A biosensor engineering strategy for improved cell-based therapy

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Technology description

A sophisticated multiplexed biosensor system that can activate a downstream promoter to effect diverse custom biological functions. #therapeutics #cellsignaling #healthcare #diagnostictool

BACKGROUND

The market for cell-based therapeutics has gained wide recognition in the healthcare industry. One example is CAR T cell therapy which involves removal of T cells from patient's blood, transduction with a viral vector containing the CAR, expanding the T cells, and patient infusion. The CAR contains fragments that improve the ability for T cells to recognize tumor antigens and target cancer cells. Harnessing the therapeutic capability of such cells holds huge potential for treating many diseases beyond cancer, like infections, autoimmunity, metabolic diseases, and tissue degeneration as well as for realizing tissue repair and regeneration. However, a lack of control over the cellular response via CAR produces significant scientific and regulatory hurdles that hinder their adoption as a viable platform for therapeutic applications. For example, activating an intended gene, or an "off-target activation," could prove to have deleterious health effects. There are numerous ways to address this need, one of which might be to incorporate a signaling system where two distinct molecules are required for signaling to occur.

ABSTRACT

Northwestern inventors have developed a novel strategy using Boolean logic that improves the safety of cell-based therapeutics while diversifying the range of biological outputs that can be achieved. the technology that they developed uses synthetic receptors, named modular extracellular sensor architecture (MESA), that can be multiplexed to create more stringent cell signaling controls. In a preliminary study, the team designed a multiplexed system of two self-contained receptor and signal transduction system platforms wherein the two receptors each sense a distinct soluble molecule (ligand). Binding of these ligands to each receptor results in the release of intracellular signaling molecules that enter the nucleus and induce targeted gene expression. In this multiplexed system, however, cell signaling occurs only if both receptors are active at the same time. This is the first system that has been developed where the detection of multiple, soluble ligands has been coupled to a user-defined signaling output. Using various MESA receptors and ligand combinations also makes it possible to generate customizable signaling outputs, increasing the versatility of the system.

Application area

Immunotherapy and other cell-based therapies

Advantages

Increased control of downstream effects of engineered receptors
Cutomizable output with respect to transcriptional target
Level-matching: signaling from the promoter is only activated once a threshold level of both ligands is reached

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