Researchers engineer synthetic pathways for new antibacterial treatments

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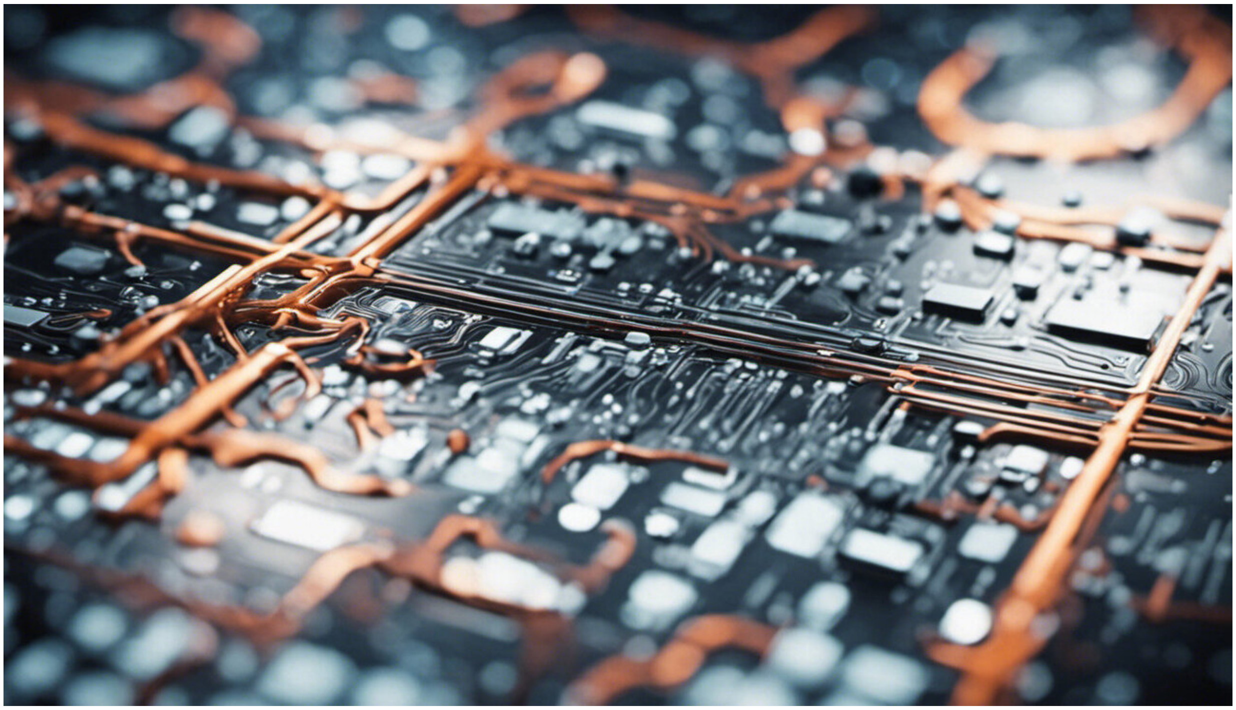

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Bacteria, for the most part, thrive in extreme temperatures and in arid conditions. But some types of bacteria have the capacity to do this and more: they grow within diverse environments and adapt easily. One such species is the Bacillus subtilis. Known to make its home in soil and in water, researchers have also found evidence that B. subtilis is frequently present in the human gut.

B. subtilis forms endospores that can protect it from nutrient deprivation. Researchers have seized on this and frequently use the genetically controllable bacterium as a cell factory in biotechnology. Enter BASYNTHEC ('Bacterial synthetic minimal genomes for biotechnology'), a project launched in 2010. It sought to develop a model-based approach for engineering B. subtilis and create synthetic modules for producing metabolites and proteins of interest. Ultimately, the research could lead to new antimicrobial treatments for bacterial infections.

But the results could also lead to better strain safety, reducing the ability of strains being able to survive and diminishing the unwanted side effects that all natural organisms have. This, in turn, would lead to both fewer accidental gene transfers and unwanted interactions with the environment, humans or products.

The project is supported under the 'Knowledge-based bioeconomy' theme of the Seventh Framework Programme (FP7). Led by the Institut National de la Recherche Agronomique (INRA) in France, the project partners used computational and experimental biology with novel high-throughput methodologies to alter and reduce the chromosome of this particular strain 'à la carte'.

The team produced, collected and subjected hundreds of deleted strains (strains in which part of a single chromosome has been lost) to high-throughput screening for antimicrobial targets and other applications. The BASYNTHEC team also engineered synthetic pathways for protein translation and for production of vitamin B5, enabling the researchers to test their full potential. A patent application based on this work has been filed.

The consortium started from the conviction that it was necessary to identify both new antimicrobials for bacterial infection treatment, and targets within the bacterial cell for antimicrobials. The deletion strains generated in the study allowed the researchers to determine which strains are relatively resistant to Sublancin 168, a B. subtilis-triggered antimicrobial peptide that has the capacity to destroy several certain organisms.

There are many companies manufacturing enzymes for the pharmaceutical industry. The Bacillus species is already recognised for its low cost and efficiency in production chains, but there is still room for improvement - for example by eliminating the unwanted side effects during production. The team is hopeful that combining the BASYNTHEC modelling framework with validated and less complex bacterial strains will encourage scientists to use it as a generic biotechnological platform for better control and cell metabolism manipulation during industrial processes.

The BASYNTHEC team brought together experts from Novozymes A/S (Denmark), INRA Transfert (France), Ernst-Moritz-Arndt-Universität Greifswald (Germany), Academisch Ziekenhuis Groningen (Netherlands), DSM Nutritional Products (Switzerland), Eidgenössische Technische Hochschule Zürich (Switzerland) and the University of Chicago (United States).

More information: BASYNTHEC: www.basynthec.eu/
Institut National de la Recherche Agronomique (INRA): www.inra.fr/en/

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