic agent are its inability to cross the blood brain barrier, difficulties and costs associated with large-scale production of a glycosylated protein and the variations of half life on administration.

The development of RAGE small molecule antagonists represents an exciting opportunity for the treatment of the numerous diseases associated with RAGE activation.

>>>progress

The team has cloned the gene for human RAGE and developed a number of constructs of sRAGE incorporating its various extracellular domains. The minimum requirements for ligand binding of sRAGE, including domain construct size and level of glycosylation are being characterised. Structure determination will also be undertaken. Following elucidation of the structure of sRAGE at the atomic level, WABRI will apply its advanced drug discovery capabilities to fast track the development of new therapeutics for a range of RAGE related diseases.

>>>intellectual property

No IP protection has been sought for this work at this stage. All rights to exploit the technology vest with the Western Australian Biomedical Research Institute through Curtin University of Technology.

>>> expected outputs of the project

The development of therapeutics to attenuate inflammatory responses in a number of diseases including rheumatoid arthritis, sepsis, atopic dermatitis, multiple sclerosis, Alzheimer's Disease and diabetes.

>>>further information

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