ENGINEERING BIOLOGY EXPLAINED

A summarised guide to engineering biology

2019

Foreword

The 21st century is proving to be one of the most exciting and prolific periods of innovation in biosciences and healthcare, and UK bioscience companies are at the forefront of this innovation.

These companies are a key part of the UK Bioindustry Association (BIA)'s membership, and we provide a home for them through our Advisory Committees and working groups on antimicrobial resistance, cell and gene therapy, engineering biology and genomics.

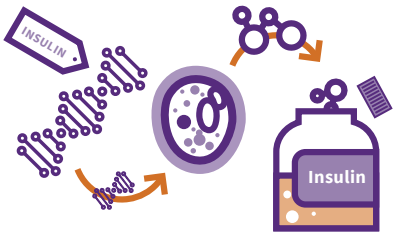
We are delighted to publish this short summary of **A guide to engineering biology and UK excellence in the field** as an accompaniment to our Explainer series, within which we describe what these four strategic technologies are all about, and showcase the important contributions being made by some of the UK bioscience firms who make up our dynamic and innovative membership. You can access the full versions of these Explainer documents on our website, or get in touch with us if you would like some hard copies.

We hope you enjoy reading them.

Steve Bates OBE CEO,
UK Bioindustry Association

What is engineering biology?

Engineering biology and its applications span medicine, agriculture, energy, manufacturing and almost every other industrial sector and UK companies are leading the way in this engineering biology revolution. Scientists are already able to insert corrected copies of defecting or missing genes into patients with certain genetic diseases, with extraordinary results. Genome editing techniques allow scientists to accurately and rapidly cut out, replace or repair specific bits of genetic material (DNA). One recently-developed tool, known as CRISPR-Cas 9, can be used like a pair of molecular scissors, and other tools can switch genes on or off.

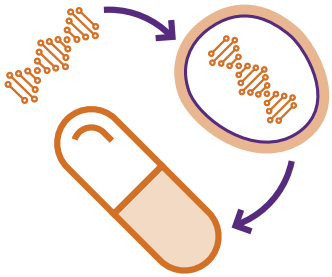


Engineering biology (also called 'synthetic biology'), is industrialising DNA sequencing, manufacture and editing, making all of it cheaper and more accessible. Applications of this technology are as wide as they are various, including reprogramming mosquitoes to limit the spread of disease, reprogramming immune cells to detect and fight cancer, and using gut bacteria to deliver targeted therapeutics.

Prokarium

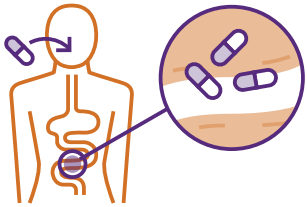
London-based Prokarium is developing a new, more convenient way to produce and administer vaccines. Prokarium's oral vaccine delivery platform uses a modified, harmless version of Salmonella bacteria to carry the genetic instructions for a vaccine to the site where it can have the greatest effect.

The modified bacteria are swallowed in a capsule and pass through the stomach and into the small intestine, where the vaccine is expressed and triggers a powerful immune response. Prokarium's lead programme is a vaccine against typhoid fever, and the related para-typhoid strain. The company claims that its Vaxonella platform could halve manufacturing and distribution costs, significantly increasing the number of people who can access vaccines. "The vaccination approach to typhoid and para-typhoid is very important from a global health perspective," says Ted Fjallman, Prokarium's CEO. Prokarium's typhoid vaccine candidate has been safely dosed to nearly 500 volunteers during Phase I and Phase II clinical trials. In February 2018 Prokarium raised $10 million from international investors.



CHAIN Biotechnology

CHAIN Biotechnology, a privately-held microbiome company based in Marlow, uses harmless Clostridia bacteria as mini drug factories in the gut. To-date, CHAIN has raised approximately £3M from equity investment and grant support from Innovate UK. CHAIN has assembled a team of Clostridia experts to engineer the bacteria to produce useful metabolites and biologics that confer further health benefits.



The genetic instructions for production of each bioactive are hardwired into the chromosome and only switched on during growth in the gut. CHAIN's lead product is a candidate for inflammatory bowel disease (IBD). Clostridia are engineered to produce a metabolite called beta hydroxybutyrate (BHB) that reduces inflammation. Using this Trojan-horse approach to drug delivery overcomes many of the difficulties in delivering effective therapeutics to the lower gut, notably the risk of degradation in the stomach and absorption in the small intestine. CHAIN's technology has the potential to be highly disruptive both in terms of cost and efficacy for the treatment and prevention of chronic gut-related diseases, and also for a range of conditions linked to disturbances in the gut microbiome.

