Small molecule inhibitor for blood cancer

The Problem

- Acute myeloid leukemia (AML) is a devastating, deadly disease:
  - Overall 5-year survival: 40%
  - 5-year survival (>70yo): 2-5%
- Curative treatment is toxic and half of patients cannot receive it due to age and pre-existing conditions – these patients receive venetoclax as standard of care, which is non-curative.
- Many new and emerging treatments are mutation-specific and treat only subsets of patients.

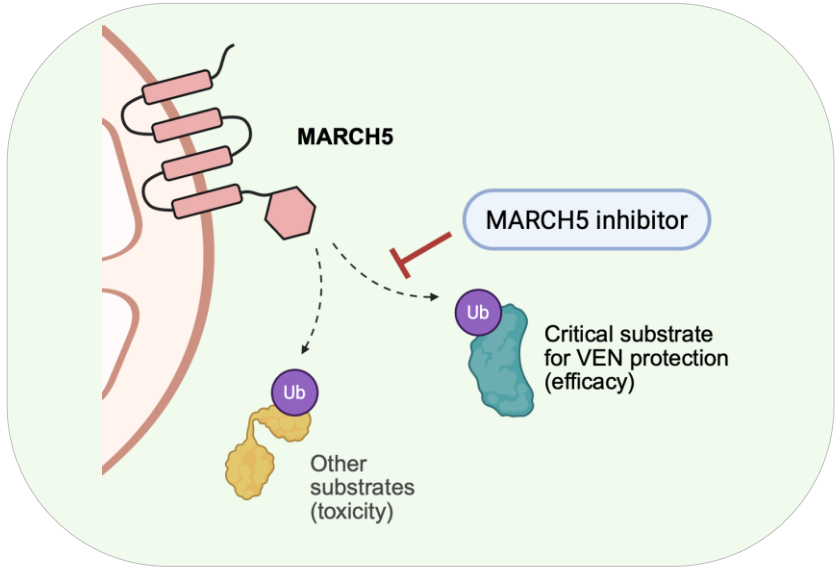
The Solution

- Unbiased genetic screens (including ours) have identified that genetic deletion of MARCH5 sensitises cells in a dose-dependent manner to BH3-mimetics, including venetoclax.
- A first-in-class oral, small molecule inhibitor of MARCH5 would represent a mutation-agnostic approach and could improve clinical outcomes for patients with AML and other blood cancers, as well as enhance the efficacy of venetoclax.
- We have identified an interface critical for MARCH5's venetoclax sensitization phenotype, providing a unique starting point for generating chemical matter.

Our Program

- MARCH5 is a rational, structure-enabled target by NMR
- We are conducting a high throughput screen in parallel with fragment (and/or DEL) screens
- We have the necessary tools and assays to support a follow-up hit-to-lead campaign
- We are developing *in vivo* small animal models to validate and inform drug design

Seeking ***partnerships and investment*** to progress our drug discovery program



We have identified an interface of MARCH5 that drives sensitivity of cancer cells to a BCL2 inhibitor and are conducting a structurally-enabled drug discovery program.

Our Team

Dr. Tom Lew, Haematologist, Molecular biology
A/Prof. Jeff Babon, Structural biology
A/Prof. Brad Sleebs, Medicinal chemistry
Prof. David Huang, Global cell death
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