Яковлев Владимир Андреевич
Тюменский государственный университет
Институт Биологии
Кафедра иностранных языков и межкультурной
профессиональной коммуникации
Студент специалитета
Группа 26БиБс185
stud0000203661@study.utmn.ru
Гаркуша Надежда Анатольевна
Тюменский государственный университет
Институт Социально-Гуманитарных Наук
Кафедра иностранных языков и межкультурной
профессиональной коммуникации
Доцент, канд. пед. наук
n.a.garkusha@utmn.ru

Синтетическая биология: достижения и основные аспекты развития. Достоинства и недостатки производства

Yakovlev Vladimir Andreevich
University of Tyumen
Institute of Biology
Foreign Languages and Intercultural
Professional Communication Department
Student of 26BiBs185 gr.
stud0000203661@study.utmn.ru
Garkusha Nadezhda Anatolievna
University of Tyumen
Institute of Social Sciences and Humanities
Foreign Languages and Intercultural
Professional Communication Department
Associate Professor, Candidate of Pedagogic Sciences

n.a.garkusha@utmn.ru

Synthetic Biology: Achievements and Main Development Aspects. Advantages and Disadvantages

Аннотация. Данная статья посвящена достижениям в синтетической биологии. В статье представлена информация как об общем развитии синтетической биологии, так и о конкретных разработках в этой области. Основная цель данной статьи это сбор информации о достижениях синтетической биологии, а также выявление преимуществ и недостатков проектов, созданных с помощью синтетической биологии.

Ключевые слова: синтетическая биология, биотехнология, генная инженерия, ген.

Abstract. This article is devoted to advances in synthetic biology. The article presents information about the general development of synthetic biology and specific developments in this area. The main purpose of this article is to collect information about the achievements of synthetic biology, as well as to identify the advantages and disadvantages of projects created with the help of synthetic biology.

Key words: synthetic biology, biotechnology, genetic engineering, gene.

Introduction

Imagine a future where synthetic jellyfish roam waterways looking for toxins to destroy, where eco-friendly plastics and fuels are harvested from vats of yeast, where viruses are programmed to be cancer killers, and electronic gadgets repair themselves like living organisms.

Synthetic Biology History

Welcome to the world of synthetic biology, or ‘synbio’, where possibilities are limited only by the imagination. Its practitioners don’t view life as a mystery but as a machine – one that can be designed to solve a slew of pressing global health, energy and environmental problems.

The front man for the field would have to be the audacious Craig Venter. In 2010 his team created the world's first synthetic life form – a replica of the cattle bacterium Mycoplasma mycoides. Dubbed 'JCVI-syn 1.0', its DNA code was written on a computer, assembled in a test tube and inserted into the hollowed-out shell of a different bacterium. Its creators embedded their names in watermarks in the DNA, along with two quotes. From writer James Joyce: "To live, to err, to fall, to triumph, to recreate life out of life." From pioneering quantum physicist Richard Feynman: "What I cannot create, I do not understand."

For Venter this was just one of many firsts. He holds joint credit for the first sequencing of the three-billion-letter DNA code of the human genome in 2001; in 2007 he became the first human to have their individual genome sequenced.

In 2016 he announced the answer to the meaning of life. It's 473 – at least for M. mycoides. That's the minimal number of genes the bacterium needs to survive. Venter's team discovered this by stripping down JCVI-syn 1.0 to create JCVI-syn 3.0. The leaner life form has about half as many genes as its precursor.

Synthetic biology gets less attention than genetic engineering but practitioners use many of the same techniques. There are long-standing examples, like Golden Rice engineered to produce vitamin A, which could be tagged with either label.

Historically, genetic engineers have tinkered with organisms. Synthetic biologists have a far bolder mindset. As Polish geneticist Wacław Szybalski put it at a conference back in 1973: "Up to now we are working on the descriptive phase of molecular biology … But the real challenge will start when we enter the synthetic phase … We will then devise new control elements and add these new modules to the existing genomes or build up wholly new genomes."[2, c. 1]

Finally, Szybalski predicted, the work would move to building "other organisms".

