Charting metabolic maps in the pursuit of new vaccines and antimicrobials

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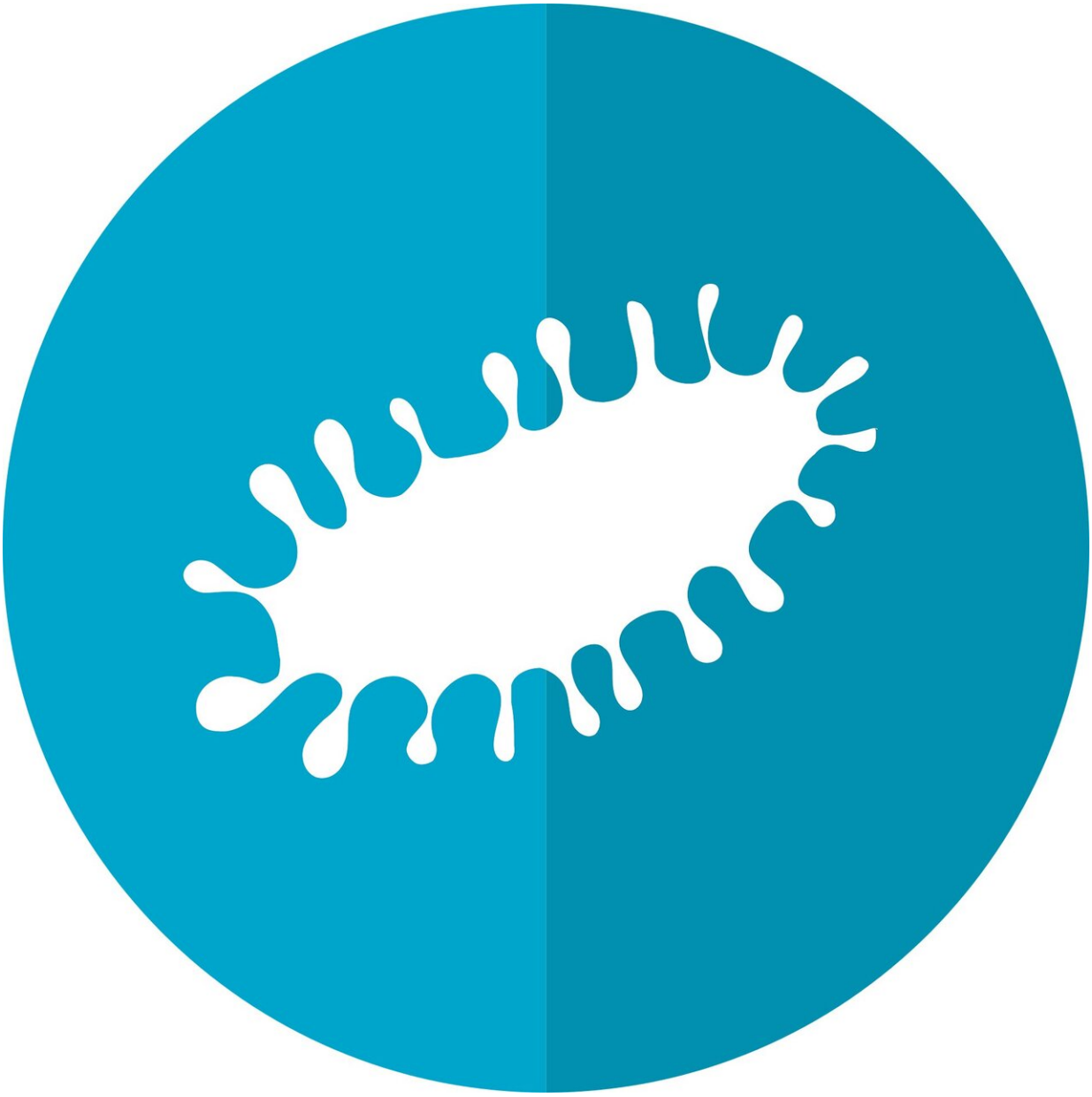

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A study in *Cell Reports* maps genes essential for the metabolic function of M. agalactiae and M. pneumoniae, two common bacteria that infect livestock and humans respectively. The map of M. agalactiae reveals insights that unlock routes to explore new vaccines and antimicrobials for veterinary applications. The results can also be used to finetune a re-engineered version of M. pneumoniae so that it can treat human lung diseases in the future.

The new methods used in the study could be useful for other researchers to quickly evaluate a microorganism's active metabolism, boosting chances of finding new applications using microbes.

Bacteria are versatile living organisms that can colonize a huge range of environments, hosts and tissues. Much of this success is thanks to their metabolic plasticity, which has been shaped by evolution over millions of years.

Microbial metabolic pathways can be exploited for industrial applications, such as using bacteria to dye jeans with their trademark indigo hue. It is also increasingly important in healthcare, with previous studies linking microbiome metabolism with the human body's ability to absorb therapeutic drugs.

Current approaches to charting microbial metabolic pathways are expensive, tedious and time consuming, hindering the development of new applications such as vaccines or antimicrobial substances. New tools are needed to build an accurate map of all the chemical reactions that take place in a particular strain of bacteria with no dead ends or futile loops.

In a study published today in the journal *Cell Reports*, researchers at the Centre for Genomic Regulation in Barcelona describe a new method for determining active metabolic pathways in microbes using cutting-edge techniques from genomics and proteomics.

The researchers first tested their methods by mapping the metabolic pathways of Mycoplasma pneumoniae, a bacterium with a small genome that commonly causes mild infections of the respiratory system, and whose metabolism has been comprehensively documented in the past. Its active metabolic pathways agreed with experimental data.

They used the same methods to document the relatively unknown pathways of Mycoplasma agalactiae, a common source of infections in goats and sheep with significant health and economic ramifications for livestock. Despite M. agalactiae and M. pneumoniae sharing much of each other's genome, their metabolisms took substantially different pathways, highlighting the complexity of predicting metabolic networks based on genomic information alone.

"Microorganisms are a treasure trove for finding new applications for healthcare and industry. Having new tools to capture a global picture of the activity and directionality of microbial metabolic networks is key to making the most of these natural resources," says Ariadna Montero Blay, Ph.D. student at the Centre for Genomic Regulation and first author of the study.

"Our findings for Mycoplasma agalactiae could have a great impact in the veterinary field in the generation of novel antimicrobials based on toxic metabolites or attenuated vaccination strains with knock-down of essential metabolic genes or re-engineered metabolic fluxes."

The results of the study may be used to fine-tune a re-engineered version of M. pneumoniae so that it may one day be used to treat human lung

diseases, a long-term objective of the research group.

"While this is still years away, we can use these methods to identify important metabolic routes and block them, which could increase the specificity and effectiveness of using Mycoplasma as a live pill," says Luis Serrano, ICREA research professor, director of the CRG and last author of the study. "Our study highlights the ingenious new methods in science that are reducing time and costs and accelerating new discoveries."

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