Potential New Treatment in EGFR-TKI Resistant Cancer

Epidermal Growth Factor Receptor (EGFR) drives cancer progression in a large number of solid tumors. EGFR inhibitors are the standard of care for most of these patients. Patients may respond to treatment initially, but nearly all will develop resistance within a year.

The Solution

EGFR activity is important for driving tumor growth, but the protein itself is essential for the tumor’s survival. University of Michigan team Mukesh Nyati, Ph.D. and Theodore Lawrence, M.D., Ph.D., found that degrading EGFR kills cancer cells selectively by specifically targeting this receptor, which is more effective than inhibiting EGFR alone.

Nyati and Lawrence developed the peptide Disruptin and two small molecules that are selectively effective in inducing phosphorylated-EGFR degradation in tumors, including tyrosine kinase inhibitors (TKI)-resistant tumors.

This new approach will be more effective and less toxic to normal tissues than current strategies being used because of the extraordinary selectivity of the novel peptide, Disruptin.

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.
**A new treatment for EGFR-TKI resistant cancer**

benefits patients with no long-term treatment options. Disruptin, a novel peptide, and two small molecules are effective in inhibiting EGFR in tumors without manifesting toxicities or affecting the EGFR in adjacent host tissues.

**Significant Need**
The peptide drug provides a treatment option for EGFR-driven TKI resistant patients who currently don’t have any other therapeutic alternatives.

**Compelling Science**
Disruptin and two small molecules are already developed and tested.

**Competitive Advantage**
Disruptin does not affect the EGFR in adjacent host tissue and does not manifest toxicities seen with other agents.

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**MTRAC Project Key Milestones**

- Conduct in-vivo studies to assess pharmacodynamics (PD) of Disruptin in TKI resistant tumor model
- Establish correlation between dose and duration of treatment (schedule) with PK in TKI xenograft mouse model
- Conduct in-vivo tests to assess pharmacokinetics (PK) of Disruptin in C57 mice
- Determine the maximum tolerated dose
- Compare efficacy of Disruptin with standard of care to determine therapeutic index in TKI resistant EGFR dependent tumor models

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**Overall Commercialization**

- **Regulatory Pathway**: Begin discussions with regulatory consultants regarding the quickest path to an Investigational New Drug (IND) approval.
- **Completed Business Formation**: Experienced senior management team assembled, papers have been formally filed for a bio-tech startup called PI Squared.
- **Engage Investors**: A number of investors interested in PI Squared.
- **Product Launch**: Disruptin

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**MTRAC funding and guidance** helped us determine the milestones to fill gaps in the technology, and form the best team to successfully move our research to the next level.