Novartis and Dana-Farber renew decades-old cancer alliance [1]

Discovery [2]

Malignant rhabdoid tumors (MRT) are tragic. They riddle the kidneys and other tissues of young children, causing death in a majority of cases less than a year after diagnosis.

No precise therapies are approved for the rare cancer. To change that, Sunkyu Kim of Novartis Institutes for BioMedical Research (NIBR) and Dr. Charles Roberts of Dana-Farber [3] Cancer Institute paired up to tackle the challenge of discovering a targeted therapy that can help patients with MRT.

Their research aimed to exploit a recently discovered molecular weakness in MRT. Loss of the tumor suppressor gene SNF5 in this cancer type makes it addicted to cyclin D1/CDK4 for growth. Take away this fuel and tumor growth stops, their lab experiments showed.

Kim and Roberts saw surprising potential of a compound in models of MRT in complementary studies, giving Novartis and Dana-Farber confidence to begin a clinical trial in children with the disease.

“It’s too early to say whether this trial will show benefits for patients,” says Roberts, “but these are patients who are essentially facing a death sentence.”

This is just one example of the impact that the long-standing research alliance between Novartis and Dana-Farber is having in the fight against cancer. To seek further advances, Novartis and Dana-Farber have renewed their relationship for the fourth time. The new agreement, which begins in January 2015, builds on 22 years of collaboration between the partners. Their previous efforts have supported work on numerous compounds in development and targeted medicines.

“This is an avenue for academics to take a scientifically tractable idea with clinical implications and enable the translation of that first into translational research studies and eventually into clinical trials,” says Dr. William Sellers, Vice President and Global Head of Oncology, who leads the alliance with Dana-Farber for Novartis.

The agreement is unique for its longevity and open scientific exchange. In contrast to limited, short-term research agreements between academia and industry, Dana-Farber and Novartis investigators have worked together over the course of two decades to solve difficult problems inherent to drug discovery.

Tom Roberts, a longtime Novartis research collaborator, studies the molecular roots of cancer at Dana-Farber Cancer Institute.
(Photo courtesy of Dana-Farber Cancer Institute)

The collaboration focuses on discovery of new molecular targets in specific tumors, against which “smart” cancer therapies can be directed, as well as assessing whether experimental compounds are successfully attacking those targets. Novartis will fund Dana-Farber projects in such areas as genomic description of tumors, biomarkers predicting sensitivity to drugs, research on combination drug therapies, probing mechanisms by which cancers become drug-resistant, and devising novel cancer model systems.

Tom Roberts, co-Chair of Cancer Biology at Dana-Farber, has worked with Novartis for decades. Roberts and Novartis’ Sellers, a former Dana-Farber principal investigator, have focused their research on the role of the PI3K/ATK/mTOR pathway, the most common molecular pathway to go awry in cancer.

Novartis has compounds targeting this pathway in trials, including one that targets the specific PI3Ka protein that Roberts and his colleagues have studied.

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“I’m struck with just how difficult it is to make a truly successful cancer drug,” says Tom Roberts, who co-leads the alliance for Dana-Farber with his colleague Dr. David Livingston. “I think the value to patients is that this relationship between Novartis and Dana-Farber significantly facilitates this extremely challenging process.”

Novartis investigator Zainab Jagani and Dana-Farber’s Charles
Roberts represent the future of the alliance. They and their colleagues recently published a paper in Proceedings of the National Academy of Sciences, highlighting a new drug target. The target is a key part of the SWI/SNF chromatin remodeling complex. Cancer-related mutations to SWI/SNF are found in about 20 percent of all cancers, including some cases of lung cancer and almost all instances of MRT.

Jagani is doing early experiments with an eye toward translating hers and Roberts' findings into additional potential therapies. "The synergy between fundamental cancer research and its application into therapeutic strategies through these collaborations provides a great opportunity to accelerate the discovery of novel cancer treatments," she says.

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Tags:
Novartis Institutes for BioMedical Research [4]

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[1] https://www.novartis.com/stories/discovery/novartis-and-dana-farber-renew-decades-old-cancer-alliance
[2] https://www.novartis.com/stories/discovery
[3] http://www.dana-farber.org/
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