MONASH University

Engineering a safer mineralocorticoid receptor antagonist for heart failure

THERAPEUTIC: CVD

Product Type	Small molecule
Indication / ROA	Cardio-vascular diseases such as heart failure, suitable for high risk HF patients with co-morbidities such as renal disease or diabetes/oral delivery
Target / MoA	Tissue-selective mineralocorticoid receptor (MR) antagonists, targeting heart but not kidney
Development Stage	Lead series
Brief Description & Differentiation	Current MR antagonists have proven clinical benefit in >30% patients with heart failure and cardiovascular disease. However, their clinical use has been severely limited by safety issues, in particular, an increased risk of hyperkalemia (increased serum potassium), a serious on-target side-effect caused by MR blockade. Hyperkalemia is associated with cardiac arrhythmia and increased all-cause mortality. We are developing new compounds that are potent inhibitors of cardiac MRs, but are less active against MRs in the kidney. Retaining normal MR biological function in the kidney will avoid the cellular mechanism that causes hyperkalemia (unlike current MR antagonists).
Research Team	Prof. Jonathan Baell (Monash Institute of Pharmaceutical Sciences), Dr. Morag Young (Hudson Institute for Medical Research)
Intellectual Property	• New composition of matter potential • SAR strategy, key biological assays and preclinical models are established in house for drug optimization.
Key Publications	Yan J. & Young MJ (2016) *Current Opinion in Pharmacology 27*:78–85
Future	Partner to advance lead series and develop a drug candidate that is potent and selectively targets cardiac MR.

➢ Key Data

Proof-of-Concept: Preliminary compounds have been developed that are several fold more selective against mineralocorticoid receptors in heart versus kidney cells.

We have developed further analogues with improved potency and are currently working to maximize selectivity and establish efficacy *in vivo*.