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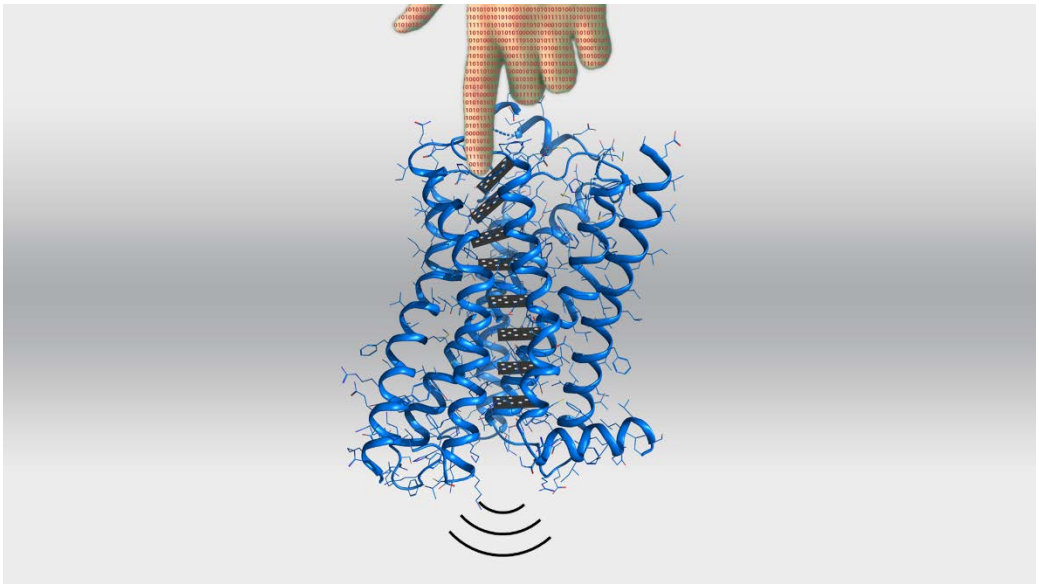
Licensing Opportunity

TTO – Technology Transfer Office

Method for engineering fine-tuned protein variants



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Keywords

Allosteric regulation
Biosensor
GPCRs
Protein active state
Protein variant

Intellectual Property

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Publications

Kuang-Yui et al, Nature Chemical Biology (2020)
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Description

In many protein families, such as GPCRs, function is triggered by conformation switch between active and inactive state and its dependence on ligand binding is determined by allosteric regulation. Residue coupling is physically connecting extracellular and intracellular regions of the protein and enables allosteric communications, but its detailed implication in terms of structure and sequence remains unclear.
Here, we propose a method and a software for generating protein variants with fine-tuned properties, by identifying and targeting coupled allosteric sites, and applying in silico mutations. Then, a score is computed to characterize each variant in terms of constitutive or ligand-related activity.

Advantages

Our method allows to engineer highly specific properties without having to design protein from scratch which is very challenging. Furthermore, it can be applied to any protein with available homolog protein structures, and is not limited to

proteins for which 3D data structure has been characterized.

Applications

- Design of novel biosensing protein (e.g. for drug detection) or protein therapeutics with enhanced sensitivity to stimulus (e.g. Dopamine receptor in PD).
- Protein active state structural characterization or strong inhibitors identification taking advantage of increased ligand free stability and activity.
- Function prediction of protein genetic variants for improved personalized medicine approach.