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Programmable control of intercellular signals using protein-protein interactions

Stanford researchers have developed a new phospho-responsive system to control protein secretion and surface expression of any tagged protein of interest. The invention enables complex control of multiple proteins.

While tissue engineering holds immense promise in many therapeutic applications including transplantation and cancer immunotherapy, the immune system remains a major challenge. To address this issue, Stanford researchers have previously developed a generalized protease-responsive platform, called RELEASE, to control the secretion and display of surface proteins. Building upon it further, now they have developed a new design to attach a phospho-responsive peptide to RELEASE. Upon phosphorylation of this peptide, 14-3-3 proteins (native scaffolding proteins) will be recruited to the construct, inhibit the retention activity of RELEASE, and result in desired protein secretion. The system also allows for implementation of complex boolean logic by using a phospho-peptide that is constitutively phosphorylated (always ON), but can be removed using proteases. These protein-based circuits have advantages such as fast operation, compact delivery and robust performance compared to traditional synthetic circuits.

Stage of Development
Research - in vitro

Applications

- Cell transplantation
- Stem cell differentiation
- Cancer immunotherapy

Advantages

- Uses native signal transduction pathways
- Programmable control over expression of multiple proteins
- Modularity: local control of the immune microenvironment
- Increases the number of available sensors to activate protein secretion
- Concentration-dependent sensing of a single input, to control the expression of multiple outputs
- Fast operation, compact delivery and robust performance

Innovators

- Alex Vlahos
- Xiaojing Gao
- Connor Call

Licensing Contact

Seth Rodgers

Licensing Manager, Life Sciences

Email