Synthetic biologists, quips Vickers, "are largely biologists masquerading as engineers or vice versa". While they work with biology – genomes (DNA codes), transcriptomes (parts of the DNA that are uploaded) and proteomes (what proteins

are being made) – they like to translate that work into engineering concepts and language.

In genetics speak, for example, regulatory stretches of DNA are called ‘promoters’; they are in turn regulated by ‘repressor’ or ‘inducer’ molecules. In synbio speak, promoters are called ‘switches’ and the molecules that regulate them ‘actuators’. Working circuits of switches and actuators are ‘logic gates’.

Is designing a tailor-made organism as straightforward as putting together some circuit components? No, says Vickers, life is much messier. “We would like to be able to treat biology like it’s an electrical circuit, but biological complexity is confounding much of the time.”

Synthetic biologists develop their projects through standard engineering cycles of ‘design, build, test’. The design phase involves computer modelling of the components’ behavior. The build stage involves the genetic engineering. The test step assesses if it works – and all too often unpredicted DNA interactions and toxicities mean it does not work as expected. [4, c.2]

Even the simplest biological organisms have DNA sequences no one entirely understands. Take Venter’s minimalist life form, JCVI-syn 3.0, with its 473 genes. While all these genes are necessary for the bacterium to live, the team – which has spent decades studying M. mycoides – has no idea what a third of them do. “As a synthetic biologist I find this so humbling,” Vickers says.

If the genetic logic of simple bacteria is mysterious, synthetic biologists are likely to encounter far more spanners in the works as they attempt to move up the evolutionary tree.

Here the ‘Yeast 2.0 project’ may help. This international initiative is rebuilding the yeast genome from scratch. Think of it as building a custom model racer rather than tinkering with a stock car. By starting with the nuts and bolts, scientists may be able to overcome the tangled legacy of millions of years of evolution to engineer a super-sleek genome in which they know how every gene contributes to life.

At least, that’s the hope.

Life may turn out to be harder to tame than the synthetic biologists initially thought. Nevertheless, they have already scored some impressive runs and their imagination remains unfettered – with a wild array of projects on the drawing board that span the solidly utilitarian to the truly fantastic.

Artemisinin

Synthetic biology's greatest success story so far is the synthesis of artemisinin, the key ingredient in today's best malaria drugs. Its large-scale production was made possible by Jay Keasling and colleagues at the University of California, Berkeley, who worked out how to make it using the humble yeast.

Artemisinin was first isolated from the sweet wormwood plant, Artemisia annua, in the early 1970s by Chinese chemist Youyou Tu – a discovery that would ultimately win her a share of the 2015 Nobel Prize in Medicine.

When she first isolated artemisinin, Tu was part of a secret government project to help China's North Vietnamese allies, who weren't just battling human foes but strains of malaria resistant to chloroquine, the most widely used malarial medicine. Searching for alternatives in traditional Chinese medicine, Tu found her breakthrough in The Handbook of Prescriptions for Emergency Treatments, written some 1700 years ago by physician Ge Hong.

The prohibitions of the Cultural Revolution prevented Tu from publishing her work till 1981, when it provided a shot in the arm for the battle against chloroquine-resistant malaria across Asia and Africa. By the early 2000s, the World Health Organisation was recommending artemisinin-based medicines as first-line treatments. Its supply, however, was limited and erratic due to the vagaries of growing sweet wormwood. In 2001 Keasling and colleagues set out to find a cheaper and more reliable way to make it.

The sweet wormwood plant makes artemisinin from a precursor molecule called farnesyl pyro-phosphate (FPP). Yeast cells also make FPP, which they use as the starting material for ergosterol, a building block of yeast cell walls.

Keasling's team turned up the controls on the yeast genes that make FPP and turned down the genes that convert FPP into ergosterol. They then took a sweet

wormwood gene that turns FPP into artemisinic acid and inserted it into the yeast genome. In the lab it was a small step to turn artemisinic acid into artemisinin.

Keasling and his collaborators established a company called Amyris to commercialize synthetic artemisinin. In 2008 it handed the technology over to French pharmaceutical giant Sanofi.

