Many patients with colorectal cancer show increased levels of Epidermal Growth Factor Receptor (EGFR), a cellular protein that contributes to disease progression.

Unfortunately, the effectiveness of EGFR targeting therapies can be compromised by resistance mechanisms.

The Solution

A team of University of Michigan researchers, led by Judith Leopold, Ph.D., and Christopher Whitehead, Ph.D., is focusing on the link between PIK3A mutations/PTEN loss and resistance to EGFR targeting agents. This resistance can be overcome by inhibiting PI3K/AKT pathway signaling, which is important in regulating cell survival.

Leopold and Whitehead designed small molecules that inhibit both EGFR tyrosine and PI3 kinases. The dual inhibitor strategy would reduce side effects and drug interactions, make dosing easier, and simplify the regulatory process.

The potential of the successful combination of these therapies could significantly impact the quality and duration of patient responses to treatment in some of the most difficult and deadly cancers.

This project was funded by the University of Michigan Translational Research and Commercialization for Life Sciences Program, also known as MTRAC. MTRAC works to “fast forward” projects that have a high potential for commercial success, with the ultimate goal of positively impacting human health.

MTRAC has been made possible by the Michigan Economic Development Corporation, the Michigan Institute for Clinical and Health Research, and the generosity of friends of the University of Michigan.
Molecule offers dual targeting of EGFR and PI3K in colorectal cancer patients.

Significant Need
EGFR targeting agents have been approved for clinical use, but have met with limited success in the treatment of colorectal cancer. The novel agent being developed was designed based on the idea that dual targeting of EGFR and PI3K would be effective in colorectal cancer patients.

Compelling Science
The group designed small molecules that exhibit dual inhibition of both EGFR tyrosine and PIK3A kinases.

Competitive Advantage
This dual targeting of EGFR and PI3K will help colon cancer patients who experience PIK3A mutations/PTEN loss and resistance to EGFR targeting agents. Current therapies using EGFR targeting agents have elicited low response rates.

MTRAC Project Key Milestones
- Synthesize pre-lead agents to enable extensive PK/PD
- Compare PK and safety (MTD) parameters of pre-lead molecules
- Compare efficiccy (tumor growth delay) of pre-lead molecules
- Test two pre-lead molecules in vivo against a subset of patient-derived xenografts
- Screen a panel of patient-derived colorectal tumor models for sensitivity to EGFR and PI3K (proliferation endpoint)
- Carry out a 5-arm in vivo mouse trial to demonstrate superiority of dual targeted single molecule

Product Launch Strategy
To be determined by licensee.

Engage Investors
Subsequent to MTRAC funding, a data package will be available to attract licensors from pharma/biotech or investors interested in supporting a spin-out company.

Commercialization Strategy
Company formed in August 2015. The option to license obtained from U-M.

Regulatory Pathway
Investigational New Drug (IND) application with the FDA. Company to eventually file NDA.