CYTEIR THERAPEUTICS

The company

Cyteir Therapeutics is a clinical stage, VC-funded, private company that is a leader in the discovery and development of novel therapeutics based on the biology of DNA repair and synthetic lethality for the treatment of cancer. Our initial approach takes advantage of DNA damage overload to induce selective self-destruction of cells by targeting the DNA repair activity of RAD51.

Therapeutic approach: gain-of-function synthetic lethality

Genomic instability is caused by an imbalance between DNA damage and DNA repair. It is a key driver of many disease processes and represents a crucial vulnerability in cancer.

Normal cells have very little DNA damage and have sufficient repair capacity to handle it. Cancer cells suffer an excess of DNA damage and thus are sensitive to small perturbations in their DNA-repair capacity. By precisely targeting DNA repair, the cancer cell is overwhelmed by its own DNA damage and undergoes cell death – a therapeutic effect known as "synthetic lethality". In essence, the inhibition of DNA repair forces cancer cells to mutate themselves to death.

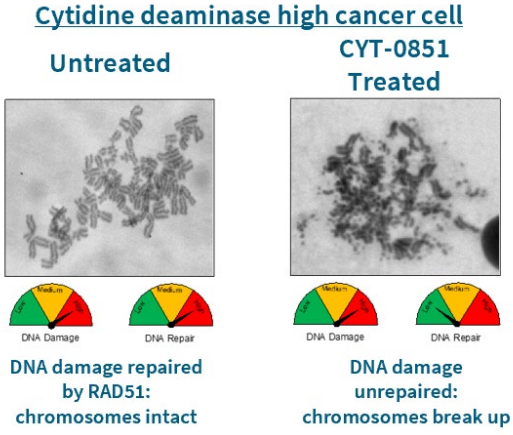
Precision targeting of DNA repair proteins in biomarker-defined diseases promises to deliver potent and highly selective therapeutics with potentially fewer side effects than traditional chemotherapy while maintaining integrity of healthy cells in the process.

A novel screening approach for DNA repair drug discovery

Cyteir has developed a unique screening system designed to rapidly identify novel DNA repair inhibitors that function with exceptional selectivity against biomarker-defined diseased tissues. This screening system utilizes primary cells derived from tissues of interest rather than traditional cell lines. Genetic constraints are engineered into the cells, which enhances the power to detect hits on the desired pathway. The power of this integrated platform is the robust ability to customize it for tissues or diseases of interest, to rapidly sort out the "true hits" from the false positives and negatives, and to dramatically reduce the number of "poor hits" that lead to failure at later stages.

Small molecules that selectively target RAD51 in cells defined by gain-of function of cytidine deaminases

Cyteir's small molecule therapeutics are selective for cancers associated with the overexpression of cytidine deaminases, a family of DNA-damaging enzymes normally present in a very small fraction of healthy immune cells. Cytidine deaminases are 'hyperactivated' in many cancers and cause widespread mutations, accelerating tumor progression and therapy resistance. DNA repair via the protein RAD51 protects cancer cells from death by cytidine deaminase generated DNA damage. Cyteir has developed a unique approach to targeting RAD51. Unlike conventional therapeutic approaches that block enzymatic activities, our strategy is designed to allow RAD51 to carry out its housekeeping functions while reducing the ability to repair DNA damage in highly damaged cells. Our lead compound, CYT-0851, is an oral drug currently in a phase I/II study enrolling at leading US research institutions.



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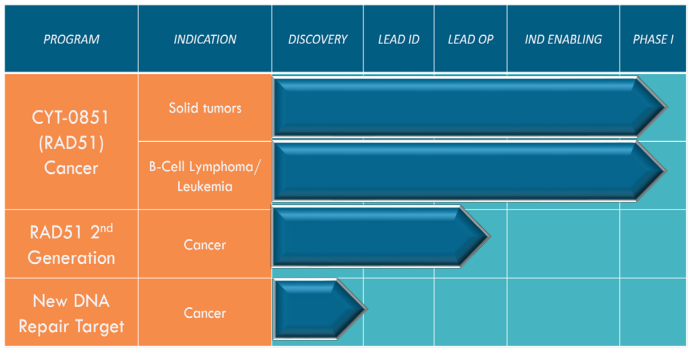
PROGRAMS



CYT-0851

- Oral small molecule inhibitor of RAD51-mediated homologous recombination
- Planned once daily administration
- Potency: 200nM in cellular assays
- Selectivity: 100x – 1000x more potent in cytidine deaminase overexpressing tumors

Phase I/II trial in relapsed/refractory NHL, CLL, multiple myeloma, advanced breast cancer, ovarian cancer, pancreatic cancer, soft tissue sarcoma, or head & neck cancer. Trial enrolling at leading US research centers.

Key publications

1. Hasham, MG, et al. Widespread genomic breaks generated by activation-induced cytidine deaminase are prevented by homologous recombination. *Nat Immunol*. 2010 Sep;11(9):820-6.
2. Lamont, KR, et al. Attenuating homologous recombination stimulates an AID-induced antileukemic effect. *J Exp Med*. 2013 May;210(5):1021-33.
3. Ward, A, et al. Targeting homologous recombination, new pre-clinical and clinical therapeutic combinations inhibiting RAD51. *Cancer Treat Rev*. 2015 Jan;41(1):35-45.

Management Team

Markus Renschler, MD
President & CEO

Chris Thomajan
CFO

Jean-Marc Lapierre, PhD
VP, Chemistry

Thomas O'Shea, PhD
VP, Preclinical Development

Susan Doleman
VP, Clinical Operations

Barbara Wan, PhD
VP, Research and Development Project Leadership

Founders

Kevin Mills, PhD
Timothy Romberger
Founded in 2012

Financings

Series A: $5.5 M (Nov 2016)
Series B: $75.2M (May 2018 – expanded Nov 2019)

Investors:

Novo Ventures
Venrock Associates
Lightstone Ventures
DROIA Ventures
Osage University Partners
Celgene Corporation

For career inquiries:
careers @cyteir.com