Biofuels

Yeast-made artemisinin captured hearts and minds by showing synthetic biology could make a life-saving malaria drug affordable. For its follow-up act, Amyris wanted to turn yeast into something equally compelling and biofuel was the answer. The Amyris scientists engineered a synthetic pathway that converted FPP into the hydrocarbon farnesene, the only biofuel sufficiently energy-dense to be approved for use in aviation fuel. Along with being a substitute for fossil fuels, farnesene also has the environmental benefit of not belching particulates and sulfur. When burned, it smells like green apples.

Venter, meanwhile, has been chasing the holy grail of turning algae into a commercially robust source of biofuel. It is a dream that over the past decades has defeated many biotech companies. Venter's company Synthetic Genomics – bankrolled by the world's largest oil and gas company, ExxonMobil – turned to synthetic biology for the answer.

Algae produce oil and require only briny water and sunlight to grow. But harvesting the oil is still expensive. To make it economically viable requires ramping up the algae's rate of growth and the amount of oil produced. Until now, it has been an either/or situation – you can double their oil output if you starve algae of nitrogen, but that cripples their growth.

The Synthetic Genomics team identified the genetic switch for producing oil in the algae species Nannochloropsis gaditana, then tweaked it to produce oil even when nitrogen is plentiful. The result, reported in the journal Nature Biotechnology in June 2017, was a doubling of the algae's oil content – from 20% to more than 40% – with no significant impact on the algae's growth. [3]

It is still not enough for commercial viability, but Venter remains upbeat that eventually algae will provide a viable alternative energy source.

Cosmetics

While profits from biofuels might still be many years away, synthetic-biology startups see more immediate returns in tooling their living factories to make high-margin commodities.

Yeast-produced farnesene is being used to make personal-care products such as vitamin E, patchouli oil and squalene, a compound once harvested from the livers of sharks, which is prized for its attributes as a skin moisturiser and other therapeutic benefits.

The chemistry that gives farnesene the smell of green apples is being leveraged at Vickers' lab at the University of Queensland. Her team has gone back to the drawing board to engineer yeast and bacteria to produce hydrocarbons like farnesene that, among other things, emit marketable fragrances.

Length is everything for this class of hydrocarbons, known as isoprenoids. Vickers says her team produces 10-15 hydrocarbon chains that not only emit nice smells but can also help make biofuels, insect repellents, vitamins and hormones used in agriculture to modify plant structure and growth.

Rubber and Plastic

Pare isoprenoids down to a five-hydrocarbon chain and you have isoprene, the raw material for rubber, which was traditionally tapped from the rubber tree. Synthetic rubber was first made in the early 1900s, and now almost all rubber comes from processing close to a million tonnes of isoprene from crude oil each year.

Genencor, a California-based company, engineered bacteria to produce isoprene in a more sustainable way. Dupont bought the company and has produced bio-isoprene to make concept tyres with Goodyear.

Synthetic biology also offers a greener option for plastics like nylon. Currently, nylon production from crude oil accounts for 10% of human-made emissions of nitrous oxide, a greenhouse gas about 300 times more potent than carbon dioxide.

Keasling's lab at Berkeley has engineered a bacterium that produces adipic acid, the molecule used to make nylon.

While the competition with petroleum-based products is fierce and dynamic, these synthetic biology products – drugs, cosmetics, perfumes and plastics – are already transforming the way we manufacture staple commodities of modern life. Synthetic biologists also have more way-out products on their drawing boards.

Cancer-killing Viruses

Timothy Lu earned a degree in computer science at MIT before moving on to medicine and a PhD at Harvard Medical School. His lab at Harvard, the Synthetic Biology Group, boasts a mix of computation, medical and biology specialists. The hybrid vigour is resulting in some dazzling devices. At the medical end of the spectrum, the team has programmed viruses to boost the immune system's ability to fight cancer. So far they have fought off ovarian cancer in mice, as published in a 2017 paper in the journal Cell.

Cancer spreads when a contingent of the immune army known as killer T- cells is not doing their job properly. Sometimes they don't detect the cancer cells; other times the cancer cells disarm their weaponry.

