A new enzymatic target for treatment of fibrosis and a series of highly potent ‘drug-like’ inhibitors of this target. These inhibitors show up to 100x greater potency than leading clinical compounds in functional assays of fibrosis. The compounds are now being assessed in animal models of fibrosis.

**THE TECHNOLOGY**

Researchers from the Monash Institute of Pharmaceutical Sciences have identified a new anti-fibrotic enzymatic target and developed a number of highly (nM) potent drug-like inhibitors (all within Lipinski’s rules) for in vivo testing.

A well-known starter compound with a previously ill-defined mechanism of action was shown by the Monash researchers to be an inhibitor of this target and to be efficacious in a bleomycin model of idiopathic pulmonary fibrosis (IPF). Monash medicinal chemists have synthesised a series of novel compounds with improved potency and selectivity. For example, MIPS-247 demonstrated dose dependant reductions in collagen production in in vitro models of fibrosis (Fig.1) and was up to 100 times more potent in the inhibition of collagen secretion from TGF-β activated myofibroblasts than leading clinical compounds, including Roche’s Pirfenidone and Shire’s FT011.1,2

The Monash compounds are now being assessed in animal models of fibrosis, including IPF, LAD-ligation, urinary ureteral obstruction, etc.

**THE OPPORTUNITY**

Monash is seeking a partner to complete preclinical assessment of its advanced lead series, nominate a clinical candidate and undertake clinical trials.

The researchers together with the Faculty of Pharmacy and Pharmaceutical Sciences have extensive academic and industrial experience in medicinal chemistry and in taking molecules from the research laboratory into the clinic.

**References**


**Figure 1**: A & B: MIPS-247 shows dose dependent reduction in collagen production in TGF-β and Ang II stimulated rat neonatal cardiac fibroblasts (NCF). C: MIPS-247 shows dose dependent reductions in Ang II stimulated hypertrophy in rat neonatal cardiomyocytes (NCM).

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