Vibrio natriegens: Low-cost microbe could speed biological discovery

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Credit: Pixabay/CC0 Public Domain

Cornell University researchers have created a new version of a microbe to compete economically with E. coli—a bacteria commonly used as a research tool due to its ability to synthesize proteins—to conduct low-

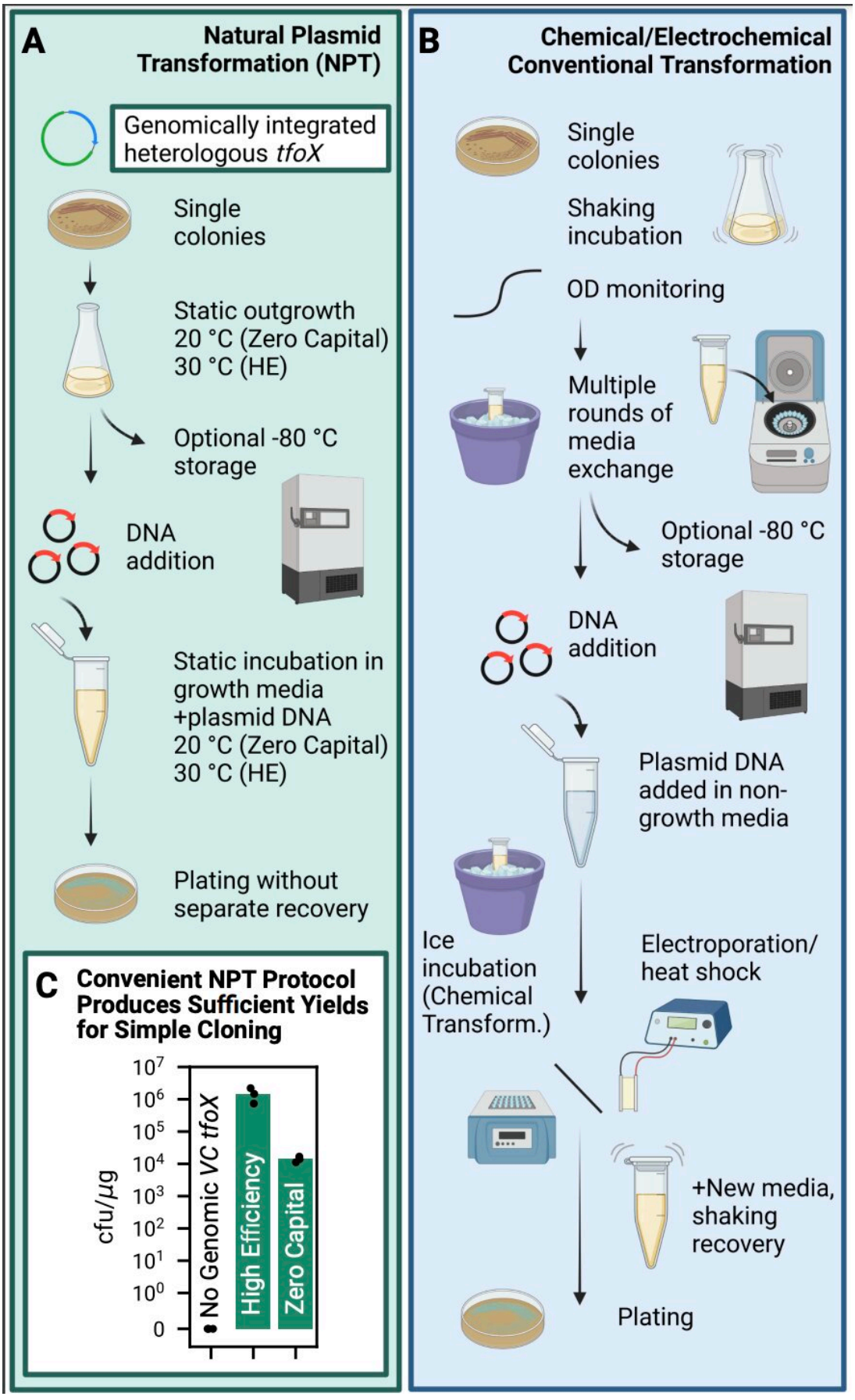
cost and scalable synthetic biological experiments.

As an inexpensive multiplier—much like having a photocopier in a test tube—the bacteria Vibrio natriegens could help labs test protein variants for creation of pharmaceuticals, synthetic fuels and sustainable compounds that battle weeds or pests. The microbe can work effectively without costly incubators, shakers or deep freezers and can be engineered within hours.

The research was published Feb. 13 in *PNAS Nexus*.

"It's really easy to produce," said lead author David Specht, a postdoctoral researcher in the laboratory of Buz Barstow, assistant professor of biological and environmental engineering.

To study proteins for creating medical cures or fashioning fuels, researchers use a plasmid (a small piece of DNA) that acts as the instruction manual to make the molecular machine—a protein—of interest. Currently, when researchers place a plasmid into E. coli, they can create many copies to test several variants.


A
Natural Plasmid Transformation (NPT)
Genomically integrated heterologous tfoX
Single colonies
Static outgrowth 20 °C (Zero Capital) 30 °C (HE)
Optional -80 °C storage
DNA addition
Static incubation in growth media +plasmid DNA 20 °C (Zero Capital) 30 °C (HE)
Plating without separate recovery
C
Convenient NPT Protocol Produces Sufficient Yields for Simple Cloning
cfu/μg
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
0
No Genomic VC tfoX
High Efficiency
Zero Capital
B
Chemical/Electrochemical Conventional Transformation
Single colonies
Shaking incubation
OD monitoring
Multiple rounds of media exchange
Optional -80 °C storage
DNA addition
Plasmid DNA added in non-growth media
Ice incubation (Chemical Transform.)
Electroporation/ heat shock
+New media, shaking recovery
Plating

Vibrio natriegens genomically engineered for natural competence is transformable via direct addition of plasmid DNA to cells growing in a minimal competence media. Credit: Specht et al

E. coli cells help molecular biologists multiply and manipulate plasmids for protein engineering, but the process is expensive since they often purchase the bacteria from manufacturers, must keep it cold and maintain rooms of expensive equipment to sustain it. A modified E. coli, used for this purpose, is also very fragile.

"As scientists, we don't often know precisely what those regulatory or molecular sequences should be to achieve our goals," said Barstow. "So, we must test a lot of variants, and Vibrio natriegens allows researchers to scale up that process of testing."

The microbe V. natriegens is not complicated, Specht said. "It's so simple to make that someone with limited resources—like high school labs, home inventors or startup biological businesses—can do it," he said.

Researcher Timothy Sheppard compared the simplicity of V. natriegens in conducting synthetic and molecular experiments to using a simple writing instrument hundreds of years old. "We've found nature's pencil for cloning and conducting synthetic biology," he said.

The process is inexpensive with V. natriegens, as it requires no capital equipment purchases and it can work at room temperature. The cells produced from V. natriegens grow quickly: According to the paper, a transformation started at 9 a.m. yields visible colonies by 5 p.m., each

filled with masses of proteins.

"The microbe is a radically simple solution to a hard problem," Barstow said.

More information: Efficient Natural Plasmid Transformation of Vibrio natriegens Enables Zero-capital Molecular Biology, *PNAS Nexus* (2024). DOI: 10.1093/pnasnexus/pgad444

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