Systems genetics platform for target and drug discovery – WWP2 as a novel target for anti-fibrotic disease treatment

Problem being solved:
Fibrosis is characterized by the excessive extracellular matrix (ECM) deposition, resulting in the irreversible stiffening of the affected tissue and lead to organ malfunction and death.

- fibrotic diseases cause over 800,000 deaths per year, accounting for around 45% of total deaths
- there are currently two FDA approved new drugs for Idiopathic Pulmonary Fibrosis (IPF), but both treatments have some issues such as high liver toxicity, high dosage, photoallergic reaction, and thus long-term treatment option lacking

Solutions:
The primary challenge addressed by this application is the critical need for more effective therapies in treating fibrotic diseases, particularly IPF and CKD. The successful development and approval of the WWP2 inhibitors could address a critical unmet medical need in the fibrosis treatment market, potentially leading to rapid adoption and significant commercial success.

- employed Systems-Genetics analysis in human cardiomyopathy patients and animal models and identified WWP2 N-terminal isoform as a novel druggable target for pathological tissue fibrosis
- used AI for virtual screen followed by *in vitro* HTS screening of potential WWP2 (N-terminal isoform) inhibitors

Market Size:
The POC (in vivo) and data generated within this project will allow to position this invention as a new antifibrotic drug to be approved to be tested in humans in IPF with a market of US $4.6B in 2024 (CAGR 4.2%).

- fibrotic disease market size: USD 3.62 Billion (2023) to USD 5.56 Billion (2031) with a CAGR of 5.5%
- other disease market could potentially cover by the target discovery platform (glomerulonephritis US$748.1 million in 2023; osteoporosis US$15.8 billion in 2023)

Competition:

- Two antifibrotic therapies have been approved for the treatment of IPF: Nintedanib and Pirfenidone
- However, mechanisms of action (Pirfenidone) poorly understood and (Nintedanib) showing multiple targets with important side effect
- Majority of past IPF trials did not meet the primary endpoint. Nevertheless, a number of compounds are now under investigation in different trial settings (i.e. BMS-986020 LPA receptor-1 antagonist, ENV-101 hedgehog inhibitor etc.)

Team:

- Prof Enrico Petretto, Associate Professor, Duke NUS medical school
- Hui Mei Chen, Principle Research Scientist, Duke NUS medical school

Up-to-date as of Oct 2, 2024