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POST-DOCTORAL POSITION
ANR Project ENZINVIVO

A post-doctoral position is available for 24 months at the "UMR-Sciences pour l'Œnologie de Montpellier" (UMR INRA 1083), in the Microbiology team, starting approximately in March 2017.

This work is part of a project financed by the "Agence Nationale de la Recherche" (ANR) (for details see ENZINVIVO project http://www.agence-nationale-recherche.fr/fileadmin/aap/2016/selection/aap-g-anr-DS10-selection-2016.pdf).

Enzyme reactions have long been analyzed in vitro, using pure enzymes and diluted buffer conditions. Due to the large amount of data generated and collected with thousands of enzymes, enzymology has made tremendous progress on understanding the incredible power of biocatalysts. However, dilute, in vitro conditions are far from the surroundings of natural enzymatic reactions that take place inside cells. The cellular medium is more accurately described as a heterogeneous crowded gel, dense and filled with all sorts of macromolecules and cellular lipidic organelles which may result in some partitioning effects and changes in diffusion. Therefore, enzymatic parameters determined using classical enzymology setups may not perfectly represent the real, in vivo based, rate and equilibrium constants. Although some advances have been made toward the comprehension of viscosity and crowding effects, we are still far to derive rate and equilibrium parameters from in vivo enzymatic reactions.

The project ENZINVIVO will address this issue focusing on two isoforms of phytoene synthase (carotenoid biosynthesis) as model enzymes. The enzymatic properties of these enzymes will be investigated in vitro, through a set of measurement in environments of increasing complexity and *in vivo* expressing the carotenoid biosynthesis pathway in *S. cerevisiae* and using synthetic biology tools and concepts to tune, at will, substrate and enzyme levels.
We aim at deciphering:

- how the intracellular medium influences enzymatic reactions.
- how can we build an in vivo approach to measure enzymatic parameters.
- how general models of enzymatic equations can be rewired to account for the complexity *in vivo* approaches. Our work will notably verify (or not) whether a Michaelis-Menten description of the kinetics remains valid in vivo.

The candidate will be first responsible for the construction of engineered strains with fine-tuned or inducible expression of CtrE (geranylgeranyl pyrophosphate synthase, GGPP synthase) to modulate intracellular concentration of GGPP, substrate of the phytoene synthase in a range consistent with its K_M. Then, he/she will be in charge of analyzing the consequences of the heterologous pathway on the yeast physiology through multi-levels characterization of the recombinant strains.

Personal Qualifications

- ✓ A PhD in the fields of molecular biology, genetics or related fields
- ✓ Solid experience in metabolic engineering, omics approaches, and microbiology are highly desirable.

- ✓ Skills in yeast metabolism and experience in multi-partners collaborations will be also strongly appreciated.
- ✓ Ability to lead good oral and written communication skills, engaged and highly motivated.

Candidates please send a letter that describes your scientific interest and research experience, together with your CV, list of publications and the names of three references to Drs. Carole Camarasa (carole.camarasa@inra.fr) and Virginie Galeote (virginie.galeote@inra.fr).

Application deadline: 01/04/2007. Applications will be reviewed on an ongoing basis.