UNIVERSITY OF MINNESOTA
Driven to Discover℠

T cell receptors for engineered T cell therapy

Mesothelin-specific T cell receptors for cell engineering and cancer therapy

IP Status: Provisional Patent Application Filed

Applications

- Cell therapy of T cells targeting solid tumors with advanced malignancy

Key Benefits & Differentiators

- **Intracellular antigen targeting:** by modifying cells to express tumor-reactive T cell receptors (TCRs) instead of using CAR T cell approaches
- **Durable therapeutic responsive:** TCRs can recognize not only tumor cells, but also stromal cells in the tumor microenvironment, thereby engaging the immune system in ways that are distinct from CAR-based approaches. Further, tumor-reactive T cells that express TCRs are capable of eradicating solid tumors in clinical trials.

Technology Overview

Immunotherapies such as checkpoint blockade and chimeric antigen receptor (CAR) T cells have shown to be effective therapies for certain cancer types. However, pancreatic ductal adenocarcinoma (PDA) and other high malignancy solid tumor types fail to respond to this approach. To address this issue, several researchers have proposed the use of T cell therapy using TCRs of high affinity against tumor antigens to overcome the solid tumor-induced immunosuppression. However, TCR modifications can lead to serious adverse responses in patients such as unwanted toxicity and rapidly induce T cell exhaustion, due to chronic TCR signaling resulting from high affinity TCRs.

Seeking new therapeutic solutions researchers at the University of Minnesota have identified unique TCRs that are specific for an overexpressed tumor antigen Mesothelin. Mesothelin is overexpressed in most pancreatic and ovarian cancers, as well as many other cancers including subtypes of breast and lung cancer and AML. Here, T cells can be genetically modified to express a Mesothelin-specific TCR and transferred into patients with advanced disease for therapeutic benefit. In highly aggressive animal models of ovarian and pancreatic cancer, such an approach can lead to durable therapeutic responses for advanced intractable malignancies and is safe. This technology includes sequences of top candidate human mesothelin specific TCRs, which can lyse pancreatic and ovarian cancer cell lines in vitro. The proposed approach of using tumor-reactive TCRs in combination with novel strategies identified has a high potential to develop into effective durable cancer therapeutics since T cells which express tumor-reactive TCRs have repeatedly demonstrated the capability to eradicate large, bulky solid tumors in patients.

Phase of Development

TRL: 2-3
Strong preclinical data demonstrating T cells modified to express tumor reactive TCRs can lead to durable therapeutic responses in preclinical models of both ovarian and pancreatic cancer. Additional data on how to further engineer T cells to be refractory to inhibitory signaling in the tumor microenvironment and how to combine engineered T cell therapy with other approaches leading to robust and durable anti-

Technology ID
2020-202

Category
Life Sciences/Biologics
Life Sciences/Human Health
Life Sciences/Pharmaceuticals
Life Sciences/Therapeutics

Learn more

tumor responses may be disclosed (manuscripts in preparation).

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

Please contact our office to share your business' needs and learn more.

Researchers

- **Ingunn Stromnes, PhD** Assistant Professor, Department of Microbiology and Immunology

References

1. Rollins, M.R., Spartz, E.J. and Stromnes, I.M.(2020) , https://doi.org/10.1002/cpim.97, Current protocols in immunology
2. Stromnes, I.M., Schmitt, T.M., Chapuis, A.G., Hingorani, S.R. and Greenberg, P.D(2014) , https://doi.org/10.1111/imr.12141, Immunological reviews
3. Stromnes, I.M., Schmitt, T.M., Hulbert, A., Brockenbrough, J.S., Nguyen, H.N., Cuevas, C., Dotson, A.M., Tan, X., Hotes, J.L., Greenberg, P.D. and Hingorani, S.R(2015) , https://doi.org/10.1016/j.ccell.2015.09.022, Cancer cell
4. Anderson, K.G., Voillet, V., Bates, B.M., Chiu, E.Y., Burnett, M.G., Garcia, N.M., Oda, S.K., Morse, C.B., Stromnes, I.M., Drescher, C.W. and Gottardo, R.(2019) , https://doi.org/10.1158/2326-6066.CIR-19-0258, Cancer immunology research
5. Stromnes, I.M., Burrack, A.L., Hulbert, A., Bonson, P., Black, C., Brockenbrough, J.S., Raynor, J.F., Spartz, E.J., Pierce, R.H., Greenberg, P.D. and Hingorani, S.R.(2019) , https://doi.org/10.1158/2326-6066.CIR-18-0448, Cancer immunology research