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Extended Abstract

Biosynthesis of Drugs through Synthetic Biology: From the Assembly of a Synthetic Genome to the Purification of the Drug

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Abstract

Today, bacteria are programmed to produce metabolites, proteins, biofuels, biomaterials, pharmaceuticals, antibiotics, and medicines, thanks to innovative research in synthetic biology. Where a tool called minimal genome can play an important role in the design, construction and assembly of fully synthetic genomes, which do not exist in nature, which once introduced into a previously treated biological system 'host cell' (example: bacteria and / or yeast) result in a synthetic organism, which also does not exist in nature, conceived in the computer, where it is simulated from the interaction and expression of its genes, the optimization of some product of interest, growth rate and others so many physiological and phenotypic characteristics that do not follow the traditional method of genetic engineering and the engineering of metabolic pathways, based on trial and error.

What makes the design and creation of synthetic organisms (in silico) a more attractive and promising alternative for the pharmaceutical industry, to have a faster, more economical, more sustainable but above all, more innovative drug biosynthesis. But the innovative process does not stop until there, thanks to Systems Biology, we can now model and simulate processes that have to do with clinical tests, drug discovery, and drug metabolization by biological systems, all this helped with omic sciences (metabolomics, fluxomics, phenomics, reactomics, etc.)

Where the Synthetic Biology together with the Systems Biology and the omic sciences, offer us a biosynthesis of drugs, from the conception of a production by new biological systems (synthetic organisms) the modelling of the metabolism of the drug, selection of therapeutic targets, even to get to design new antibodies (aptamers). Not for anything, today the commercial market of Synthetic Biology is one of the most millionaires whose projections are of a growth of 45% per year, where not even the oil and traditional big pharma markets have.

Introduction

Microbes are master chefs of the bimolecular world; collectively, they harbour the power to supply a huge array of unknown substances, a number of which can have therapeutic or other useful properties. In checking out useful products, a team of chemists at Illinois have discovered an entire new class of microbial recipes.

"The quite reactions that these enzymes do are mind-boggling . . . when we first saw them, we were scratching our heads," said Howard Hughes Medical Institute (HHMI) Investigator Wilfred van der Donk, who led the study. "Then we had to painstakingly prove that the reactions we thought the enzymes were doing are indeed carried out." Van der Donk, who is also the Richard E. Heckert Endowed Chair in Chemistry and his colleagues at Illinois, collaborated with the laboratory of HHMI Investigator and University of California, l. a. Professor of Biological Chemistry and Physiology Tamir Gonen to confirm their findings, which were published this week in Science. The work was supported by HHMI and the National Institutes of Health. First author Chi Ting and van der Donk are members of a search team at the Carl R. Woese Institute for Genomic Biology that aims to get new natural products--the potentially useful substances produced by microbes--by exploring their genomes, a technique called genome mining.

"Genome mining allows you to start looking for compounds where you have absolutely no idea what they are going to be," van der Donk said. "Many labs in [our team] try to seek out new antibiotics by genome mining . . . you search for unusual things where we do not know what's being made, then you are trying to form the compound during a friendly organism." Cells use special chemical ingredients called amino acids to make proteins, which are the most structure and internal machinery of living things. Proteins are long chains made up of the twenty different types of amino acids; peptides are shorter chains. Some types of microbial natural products are formed from small peptides embellished with aftermarket chemical parts. Proteins and most peptides are assembled by ribosomes, giant cellular machines that act like pastry chefs at a bakery. Following the recipes written in genes, ribosomes can link together any sequence of amino acids; ribosomes are efficient and versatile. Other peptide-based natural products are made by teams of specialised enzymes, which act sort of a home baker with a favourite recipe learned by heart--these enzymes don't follow a template, instead creating the same types of linkages and modifications over and over to make just one product. "In natural product biosynthesis, both pathways are wont to make natural products," van der Donk said. "And now we stumbled across something that has features from both."

The researchers made their unexpected discovery while examining a cluster of genes found within the bacterium Pseudomonas syringae, which infects plants. They had found that their cluster of genes included one that held the knowledge for a peptide made by a ribosome, while another coded for an enzyme that would add another amino acid onto the peptide chain. The pastry chef was assembling dough to make bread, but handing it over to a home baker to finish preparation. "In retrospect it's just a very clever way of doing things," van der Donk said. "Having an enzyme which will do that to a pre-existing peptide means now you'll use it as a scaffold and just keep making the natural product time and time again." the sort of synthetic process they found in Pseudomonas works this manner because once the new aminoalkanoic acid is added to the peptide, it's modified in a series of steps then broken off, returning the first ribosomal-created peptide back to the starting step. In this way, it is a bit like sourdough starter. As long as it remains active, it doesn't need to be recreated from scratch to make each subsequent batch of bread.

To fully describe their natural product and its synthesis, van der Donk's team wanted to urge a far better check out its structure. However, the molecule proved too unstable to use traditional techniques. The researchers reached out to Gonen, whose lab had recently applied a cutting-edge approach--using electron microscopy on flash-frozen microcrystals of purified substances--to the determination of the structures of small molecules. "Once you've made the natural product, now you would like to work out what it's our collaborators wanted to point out the utility of this method for an unknown molecule of natural origins," van der Donk said. "This was really a win-win situation for both labs. I think the entire natural products community probably will want to start out using this system." Now that van der Donk and his team are conscious of the existence of this alternative pathway for synthesis, they need already found other samples of similar mechanisms, including the assembly of an anti-tumor compound by a soil microbe. In addition to expanding the power to acknowledge gene clusters that make promising natural products, the researchers are excited about finding new ways to place pathway to use.

"We're also excited on how we'd be ready to use this for synthetic biology," van der Donk said. "Because the overhead, the quantity of resources that need to enter to form a natural product, is fairly low here. You make this peptide, a couple of enzymes, and outcomes rolling an anti-tumor compound. There's a lot of interest immediately in engineering bacteria to possess anti-cancer activity, and this is often relatively low-hanging fruit with reference to making the organism make the molecules for you."

Biography

Francisco is a Synthetic Biologist from University College London (UCL) he is currently CEO & Founder of the Synbiomics Group, a corporate that brings together STEAM Sciences Startup’s (many of which he has founded and directed), Last year, MIT Media Lab invites you to participate in the Global Community Bio Summit, space for the community Global Biologists, Biotechnologists, Biohackers, Biomarkers and other members of the Biotech field. He was recently named as one of the Young Leaders in Biotechnology and Bio economy in the Latin America Region. He has toured more than 15 countries in which he has participated as a keynote speaker, lecturer, panelist and member of the Biotechnology Advisory Board in congresses, forums, workshops and medical fairs. In these events he promotes the development and proper use of the achievements of Synthetic Biology, highlighting the ethical, moral and humanitarian aspects in its importance in global regulation and rational use in humans.