Docket #: S19-343

STASH Tag: A chemigenetic system for control of protein localization

Overview
Researchers in the laboratory of Stanford's Crystal Mackall have developed a molecular biology technique to sequester proteins of interest into intracellular compartments- making it a powerful tool for protein characterization, while also enabling safer use of protein-based therapeutics. This technology supports precise, drug-induced control of engineered gene and cell therapies, which can help improve on existing safety profiles for novel treatments.

Technology
The Intracellular **S**torage by **TA**rgeted **SH**uttling (STASH) system uses retention tags to drive target proteins to an intracellular compartment of choice. That sequestration is inducible, driven by the administration of a pharmacological agent that inhibits cleavage of the retention tag.

Related Technology
Stanford Docket S20-432- STASH system: Enriching genetically modified cells with a single selectable surface marker

Stage of Development: Research - in vitro

The inventors demonstrate that the inducible STASH system can be used to drive on-demand shuttling of CAR-T receptors away from cell membranes in various cell models, regulating production of inflammatory cytokines and cytotoxicity to potentially improve the safety profile of CAR-T therapies. Applications for the system in research models are also broad, with customizable, modular construction of engineered proteins that can shuttle cell surface receptors, secreted proteins, and other molecules of interest to desired intracellular compartments.

Check Docket 17-501: SMASh_CARs: A "drug off" chemogenetic system for regulating CAR T-cell therapy, a related technology from the Mackall laboratory to

tune CAR-T activity.

Applications

- CAR-T, TCR, and NK cell therapy
- Cytokine therapy
- Gene therapy
- Viral vectors
- Gene engineering
- Molecular biology research tool for protein characterization

Advantages

- Cell surface receptor localization
- Reversible control of protein localization
- Wide dynamic range of expression
- Well tolerated and FDA-approved small molecule inhibitor

Publications

- MacKall, C., Majzner, R., Labanieh, L., & Lin, M. (2024). *U.S. Patent Application No. 17/767,818*.

Patents

- Published Application: WO2021072250
- Published Application: 20240082399

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