CHEMICAL BIOLOGY

Collaborating on cellular control

New Centre for Living Technologies engineers new properties into living cells

Tom de Greef

The Dutch "polder"-mentality – the ability to work together for the common good – happily permeates all walks of Dutch life, including scientific collaboration. Knowing that you can achieve more together than you can alone, has triggered a powerful new partnership: The Centre for Living Technologies. A collaborative synthetic biology research program that connects TU/e, Wageningen University Research (WUR), Utrecht University (UU) and University Medical Centre Utrecht (UMCU). Together, these four institutions aim to develop bio-based technologies to improve the health of people, animals and the environment by engineering new properties into living cells.

"MICROBES IN A MIX ARE A BIT LIKE TODDLERS AT AN UNSUPERVISED PARTY"

Tom de Greef, associate professor of Synthetic Biology, is leading this collaboration from the TU/e end. Using synthetic biology, the collaborators will work together to create materials that can mimic, enhance and increase the functionality of living cells. These materials can then be used in a therapeutic way in the body or to create advanced materials that can help solve environmental problems.

CELL AS COMPUTER

De Greef's lab specializes in biological computing within the synthetic biology field. "We engineer cells to perform the very familiar functions of a computer, such as logical reasoning, analytics, recording of signals and storage of data," he explains. The translational possibilities for this emerging field where synthetic biology and computing meet, are vast. Combining their joint strengths, the collaborators have chosen two topics that they believe may contribute to addressing challenges in the field of health and the environment: "Smarter cellular therapies" and "Policing the microbial soup."

SMARTER CELLULAR THERAPIES

Together with Lukas Kapitein, professor of molecular and cellular biophysics (UU), the first project focuses on elevating existing cellular therapies – treatments where living cells are engineered to fight disease and then are administered to patients – to the next level of sophistication. De Greef: "First-generation cellular therapies are in the clinic, but these are relatively simple. They are programmed to detect single antigens and, in a limited way, destroy diseased cells." The collaborators will focus on engineering designer cells to recognize and respond to multiple antigens resulting in targeted and more accurate therapies. This generation of smarter cellular therapies would be responsive and capable of tackling cancer cells that are constantly adapting to survive and outwit anti-cancer therapies. "It's a kind of engineered intellectual match between the therapy and the cancer cell," says De Greef.

POLICING THE MICROBIAL SOUP

Humble and often overlooked microbes could help to solve the biggest problem facing humanity today: global warming. Professor of microbiology at WUR, Diana Machado de Sousa knows that a side effect of culturing certain microbes in a mix, is the conversion of greenhouse gases into biomass. Using such a microbial mix or microbial soup to "eat" carbon emissions and produce a sustainable biofuel could be an important tool in reducing atmospheric CO_2 levels and thus counter global warming.

Unfortunately, the unstable nature of the mixture hampers large-scale application of microbial soups. De Greef: "Combining specific microbes produces this very welcome side effect, but their very co-existence also leads to each species influencing the other. That makes the combined culture unstable, destructive and volatile and thus unfit to be used at scale." He has an insightful metaphor at hand: "It's a bit like toddlers at an unsupervised party. It can all go great for a while, but at some point, things are pretty sure to take a turn for the worse." Together with Machado de Sousa, De Greef is engineering so-called policing microbes (comparable to parents at the party) who can control microbial interactions by detecting certain signals. "Receiving a signal that one species is growing too fast will trigger the policing microbe to send a stop signal, thus slowing down the overactive growth," explains De Greef. Adding such an engineered police force will result in a stable product that can be part of the toolkit to help combat global warming.

JUST AN ENGINEER

Without the deep commitment to collaboration and the structure provided through the living technologies collaboration, these projects would not be possible. "I am just an engineer," says De Greef. "I taught myself how to modify organisms, so for me it's easy to apply this to different societal problems." Beyond joint projects, this collaboration is also focused on training the next generation of scientists, sharing facilities and stimulating spin-off collaborations. The return on investment of a collaboration like this is predicted to be significant and long lasting with ripple effects that will spread across the scientific community and stimulate further advancements for society.