

Stage M1 Ingénierie de la Santé 2018

Caractérisation d'enzymes ancestrales ressuscitées.

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Summary: Allostery is one of the most effective mechanisms for regulating protein activity. This regulation is due to the binding of a ligand to one protein site which affects the catalytic site by long range distance effects. Numerous studies have been conducted to understand the fundamental basis of allosteric regulation. Nevertheless, some aspects of the allosteric modulation are still poorly understood. In particular, the genesis of the allosteric mechanisms remains unknown. The evolutionary structural and biochemical approach used during the training period is based on ancestral protein resurrection.

How does protein sequence resurrection work? This is a stepwise process relying on the phylogeny of the studied proteins. Then, the more probable ancestral sequences at each nodes of divergence are calculated. In a last step, the inferred ancestral gene, which codes for an ancestral protein, is synthesized and then expressed.

The candidate will purify and characterize enzymatic properties and allosteric behavior of ancestral dehydrogenases involved in the metabolism. The candidate will also participate in the screening of crystallization conditions in the presence of enzymatic inhibitors.