Metabolic Targets for Cardiometabolic Diseases

Problem being solved:
Heart failure with preserved ejection fraction (HFpEF) presents several unmet needs that researchers and clinicians are actively addressing:

- Diagnostic bio-markers: there is a lack of the specific bio-markers for HFpEF
- Undesirable clinical outcome: Angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), and beta-blockers have shown limited efficacy in HFpEF
- Clinical trial design challenges: The heterogeneity of the patient population and ambiguous endpoint selection complicate the evaluation of treatments for this complex heart failure condition

Solutions:
The team has explored various methods in targeting metabolic targets for cardiometabolic diseases

- Novel BDK (Branched-chain alpha-ketoacid Dehydrogenase Kinase) inhibitors for heart failure targeting BCAA (branched chain amino acid)
- Glucagon receptor antagonist for heart failure with preserved ejection fraction, where cardiomyocyte-specific genetic deletion of the glucagon receptor or treatment with a glucagon receptor antagonist significantly ameliorated HFpEF manifestation
- Method and expression vector for RBFox1 to promote heart muscle cell maturation and treatment of heart failure

Market Size:

- Heart failure affects around 64 million individuals globally, and prevalence is expected to increase by 46% between 2012 and 2030
- Global heart failure market valued at $31.9 billion in 2022 (CAGR >5%) during 2022-2032

Competition:
The Duke-NUS team has acquired an in-depth understanding of the biological pathways involving in cardiometabolic diseases

- The team's revelation that chronically elevated BCAA level leads to pathologies
- Boehringer Ingelheim developed a small molecule targeting sodium-glucose cotransporter 2 (SGLT2) inhibitor (T2D) with potential applications in HFpEF
- To-date, there are no specific small molecules approved solely for the treatment of heart failure with preserved ejection fraction (HFpEF)

Team:
Wang Yibin, Professor, Signature Research Programme in Cardiovascular & Metabolic Disorders, Duke NUS

Up-to-date as of Oct 2, 2024