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DRUG AND BUG INTERACTIONS WIN LIFE SCIENCES PRIZE

A conversation with **ATHANASIOS TYPAS**, group leader in the Genome Biology Unit at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, and winner of the 2022 Liliane Bettencourt Prize for Life Sciences from Fondation Bettencourt Schueller

The Liliane Bettencourt Prize for Life Sciences has recognized and celebrated young European researchers since 1997. Awarded by Fondation Bettencourt Schueller, the prize highlights the innovative research and discoveries, international publications, and leadership skills of scientists under the age of 45, and is accompanied by a €300,000 grant. Athanasios (Nassos) Typas discusses his research on drug-bacterial interactions and their impact on the human microbiome.

Tell me about your work?
I study how bacteria interact with each other, their environment and their host. I am particularly interested in how interactions with drugs can affect microbes in the human gut, where commensal bacterial communities play pivotal roles in our health and well-being.

I look at modes of drug resistance, metabolism of drugs by microbes, and the collateral damage to our gut flora caused by drugs intended to act in other parts of the body. For example, my team discovered how large numbers of therapeutic medicines can actually inhibit the growth of gut bacteria.

What drew you to this research?
I am fascinated by the functional diversity of microbes and the multiple paths that evolution has taken to solve similar problems. A driving force in my lab has been to come up with experiments to investigate these bacterial genetic mechanisms and interactions.

These tests can also explore the mechanisms that drive some of the important relationships we see in microbiome data, such as how the gut microbiome composition changes with different diseases. These relationships are usually presented as associations. But our experiments can address causality — such as whether a specific disease or its treatment is responsible for a microbiome change. This has made the mirobiome field more molecular and mechanistic.

And the work that won the prize?
As part of the award, you have to pitch a proposal, which is then funded if you win. So, the prize will allow us to create and examine model bacterial species for the gut.

Between 500 and 1,000 bacterial species make up the complex communities of our microbiome. These are very diverse and the details of their genetics are mostly unknown. I call this dark genetic matter.

My team and I aim to develop the genetic tools, functional knowledge and resources we need to assess how drugs influence some key microbes, and how this affects health.

Working in two species of bacteria — *Phocaeicola vulgatus* (until recently known as *Bacteroides vulgatus*) and *Bacteroides uniformis*, we will map gene function and organization in a systematic way. We will also create publicly available genetic tools and mutant libraries for other researchers to study these organisms further, and use the information to chart their cellular networks and highlight different aspects of their underlying biology.

Why these two bacteria species?
These two species of bacteria represent two main genera of the most prolific bacterial phylum in the microbiome, the Bacteroidota. Although there are vast differences between the microbiome of different individuals, these species are found in most people.

We can build on current genetic tools to study these two species, and they are relatively easy for researchers in other labs to cultivate and work with. There are many other species we could have picked, but we want to produce a roadmap for establishing new model organisms from scratch that other labs can apply to develop further model species. We hope this work will eventually lead to a map of functional units and metabolic pathways across most, if not all of the microbiome species.

Why is this work important?
We need to better understand each individual species within the community before we can fully appreciate the complexities of the interactions between each species in a healthy gut environment, as well as the response to different pathogens and drugs.

Phocaeicola vulgatus and *Bacteroides uniformis* are efficient colonizers of the gut and robust members of the community, both in vivo and in vitro. So, they are a likely species that could be introduced and accepted into new communities. They could potentially carry functional traits we want to introduce into the gut, such as specific enzymatic function to metabolize toxic metabolites left after degradation of foods or drugs — helping to harmonize the microbiome community. But this is a long way into the future. We have to prepare the foundations first.

What does the Liliane Bettencourt Prize for Life Sciences mean to you?
I am delighted and honoured, and it was great to see the recognition for my team's work and that the questions we try to answer are relevant to others. Prizes are always given to individuals but research is not done by individuals. Our work has been done by teams of people working closely in collaboration with many other labs. We will continue to work with other EMBL teams to develop data-driven approaches to piece this puzzle together to improve human health.

Fondation Bettencourt Schueller

Prix Liliane Bettencourt *pour les sciences du vivant*

2022 LAUREATE

Athanasios Typas

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Heidelberg, Germany

Establishing model species for studying the human gut microbiome and characterizing its dark genetic matter

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