To improve their kill rate, Lu's group loaded a virus with a gene circuit that carries alarm signals called cytokines. When the virus infects a cancer cell, the circuit sends an alarm that alerts killer T-cells to the cancer. It also releases a compound to stop the cancer cell from disarming the killer T-cell.

The gene circuit only responds in the presence of two cancer-specific proteins – myc and E2F – to ensure normal cells infected by the virus do not end up as collateral damage. The genes operate like a 'logic gate' in an electronic circuit, with the virus unleashing its payload only when both proteins are detected. "Computing language makes the design process easier," says Lu.

Jellyfish Sentinels

Believe it or not, Nina Pollak at the University of Sunshine Coast in Queensland is synthesising jellyfish to clean up toxic spills.

In 2012 the Austrian-born scientist was inspired by a bold study, published by Kevin Kit Parker at Harvard's Wyss Institute for Biologically Inspired Engineering. Parker's group had transformed rat heart muscle cells into a swimming creature dubbed a 'medusoid' (medusa being the scientific name for the typical form of a jellyfish).

Beginning with a computer design, the researchers laid rat heart muscle cells on a scaffold of silicone polymer shaped like an eight-petalled flower. The creation could be made to swim with pulses of electricity: flowing current caused the muscle to contract; when the current stopped it relaxed and the medusoid's elastic silicone pulled it back to its original shape. The motion echoed that used by jellyfish to propel themselves.

Parker's goal with the medusoid was to model the beating of a heart and test new drugs; Pollak envisioned the possibility of creating an aquatic rover to detect and clean up ocean pollutants. Her approach relies on coaxing mouse embryonic stem cell to form heart cells whose beat should provide locomotion. The stem cells will also be engineered to carry a gene that senses toxic organophosphate – a pesticide common in agricultural run-off – and other genes that can then break toxic chemicals down. The end result: a jellyfish-like organism that can hunt and destroy pollutants.

The ambitious project seems set to consume the rest of Pollak's working career – a worthwhile cause, she says, if it delivers a solution for toxic spills. "There is heaps going on in synthetic biology. It's about combining what we already know to make something new and great."

Conclusion

So will the glowing vision of the future offered by synthetic biology become a reality? A large part of the answer depends on how readily society will accept artificial life forms in our midst. Another part comes down to simple economics.

The history of artemisinin and biofuels is instructive. Large investments in synbio companies to commercialize these products have failed to deliver the expected returns.

The price of natural artemisinin in 2011 was more than US$800 a kilogram. With the cost of producing synthetic artemisinin about US$350 a kilogram, pharmaceutical maker Sanofi invested big in facilities for large-scale production. Then increased cultivation of sweet wormwood and a series of bumper harvests saw the cost of making natural artemisinin crash to less than US$200 a kilogram.

The same forces of supply and demand have hindered biofuels. In 2008 the future looked bright as crude oil hit US$140 a barrel, with all signs the price would only go up. Then the global financial crisis hit, followed by the natural gas fracking boom, which slashed US demand for oil imports. By 2016 the price of crude was less than $40 a barrel, obliterating the business case for alternative fuel production.

Thus, synthetic biology is very promising, but at the moment research is hampered by the fact that the products and substances produced in this area are economically unprofitable compared to their artificial counterparts

REFERENSES

1. Ali Tavassoli(Ed.). Synthetic biology. Advance Article on the web 10th November 2009. Access mode: https://eprints.soton.ac.uk/158661/1/SynBio_review.pdf

2. Pablo Carbonell,Andrew Currin, Adrian J. Jervis, Nicholas J. W. Rattray(Eds.). Bioinformatics for the synthetic biology of natural products: integrating across the Design–Build–Test cycle. 5th February 2016. Access mode: https://www.researchgate.net/publication/303373221_Bioinformatics_for_the_synthetic_biology_of_natural_products_Integrating_across_the_Design-Build-Test_cycle

3. James Mitchell Crow(Ed.). Life 2.0: inside the synthetic biology revolution. 2018. Access mode: https://cosmosmagazine.com/biology/life-2-0-inside-the-synthetic-biology-revolution