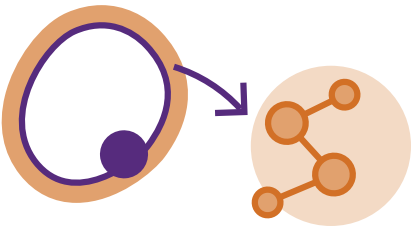
Green Biologics

Oxfordshire-based Green Biologics is engineering biology to manufacture cleaner, more sustainable specialty chemicals, used to make a wide range of products, from pharmaceuticals and cosmetics to paints and plastics. Chemicals such as n-butanol and acetone are currently made most efficiently, and cheaply, from petroleum oil, yet some bacteria produce these chemicals naturally. Green Biologics has evolved strains of Clostridia bacteria that are particularly good at making n-butanol and acetone, creating an efficient, high-yield fermentation process that avoids the high environmental cost of hydrocarbon-based manufacture.

The company produces these bio-based chemicals commercially at a plant in Minnesota. Green Biologics is also using a gene-editing technology, CLEAVE, to make changes to its chemical-producing Clostridia microbes even more specifically. “We can integrate new genes to programme the bug to make an entirely new product, at high yields, including products that it would not make naturally,” explains Chief Technology Officer Liz Jenkinson. Green Biologics believes its products will ultimately compete with petro-chemical based approaches. Green Biologics was founded in 2003 by serial entrepreneur Edward Green, also founder and CEO of CHAIN Biotechnology. It is funded by venture capital and grants.

CustoMem

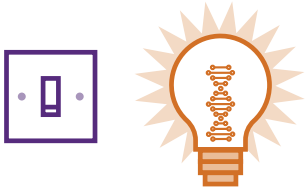
CustoMem has created a novel material that can selectively and efficiently remove dangerous chemicals from industrial waste-water. CustoMem Granular Media (CGM) is a bio-based material and can be customised to bind some of the most polluting, resistant artificial substances, in a manner that allows both the material and the pollutants it removes to be recycled. Each day, the global manufacturing industry produces millions of tonnes of water contaminated with fluorinated substances, used to make non-stick coatings, fire-fighting foam, and more. Current methods used to remove fluorinated substances from water, such as granular activated carbon or ion-exchange resins, are not particularly selective for these chemicals, and waste typically goes through high-temperature incineration which contributes to its carbon footprint. CustoMem’s Granular filter Media includes molecular binding domains that specifically capture the target chemical. The UK start-up, spun out of Imperial College London, has raised £1.5 million to date from its founders and through grants, and has already attracted large industrial players who face increasingly stringent waste regulations.



Synpromics

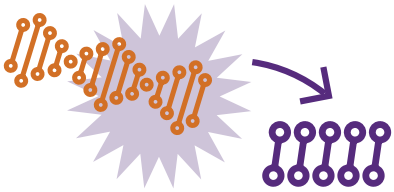
Edinburgh-based Synpromics designs and builds switches that turn particular genes on or off in specific conditions, providing a powerful way to control gene expression.

In nature, “promoters” are DNA sequences that sit alongside individual genes and control when, and how much of, that gene’s uniquely-encoded protein is made. Synpromics’ synthetic promoters are tailored to control gene expression far more precisely in order to achieve a desired outcome. For example, the company can make promoters that work only in certain tissues, such as the liver, to efficiently generate high levels of a particular protein. Synpromics’ team includes bioinformatics experts and data scientists able to integrate and interrogate a range of data sources to generate informed predictions about gene regulation in specific conditions. Synpromics’ gene-switch design capabilities have attracted over a dozen academic and industrial partners working in cell or gene therapy. The company’s promoters are patentable, thanks to their unique DNA sequences and the company is in line to receive clinical development milestones and sales royalties on partners’ eventual therapies.



Touchlight Genetics

Touchlight Genetics is one of several biotech companies seeking to transform DNA synthesis and amplification. The company uses engineered enzymes to rapidly and accurately amplify, or copy, any given DNA sequence. Its resulting ‘doggybone’ constructs are closed-ended double-strands of DNA, which can be manufactured at commercial scale within two weeks, rather than the months required for plasmid DNA production.



The doggybones are stable, reliably reproduce the DNA sequence of interest, and don’t contain any superfluous material, making them a useful substrate for cell and gene therapies. These therapies typically use modified viruses to deliver a corrected copy of a gene directly to patients (gene therapy), or into cells that are subsequently administered to the patient. Touchlight is working with pharmaceutical and biotech companies to explore applications for its doggybone DNA. In preparation for the DNA-driven future, Touchlight already has a Good Manufacturing Practice (GMP) DNA production facility and brand-new laboratories at its West London base, on the site of the historic Hampton Water Works. The company has raised £20 million since its founding in 2008.

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To access the full version of this report, take a look at our Strategic Technologies page: www.bioindustry.org/policy/strategic-technologies.html

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