



SME of the Month – CHAIN Biotechnology



Meet [CHAIN Biotechnology](#), the SME of the Month in July. The UK-based microbiome therapeutics company is focused on the development and commercialisation of live biotherapeutics, a new class of drug targeting gut-related diseases. CHAIN's technology has the potential to be highly disruptive both in terms of cost but also efficacy for the treatment and prevention of a broad range of chronic diseases. Pre-clinical tests with their lead asset showed a reduction in inflammation associated with inflammatory bowel disease. Read the full interview with this highly innovative SME below.

Why was CHAIN Biotechnology founded?

CHAIN was founded in 2014 to exploit the therapeutic potential of Clostridia bacteria found in the human gut microbiome. We aim to develop superior treatments for patients suffering from chronic and debilitating diseases.

CHAIN builds on its founder's expertise in engineering biology and fermentation with *Clostridium spp.*, a genus of industrially and medically important bacteria. We use engineering to produce therapeutic molecules that impact on the epithelial barrier, mucosal immune system, resident microbes and other organs that can be reached via neural and immune signalling networks.

The “bug is the drug” and we capitalise on unique spore-forming features of the microbe to provide targeted production and delivery of specific therapeutics to the colon. Engineering provides broad functionality in a single bacterial strain and superior therapeutic efficacy.



Edward Green, CEO & Co-Founder of CHAIN, at the 2018 Biotech SME Awards Ceremony

Which unmet medical need(s) are you seeking to address and how?

CHAIN's patented CHN-1 therapeutic targets IBD, specifically Ulcerative Colitis (UC). The bacteria have been engineered, through the addition of just one gene, to produce the new metabolite β -hydroxybutyrate (β -HB) alongside butyrate. β -HB is a ketone body normally found in the blood (from fat breakdown in the liver) and serves as an energy source as well as being a potent anti-inflammatory and neuroprotective molecule

UC is a chronic inflammatory condition associated with continuous mucosal inflammation in the colon causing patients to suffer from severe abdominal pain and bleeding. IBD impacts >5m sufferers worldwide and whereas first line treatments such as steroids and 5-ASA help manage the symptoms, they do not provide a cure. Given that relapse is common, resulting in an accumulation of tissue damage, impaired gut barrier function and life-threatening episodes, there is a clear and large unmet need for more effective treatments. UC patients also have a higher risk of developing colon cancer. Drug revenues for IBD are forecast to be \$11B by 2022 and the economic burden for US and EU is estimated to be \$60B per year.

Can you tell us a bit more about your patented platform for *Clostridium* spore assisted drug delivery and how it is compared to other approaches used to deliver therapeutics to the gut?

Biotherapeutics based on the introduction of complex microbial cocktails into the gut are the most developed, but they have had limited clinical success to date. Manufacture of commensal microbes and engraftment in the gut is problematical. Functionality is achieved through the blending of different

microbes, but the mechanisms of action are poorly understood. CHAIN use a single spore-forming *Clostridium* bacterial strain that is robust and has a safe history of use as a probiotic. Our proprietary engineering biology skills add new functionality with defined mechanisms of action. Our engineering capability supports multiple therapeutic products with broad clinical applicability. Our delivery concept provides an elegant but extremely powerful solution overcoming many of the challenges associated with conventional drug delivery to the lower gastrointestinal tract (colon). Our bacteria resist degradation in the stomach and only produce the bioactive in the colon during cell growth. Delivery is targeted and easily controlled via ingestion. Our biotherapeutics are cost-effective to manufacture and offer enhanced product stability (no cold chain logistics).



CHAIN's CADD™ platform illustration

You have a strong team of experts in synthetic biology and are using the technology in the development of advanced drugs. Can you give more details as to how you are using synthetic biology tools?

CHAIN has multi-disciplinary expertise leveraging the Founders skills in *Clostridia* plus the Board's experience in drug development. CHAIN has built a lab-based team of experts for engineering *Clostridia*.

Our platform is based on engineering *Clostridium* to produce and secrete specific drug candidates. This involves developing and implementing a suite of tools for engineering resulting in strains producing a wide range of drug modalities. All our modifications are stably integrated on the chromosome.

Synthetic (or engineering) biology is one of our core skills alongside fermentation and microbiology with anaerobic bacteria (found in the gut). We have formed a strategic alliance with the University of Nottingham who support our work on tool development. CHAIN is the only company that engineer *Clostridia* bacteria for microbiome therapeutics.

Can you outline the importance of synthetic biology in addressing future medical needs?

Synthetic biology is becoming an indispensable tool in the future of healthcare. The field isn't new, companies have been using synthetic biology principals for decades, but advances in automation, materials and genomics have allowed more coordinated synthetic biology strategies to be developed. Synthetic biology approaches will undoubtedly play major roles in future biologics, antimicrobial products, diagnostics and materials. For example, synthetic

biology is widely used for antibody design and production. Gene editing tools such as CRISPR-Cas9 underpin new breakthroughs in cell and gene therapies. We are now seeing an increase in the use of synthetic biology in the microbiome field.

Partnering with academics is part of your business strategy. Can you tell us concretely how you benefit from these business-academia partnerships?

CHAIN forms alliances with academic experts and groups in synthetic biology, the gut microbiome and disease models. For example, we work closely with the Synthetic Biology Research Centre (SBRC) at Nottingham on strain development, Oxford for pre-clinical testing and Reading for *in vitro* gut modelling. The collaborations accelerate our development work and provide important test data and validation. We also support PhD studentships and provide industry placements. Typically, we use grant funding to support collaborative projects. In addition, CHAIN promotes and markets research materials developed within the SBRC.

CHAIN has been very successful in raising grant funding. Can you tell us about your most significant funded projects?

CHAIN has recently completed a feasibility project for scale-up and manufacture of our CADD™ spores. The project was in partnership with Porton Biopharma Ltd, who are experienced with bacterial fermentation on large scales, and Scitech Engineering Ltd, who provided the design concept based on our needs. Innovate UK funded the project. We have largely de-risked spore manufacture and plan to build on this work to develop manufacturing capability.

We have an ongoing project on developing secretion mechanisms in our platform focused on therapeutic peptides. This is in collaboration with the SBRC in Nottingham. We have demonstrated peptide secretion and attracted several commercial partners who have provided novel targets for incorporation.

We have three new grant-funded projects starting in Q1 2019 that should provide further exemplification of our unique and highly differentiated platform for drug delivery. However, our key focus will be advancing our lead asset CHN-1 into the clinic.

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About EuropaBio

EuropaBio, the European Association for Bioindustries, promotes an innovative and dynamic European biotechnology industry. EuropaBio and its members are committed to the socially responsible use of biotechnology to improve quality of life, to prevent, diagnose, treat and cure diseases, to improve the quality and quantity of food and feedstuffs and to move towards a biobased and zero-waste economy. EuropaBio represents 75 corporate members and 17 national biotechnology associations and bioregions.

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