

## **T-cell Receptors Targeting CD20-Positive Lymphomas and Leukemias**

### **Summary**

The National Cancer Institute (NCI) seeks licensees for a collection of T-cell receptors (TCRs) that specifically target the CD20 antigen expressed in B-lymphoid malignancies such as non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia, and acute lymphoblastic leukemia. The TCRs are being developed as therapeutics for the treatment of lymphomas and leukemias.

### **NIH Reference Number**

E-152-2020

### **Product Type**

- Therapeutics

### **Keywords**

- T-cell Receptor, TCR, CD20, Resistant B-lymphoid malignancies, Non-Hodgkin's Lymphoma, NHL, Chronic Lymphocytic Leukemia, CLL, Acute Lymphoblastic Leukemia, ALL, Ishii, Hinrichs

### **Collaboration Opportunity**

This invention is available for licensing.

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### **Description of Technology**

CD20 is a protein expressed by wide ranges of lymphoid malignancies originating from B cells but not by indispensable normal tissues, making it an attractive target for therapies such as T-cell receptor (TCR) therapy. Current anti-CD20 therapeutics face a number of limitations. The most important limitation to current anti-CD20 therapies include cancer cells becoming resistant to the therapy. Resistance mechanisms to the existing CD20 therapies include loss of target antigen expression from the cell surface, loss of antibody epitope, or modulation of antibody epitope - all of which make the malignant cells "invisible" to antibodies. Importantly, these resistance mechanisms do not affect TCR-mediated target recognition. Epitopes for TCRs are short fragments of peptides that are

processed intracellularly and presented in the context of major histocompatibility complex. Thus, TCRs can recognize and kill leukemia and lymphoma that are no longer “visible” to existing antibodies.

Investigators at the National Cancer Institute (NCI) have developed a collection of novel anti-CD20 TCRs that can be used to treat CD20 positive lymphomas and leukemias. These novel TCRs can recognize and exert cell killing against CD20-derived epitopes even when the target protein escapes surface expression and remains in a sub-cellular compartment, such as endoplasmic reticulum or cytoplasm. These characteristics of the novel anti-CD20 TCRs allow them to overcome known resistance mechanisms associated with B-cell malignancies, making them an attractive therapy over other current CD20 therapeutics on the market.

NCI seeks parties interested in licensing to further develop this technology.

### **Potential Commercial Applications**

- The TCRs can be used as a therapeutic against B-cell malignancies such as non-Hodgkin’s lymphoma, chronic lymphocytic leukemia and acute lymphoblastic leukemia
- The TCRs can be used for treatment in
  - CD20-expressing malignancies, even if the CD20 antigen escapes the surface of the tumor cells and resides within intracellular compartments or is only partially expressed
  - CD20-expressing malignancies, even if the diseases are resistant to existing anti-CD20 antibodies through resistance to antibody-specific cytotoxicity mechanisms (such as antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity)

### **Competitive Advantages**

- The novel TCRs can recognize and exert cell killing against CD20-derived epitopes even when the target protein escapes surface expression and remains in a sub-cellular compartment, which are current limitations of CAR-T cell therapy and anti-CD20 monoclonal antibodies
- The novel anti-CD20 TCRs can specifically recognize and exert tumor-cell killing in a target-antigen-restricted manner, when CD20 expression is low, or when CD20 is expressed intracellularly
- In in vitro experiments, T cells engineered to express anti-CD20 TCR recognize and mediate cytotoxicity against cells lines that are both CD20+ and HLA-A2+ and exhibit high functional activity
- CD20 targeting TCRs are available for immediate clinical validation

### **Inventor(s)**

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### **Development Stage**

- Pre-clinical (in vivo)

## **Patent Status**

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/043,520 , Filed 24 Jun 2020

## **Therapeutic Area**

- Cancer/Neoplasm

## **Updated**

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