

Macrophage Migration Inhibitory Factor (MIF) & blocking its impact

Director:
Professor David de Kretser, AO

Executive Director:
Professor Adrian Walker

Centre Directors:
Professor Paul Hertzog
Professor Stephen Holdsworth
Dr Michael Holland
Professor Martin Pera
Professor Gail Risbridger
Associate Professor Peter Rogers

Macrophage Migration Inhibitory Factor or MIF is a natural inflammatory protein or 'cytokine' that contributes to the harmful effects of the immune system and drives inflammation and damage in diseases like rheumatoid arthritis, multiple sclerosis and lupus. MIF stimulates immune cells in the tissues affected by these diseases, and blocks the effectiveness of steroids.

Development of a MIF antagonist or mechanism to block the impact of this protein is the basis of a new treatment for arthritis and other inflammatory disease currently being developed at Monash Institute of Medical Research's (MIMR's) Centre for Inflammatory Diseases.

MIF has an unique relationship with the steroids which are often used to treat inflammatory diseases. Levels of MIF are actually increased by corticosteroids. These increased levels of MIF then limit the effectiveness of the corticosteroids. The presence of increased MIF following corticosteroid treatment means that corticosteroids work less efficiently.

Therefore, antagonizing MIF might provide a means to increase the effectiveness of corticosteroids, thus reducing the dose required to achieve a required effect. This is known as a "steroid-sparing" effect. As steroid side effects are dose dependent, steroid-sparing would be of immense value to patients.

Small molecule cytokine antagonists

The core technology for this new therapy is a small molecule cytokine antagonist. Inflammatory diseases can be successfully targeted with anti-cytokine therapies. Small molecule cytokine antagonists have never previously been developed. However it is anticipated that a simple tablet can be developed, which is both effective and economically priced, allowing more patients to receive treatment.

A Melbourne-based biotechnology company Cortical, which has been established to commercialise this therapy, is working closely with MIMR to bring this drug to market.

Cortical has major funding from a consortium of investors both in Australia and the United States and also has a \$3 million R&D Start Grant from AusIndustry to conduct Phase I clinical trials.

A model of the 3-D structure of MIF,
showing the MIF antagonists in purple

