Docket #: S23-363

Generation of antigen-specific T and B cells using engineered commensals

Researchers at Stanford have developed methods to link antigenic or immunomodulatory molecules to bacterial surface proteins of commensal bacteria that result in a high immune response when applied to an epithelial surface of a mammal.

Commensal microbiota reside primarily at barrier sites, such as the gastrointestinal tract, urogenital tract and skin, where they functionally tune the innate and adaptive immune systems. Immune tolerance to these microbes must be established at each of these contact sites. Treg cells play a major role in establishing and maintaining immune homeostasis in peripheral tissues, particularly at barrier sites where they stably reside. In contrast, T effector cells generally amplify pro-inflammatory responses in an antigen-specific manner. The authors have previously developed novel methods for stimulating and expanding antigen-specific Tregs and T effector cells with TCRs specific for a specific host antigen of interest.

Stage of Development
Research – in vitro

Stage of Research
The inventors have devised a method to present antigens linked to commensal bacterial surface proteins which results in a surprisingly high immune response triggered when the bacterial are applied to an epithelial surface of a mammal. This method comprises the expression of an extracellular bacterial protein selected from the group consisting of Accumulation-associated protein (Aap), peptidoglycan, an M protein, Lysing Motif (LysM)-containing protein and a peptidoglycan-binding protein, or a fragment linked to a heterologous antigenic molecule or immunomodulatory molecule.

Technology Reference Numbers
CZ Biohub SF ref. no. CSB-294S

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Applications

- Linkage of an antigen molecule on any bacterial surface protein or other bacterial wall molecule.
- Attachment of antigens to bacterial surface proteins.
- Fusion of an extracellular protein with a first affinity agent.
- Click chemistry compatibility that can link the antigenic molecule to a polypeptide on the bacterial surface using an alkyne or azide moiety.
- Coating bacteria non-specifically on their surface with an antigenic or immunomodulatory molecule.
- Use of non-protein molecules as antigenic molecules, i.e. lipids or polysaccharides.

Advantages

- A high immunogenic response upon application to an epithelial surface of a mammal.
- Highly flexible methodology for linking a desired antigen to a bacterial surface protein, and flexible for application in different bacterial species and strains.

Publications

- Bousbaine, D., Bauman, K.D., Chen, Y.E. et al. Discovery and engineering of the antibody response to a prominent skin commensal. *Nature* (2024).
- Goldman, Bruce. Stanford scientists transform ubiquitous skin bacterium into a topical vaccine. *StanfordReport,* Dec 2024.

Patents

- Published Application: WO2025076409

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