

## Making T cells More Suitable for Use in Cancer Immunotherapy

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**Keywords:** Therapeutics, Cancer, immunotherapy, T cell differentiation, Fas ligand (FasL), CD95

### Summary:

The [Surgery Branch](#) of the National Cancer Institute (NCI) is seeking parties interested in collaborative research to further develop, evaluate, or commercialize the prevention of T cell differentiation and effector function as part of immunotherapy.

### Technology:

NIH scientists have developed methods to make better immunotherapy by exposing T cells to Fas ligand (FasL) or Fas receptor (FasR) antagonists and agonists. Researchers have found that FasL-FasR antagonists suppress T cell differentiation leaving them in a naïve state. These T cells are a more ideal cell type for adoptive cell transfer therapies since they have not exhausted their effector functions and demonstrate greater proliferation, enhanced persistence and survival, and better activity against their target antigen when infused *in vivo* to treat cancer. Also, the prevention of T cell differentiation/effector function *in vivo* has implications for autoimmune diseases and syndromes. FasL-FasR agonists enhance T cell differentiation towards more effector-like cells. Enhancing the differentiation of T cells is expected to be useful in treating cell proliferation disorders, such as leukemias, lymphomas, or Wiskott-Aldrich syndrome.

FasL (or cluster of differentiation 95L) is a transmembrane protein in the tumor necrosis factor (TNF) family. FasR (or apoptosis antigen 1, CD95, or TNF receptor superfamily member 6) is a transmembrane protein belonging to the TNF receptor/nerve growth factor receptor superfamily. Normally, when FasL binds to FasR, a cell death signal is triggered in the cell. Antagonists of FasL-FasR interaction may include caspase inhibitors, mutated FasL/FasR, RNAi, or FasL/FasR antibodies. Agonists may include FasL/FasR encoding nucleotides.

### Potential Commercial Applications:

- Immunotherapy for cancer and other diseases or disorders using FasL/FasR antagonist exposed T cells
- Methods for generating better T cells to utilize for infusion into patients in adoptive cell transfer therapies
- Therapeutic to prevent T cell mediated toxicity *in vivo* (i.e. autoimmunity like lupus, Crohn's disease, MS, vitiligo, etc.)
- Components of a combination therapy to increase or suppress T cell differentiation and activity in patients

### Competitive Advantages:

- Some patients do not respond to T cell immunotherapy due to lack of cell persistence, survival, or activity or other reasons. Administering a FasL/FasR antagonist to a patient's T cells before immunotherapy should increase the success rate of treatment by increasing the persistence and survival of the infused cells.
- Differentiation and effector function of T cells can be suppressed by an antibody (molecular product) rather than a drug (chemical product) like rapamycin.

**Development Stage:** Discovery, *in vitro* data available.

**Patent Status:** U.S. Provisional Application No. 61/623,733 filed 13 Apr 2012.

**Related Technology:** PCT Application No. PCT/US2011/63375 filed 08 Dec 2010

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