







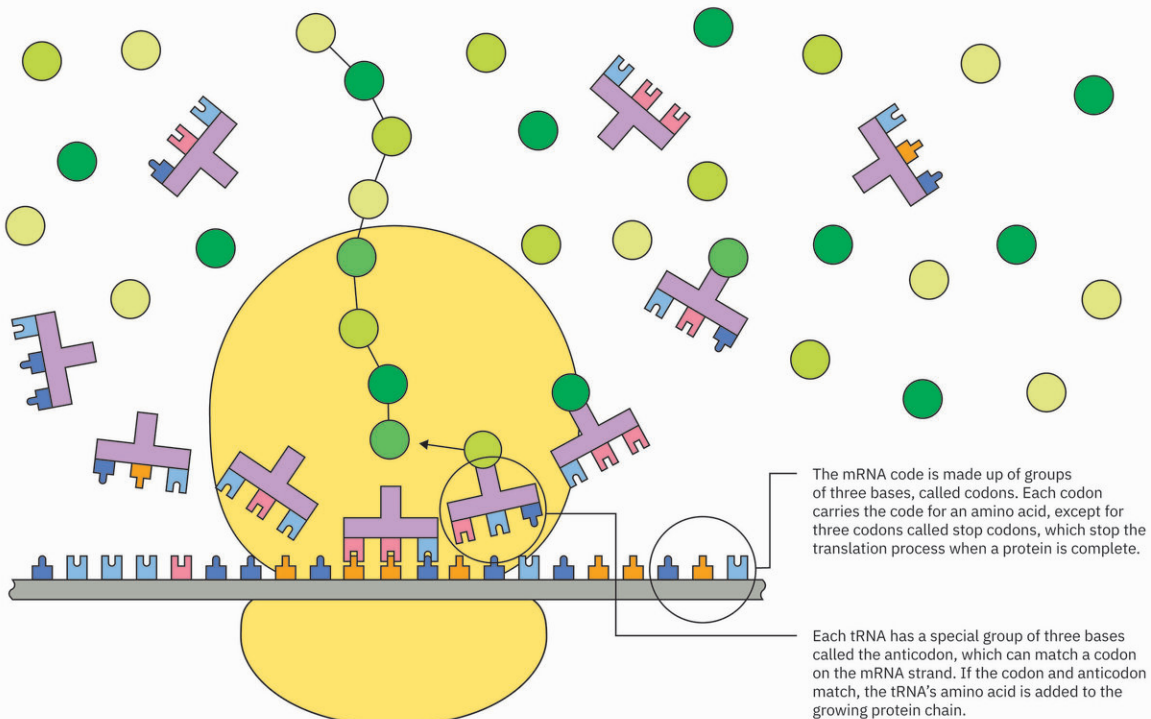
# Designer organelles bring new functionalities into cells

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## How translation works

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**Ribosome** – molecular machine where the mRNA code is 'translated' into proteins
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**Amino acids** – the chemical building blocks of proteins
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**Protein** – a chain of amino acids
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**Transfer RNA (tRNA)** – a molecule that brings amino acids to the ribosome. There are many types of tRNA, each one carrying a specific amino acid
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**Messenger RNA (mRNA)** – the molecule that carries the code for making proteins. mRNA is made using the cell's DNA as a template
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**Bases** – letters of the genetic code



The genetic code is made up of three-letter sequences called codons. Each one codes for an amino acid, except for three 'stop' codons, which signal that an amino acid chain is complete. The Lemke group were able to develop a cell organelle that uses a reprogrammed stop codon, so that it codes for a new amino acid - not one of the 20 that occur naturally in living organisms. Credit: Aleks Krolik/EMBL

For the first time, scientists have engineered the complex biological process of translation into a designer organelle in a living mammalian cell. Research by the Lemke group at the European Molecular Biology Laboratory (EMBL) - in collaboration with JGU Mainz and IMB Mainz—used this technique to create a membraneless organelle that can build proteins from natural and synthetic amino acids carrying new functionality. Their results—published in *Science* on 29 March—allow scientist to study, tailor, and control cellular function in more detail.

During evolution, the development of new organelles allows [cells](#) and organisms to become more complex, due to the ability to sort [cellular processes](#) into specific hotspots. "Our tool can be used to engineer [translation](#), but potentially also other cellular processes like transcription and post-translational modifications. This might even allow us to engineer new types of organelles that extend the functional repertoire of natural complex living systems," explains Christopher Reinkemeier, Ph.D. student at EMBL and JGU Mainz and co-first author of the paper. "We could for example incorporate fluorescent building blocks that allow a glimpse inside the cell using imaging methods."

"The organelle can make proteins by using synthetic non-canonical amino acids. Currently we know of more than 300 different non-canonical amino acids—compared to 20 which are naturally occurring. We are no longer restricted to the latter ones," says co-first author

Gemma Estrada Girona. "The novelty we introduce is the ability to use these in a confined space, the organelle,, which minimises the effects on the host."

### **Wobbly wall-less organelles**

Translation is such a complex process that it cannot be contained in one single organelle surrounded by a membrane. Therefore, inspiration was drawn from phase separation: the process responsible for the formation of membraneless organelles in vivo, such as nucleoli or stress granules. Phase separation is used by cells to locally concentrate specific proteins and RNAs. Even though these wall-less organelles have wobbly boundaries as they dynamically interact with the surrounding cytoplasm, they can still do very precise tasks. The team combines [phase separation](#) with cellular targeting to create their membraneless organelle and to make sure that only one organelle per cell is formed.

In the end, only five new components have to be engineered into a cell to build it. The assembly of these components generates a large structure, which might create some burden on the cell. In the future, the group aims to engineer minimal designer organelles, to minimise any impact on the physiology of the healthy organism.



The authors see the newly developed synthetic host as a city. On the one hand, typical cellular processes -- seen as encapsulated, isolated, and made up of non-interchangeable elements -- are represented as repetitive structures: squared, isolated blocks which are always fenced, just like membranous organelles. On the other hand, the image highlights the making of a new organelle -- a new building that is not fenced -- which is accessible to the rest of the city while having its own identity, a building which is more dynamic and flexible. Credit: Gemma Estrada Girona

Edward Lemke, visiting group Leader at EMBL, professor at JGU

Mainz and adjunct director at the IMB, led the project. He concludes: "In the end, we aim to develop a technique to engineer synthetic cellular organelles and proteins that do not affect the host machinery at all. We want to create a tool that does not have any uncharacterised effects. The [organelle](#) should be a simple add-on that allows organisms to do custom-designed novel things in a controlled fashion."

**More information:** C.D. Reinkemeier et al. Designer membraneless organelles enable codon reassignment of selected mRNAs in eukaryotes. *Science* (2019). [science.sciencemag.org/cgi/doi/...  
1126/science.aaw2644](https://science.sciencemag.org/cgi/doi/10.1126/science.aaw2644)

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