New strides in synthetic biology

Researchers are well on their way to creating entirely new biochemistries and, ultimately, artificial life. Anthony Forster, professor at the Department of Cell and Molecular Biology at Uppsala University, is one of the pioneers in this relatively new research field, known as synthetic biology. The most fundamental tool in synthetic biology is gene synthesis, which is where it all starts.

There are high hopes for what this rapidly growing research field might deliver, in the form of new solutions to major global challenges such as antibiotic resistance and the world’s energy supply.

“The possibilities are endless. Take the building blocks of biology. There are only a few of them, of course, limited by the cell’s 20 natural amino acids. But what can be produced synthetically is unlimited, and gives us totally new opportunities,” says Anthony Forster.

However, designing artificial biological systems is by no means easy. Objectives include developing new drugs, treatments and smart materials and, in the future, being able to produce new life. For over ten years, Anthony Forster has questioned the inflexibility of biology’s central dogma, represented by this flow of information in the cell: “DNA makes RNA makes protein.” He rewrote the central formulation as “DNA makes RNA makes peptidomimetic”. Peptidomimetic molecules are protein-like molecules into which he had incorporated synthetic amino acids with new properties and purely pharmacological advantages. These may be promising new drug candidates.

Unnatural amino acids are both preferred and common components of drugs. Peptidomimetics containing them enter our cells easily and are broken down only slowly. Molecules that bind strongly to the target of choice can now be evolved rapidly using genetic coding. This is inspired by nature’s ability to evolve antibodies against an infection. Something that worries him and many others is the onrush of antibiotic resistance. There is no time to waste.

The spread of antibiotic resistance is outstripping our ability to design new antibiotic molecules.

In addition to the de novo genetic codes, Anthony Forster has several groundbreaking discoveries to his name, including the discovery of the hammerhead catalytic RNA structure and the invention of external guide sequences for ribonuclease P. He has a long list of ongoing projects. A few examples are the use of metagenomics to study genes involved in antibiotic resistance, designing and assembling genetic processes and systems, and basal studies of ribosomal RNA with the objective of constructing a ribosome and a complete cell. In all his research, Anthony Forster starts from an unusual direction. Instead of looking at what works now, he asks himself what we want to work and how we make it happen.

“There is usually a solution, but it takes time, and there are often unexpected discoveries along the way. This is all part of being a researcher. As a child, I loved building with Lego. Now I get the opportunity to build with the building blocks of life instead, and to devote myself to something much more useful. Science is my passion,” says Anthony Forster.