Seed funding and a start-up help

NCATS-CCHMC cancer therapy cross preclinical Valley of Death

Collaborations, a spin-off company, and a creative approach to funding have helped the National Center for Advancing Translational Sciences (NCATS) navigate its new blood-cell cancer drug through the dreaded preclinical "Valley of Death."

NCATS, part of the National Institutes of Health (NIH), and Cincinnati Children's Hospital Medical Center (CCHMC), a teaching hospital, collaborated to develop small molecules for treating myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML).

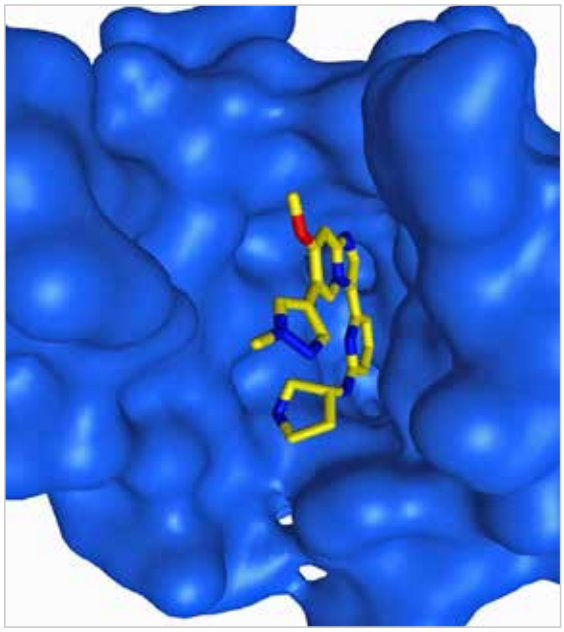
AML and MDS are blood cell cancers that urgently need improved treatments. Collectively, more than 30,000 new cases of MDS and AML are diagnosed in the United States each year. The median survival time for MDS is only 2.5 years after diagnosis, and the five-year survival rate for AML is only 27%.

Interleukin-1 receptor-associated kinase (IRAK) and FLT3 kinase enzymes play key roles in driving the progression of AML and MDS. Small-molecule inhibitors of FLT3 have shown initial promise in treating AML. However, FLT3 inhibitors have not led to long-lasting remission, since FLT3 inhibition results in increased compensatory signaling through IRAK1/4. The new treatment co-developed by NCATS and CCHMC will have potential to provide long-term benefits for MDS and AML by inhibiting both IRAK and FLT3.

The NCATS Office of Strategic Alliance worked closely with Cincinnati Children's Innovation Ventures (CCIV), a unit of CCHMC that facilitates the translation of discoveries into improved care for children, to explore pathways to support technology development through the late preclinical development phase (i.e. "Valley of Death"). This phase of product development often fails because it is significantly more expensive than early-stage discovery; it involves lengthy process development, scale-up, and toxicology testing; and it is less likely to receive federal funding.

NCATS entered into an inter-institutional agreement (IIA) that allowed CCIV to take the lead in filing patent applications, and marketing and exclusively licensing their joint intellectual property (IP) for the new IRAK/FLT3 inhibitors. CCIV filed and secured patents for the composition of matter and the methods of use for the inhibitors.

In late January of 2020, CCIV facilitated the creation of a start-up, Kurome Therapeutics, whose mission is dedicated specifically to the preclinical and clinical development of the novel IRAK/FLT3 inhibitors. CCIV facilitated series seed funding for Kurome from Cincinnati Children's and investment funds including CincyTech. CCIV also recruited an experienced entrepreneur-in-residence to manage the project operation and to coordinate product development by NCATS and CCHMC investigators.



Above: The chemical structure of a prospective drug sitting inside the protein kinase IRAK4. (Image courtesy of Cincinnati Children's Hospital Medical Center)

NCATS and CCIV worked together to enable CCHMC to enter into an exclusive license with Kurome for the IP covering novel IRAK/FLT3 inhibitors and for the treatment and diagnostic applications for AML, MDS and solid tumors. CCHMC, Kurome, and NCATS also entered into a cooperative research and development agreement (CRADA), providing Kurome with options to license future IP relevant to the inhibitors. The exclusive license agreement and the CRADA provide Kurome with a sustainable intellectual property portfolio.

Since Kurome was founded in January of 2020, it has used the proceeds from the series seed investments to fund ongoing preclinical developments by the investigators at NCATS and CCHMC, dramatically accelerating the drug development. Significant progress has already been made, as optimized drug leads have been developed and new patent applications have been filed.