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Protein evolution and molecular determinants of protein evolvability

Vendredi 29 septembre 2023 à 12 H 30

Pavillon Charles-Eugène Marchand, salle Hydro-Québec (1210)

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Résumé

Over the last decades of research on protein evolution and engineering, we have recognized that the success of protein engineering campaigns is overly different depending on the systems. What are molecular determinants to dictate the evolution of new protein functions? How we can choose the right strategies to engineer new proteins?

In this talk, I will discuss several key molecular properties that can be associated with evolvability of proteins, the ability of proteins to promptly evolve a new function. Especially, I will discuss the causes and consequences of mutational epistasis, interactions between mutational effects, that affect the pathways and outcomes of evolution. Under the prevalence of epistasis, the effects of a mutation can vary from positive to negative, and vice versa, depending on genetic backgrounds, which causes the prediction of mutational effects difficult. In-depth understanding and predicting epistasis are essential for developing better-directed evolution and protein engineering strategies. I will present statistical pictures of mutational epistasis that are observed in diverse experimental and natural evolutionary trajectories. Then, I will show several major molecular mechanisms which cause large epistatic effects, e.g., molecular conflict; two mutations perform similar molecular consequences and thus antagonize each other, reinforcing; the effect of the initial mutations is enhanced by subsequent mutations by fine-tuning the position of the initial mutation to generate synergistic effects. Finally, I will discuss potential strategies to overcome those epistatic consequences in directed evolution.

Hôte: Christian Landry

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