We have identified and validated a novel anti-fibrosis target. Inhibition of this target with proprietary small molecule lead series completely reversed cardiac and renal fibrosis in clinically relevant disease models. We now seek a partner to develop novel lead candidate inhibitors as safe and effective anti-fibrotic drugs.

**THE CHALLENGE**

Fibrosis is caused by excess accumulation of extracellular matrices such as collagen. Chronic and progressive tissue fibrosis causes pathology and dysfunction in many organ systems. Activation of the renin-angiotensin system as well as oxidative stress and inflammation pathways are all implicated in the pathogenesis of cardiovascular and renal fibrosis.

Currently, there are no specific anti-fibrotic therapies available for cardiac or renal fibroses. Angiotensin converting enzyme inhibitors and angiotensin AT1 receptor blockers improve functional parameters and overall survival (~7% reduction in cardiovascular mortality) but have only a modest effect on regressing total collagen fraction.

There is a clear need for new drugs that can reverse fibrosis in affected individuals and prevent the development of fibrosis in at-risk individuals. Ideally the drugs will be tissue-protective, acting without adversely disrupting collagen metabolism in other organs.

**THE TECHNOLOGY**

Monash Researchers have identified a new target and developed lead series inhibitors for the prevention and treatment of cardiac, kidney and other organ fibroses.

**Target**

- Target deficiency/inhibition protects against the development of cardiac and renal fibrosis in aged mice and cardiac fibrosis in Ang II-treated mice (Fig.1).
- Target inhibition completely reverses cardiac fibrosis in aged mice (Fig.2), corresponding with decreases in inflammatory and oxidative stress markers and increase in NO bioavailability.
- Target deficiency/inhibition protects against ischemia-reperfusion damage (Fig.3) and improves function of aged ischemic hearts.
- Target inhibition reverses age-mediated renal fibrosis

**Lead series**

Two structurally distinct small molecule lead series having sub-μM potency and high selectivity for the target have been developed. These have significant anti-fibrotic efficacy in a range of animal models.

**Intellectual property:** Two patent applications covering lead series composition (PCT/AU2016/050332) and use of target inhibitors in fibrosis treatment and prevention (AU Prov 2015903035).

**THE OPPORTUNITY**

We seek a partner to optimise the lead series and develop new lead drug candidate(s) against this exciting target. The Monash team has extensive experience in the target and fibrosis biology, having an array of in house models including in vitro target screen, functional assay, specific knockout models, fibrosis and other pathological models, plus target SAR and preclinical profiling.

---

**Figure 1:** Target gene deletion protects against development of age-induced cardiac fibrosis

**Figure 2:** Complete reversal of age-induced cardiac fibrosis after chronic 4 wk. s.c. infusion in 22 mth aged C57Bl/6J mice with 3 distinct classes of target inhibitor.

**Figure 3:** Large reduction in infarct volume (arrow) in target KO and inhibitor-treated mouse heart following ischemia-reperfusion.

---

**KEY CONTACT**

Dr Kathy Nielsen
Senior Commercialisation Manager
Monash Innovation
T: +61 3 9905 5918
E: katherine.nielsen@monash.edu