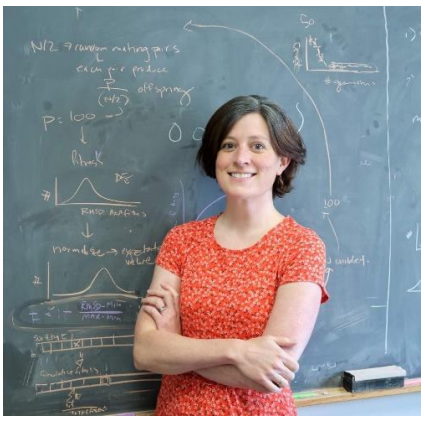
CONFÉRENCE



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Evolution-inspired engineering of allostery

LE JEUDI 11 MARS 2021 À 12 H 30

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Allosteric regulation is the control of protein activity by a site spatially distinct from the active site. This fundamental property of proteins is a basic building block for communication inside the cell, and allows cells to appropriately sense and respond to environmental change. Though allostery is a common feature of proteins, how it is encoded by protein sequence and structure remains unclear. For example, we do not know if the pattern and number of mutations influencing allostery is sparse or abundant, or if the mutations with the biggest effect on regulation are localized to the allosteric site or distributed throughout the structure. Here, we use a combination of co-evolutionary sequence analysis, domain insertion, and deep mutational scanning to better understand the structural determinants of allosteric regulation. Our results indicate that certain protein surface sites, which co-evolve with the active site, are hot spots for introducing new allostery. We also find that structurally distributed surface sites play a large role in tuning and optimizing existing regulation. These data suggest a path towards the rapid engineering or evolution of new allosteric systems.

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