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Generation of bacterial strains of production, with a growth-coupled focus to for its application in synthetic biology

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Metabolic engineering is a discipline that is based on the manipulation of metabolism through the use of recombinant DNA technologies for the production of metabolites of industrial interest. L-Alanine is an amino acid of great importance in the food, pharmaceutical, cosmetic industry and is also used as a substrate for the synthesis of thermoplastics. In E. coli, its synthesis is given from 3 compounds, L-Valine (Type I Biosynthesis), Pyruvate (Type II Biosynthesis) and L-Cysteine (Type III Biosynthesis). In all cases, highly regulated routes of biosynthesis are discussed, difficult to manipulate, redirect, and even more, about to produce. This is demonstrated by the strains conceived from a metabolic engineering approach, where the production of this amino acid has not been successful, mostly due to low production titles, or due to the inhibition of growth. Recently, through advances in systems biology and synthetic biology, the metabolism of organisms has been computationally modeled to help design production organisms from a more rational, predictive and systematic environment, qualities not always seen in biology. The present project presents a combination of methodologies that manages to turn around the design-construction-test cycle of bacterial strains of Metabolic engineering production. We started with an in silico design generated by the genomic scale model of last generation Escherichia coli (ME-iOL1554). From this, the strains were generated using molecular biology tools. The strains generated were characterized in a simple experimental system but with strict micro aerobic conditions and underwent a process of adaptive evolution in the same experimental system, managing to generate strains with fermentative pathways interrupted but that manage to grow under strict micro aerobic conditions. The strains generated produced L-alanine (although not in titles close to that predicted by the metabolic model at genomic scale), the exo-metabolomic analyzes of one of the strains show that it is igniting latent fermentation pathways not previously described. This is why this work constitutes a conceptual advance for several reasons. 1) Test the use of computer models as a design tool, a combination of systems biology and synthetic biology is achieved. Both sciences of great importance and relevance today. 2) The concept of growth-coupled (Growth-Coupled), a fundamental quality in a production strain, is experimentally validated. 3) A combination of methodologies was implemented: computational design, molecular biology, fermentations, adaptive evolution and exo-metabolomics by H1-NMR. 4) An advance was achieved in the generation of L-Alanine producing strains, however the most important result of the project was the use of computational models as a design tool and the discovery of latent fermentation pathways (ethylene glycol and methanol) in Escherichia coli, which could reinforce what has been said and proposed by other researchers. At the moment, there are two strains whose characteristics make them candidates for strains ¨Chasis¨. It is worth mentioning that the work developed is part of collaboration between the CCG-UNAM and the Department of Bioengineering of the University of California at San Diego (UCSD) who are the world leaders in Systems Biology, this project was supported by the UC- MEXUS CONACyT Collaborative Grants.

Biography

Francisco is a Biologist from the Metropolitan Autonomous University. In 2014 I made a Research Stay in the Biotechnology Institute (IBT-UNAM) in the lab of Dr. Francisco Bolívar, who in 1979, creates and organizes, based on his pioneering experiments, the first company of Genetic Engineering worldwide (Genentech, Inc.) in 2015 conducts research at the Center of Genomic Sciences in the area of Synthetic Biology and Systems Biology in collaboration with the world leaders in Systems Biology at the University of California, San Diego. He is currently a founder and researcher at the company Biolex.Corp and in September 2017 he will start a Mres Synthetic Biology at University College London (UCL).

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