

Impact case study (REF3)

Institution: University of Bristol		
Unit of Assessment: 5) Biological Sciences		
Title of case study: Commercialisation of synthetic biology research delivers sustainable economic growth and job creation in South West England		
Period when the underpinning research was undertaken: 2014 - 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Paul Race	Professor of Biological Chemistry	2009 - present
Dek Woolfson	Professor of Chemistry and Biochemistry	2005 - present
Imre Berger	Professor of Biochemistry	2014 - present
Adam Perriman	Professor of Bioengineering	2007 - present
Period when the claimed impact occurred: 2014 - 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact

Researchers at the University of Bristol's synthetic biology research centre, BrisSynBio, have created a cluster of 9 innovative life sciences companies in the city. In just a few years, this network has raised more than GBP10 million investment and created 30 new jobs. The companies span sensing, diagnostics, vaccine development, cell therapies and materials science applications of synthetic biology, to deliver benefits for medical and defence industries. Together they have swiftly transformed the city of Bristol and South West of England region into a centre of excellence for biotechnology entrepreneurship and commercialisation.

2. Underpinning research

Synthetic biology is a nascent scientific discipline that aims to make the engineering of biological systems easier, more predictable and more reliable. In 2014, researchers at The University of Bristol (UoB) won funding of >GBP13.5 million from BBSRC/EPSRC to establish BrisSynBio, a national centre for synthetic biology research [i]. Since its establishment, BrisSynBio has delivered a body of work comprising >250 publications and patents, with manuscripts in a multitude of leading international journals including *Science* and *Nature*. This portfolio of scientific discoveries has transformed the biotechnology industry within South West England, which prior to the establishment of BrisSynBio, was one of the most poorly performing regions of the UK in this area [A]. Examples of these numerous successes for UoB research include:

1. In 2014, Woolfson employed a biodesign approach to generate channel-containing α -helical barrels capable of binding a range of ligands [1]. Arrays of these barrel proteins were shown to respond to ligand binding through emission of characteristic colour changes, which could be monitored and then interpreted using machine learning algorithms. This discovery provided the core technology for the spin-out company Rosa Biotech, whose unique approach has opened up the possibility of solving biosensing challenges that were previously regarded as too complex, time consuming or expensive to address.

2. In 2016, Race and colleagues identified novel cycloaddition enzymes, which could be used to selectively cross-link a range of biological and synthetic polymers [2, 3]. In tandem with a bio-based peptide design and manufacturing platform technology, this discovery became the basis of the spin-out company Zentraxa Ltd. Zentraxa have used this polymer cross-linking approach

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to develop novel materials, including biocompatible peptide-based adhesives, which have been adopted by a number of end users in the defence and healthcare sectors.

3. In 2019, Berger and colleagues showed that it was possible to functionalise the ADDomer, an engineered multivalent protein scaffold, into a vaccine candidate to combat infectious diseases [4]. This technology became the basis of the spin-out company Imophoron. ADDomer is a thermostable, highly soluble viral capsid protein, which when functionalised facilitates epitope insertion in a library format, giving rise to a generic scaffold for displaying antigens. Each ADDomer can display up to 360 epitopes on its surface, which can be i) identical epitopes from a single pathogen; ii) diverse epitopes from a single pathogen, or iii) diverse epitopes from different pathogens. This system can consequently be used to generate ‘combo’ vaccines, which simultaneously protect against multiple diseases. Informed by high resolution structural studies of the SARS-CoV-2 spike protein conducted in the Berger laboratory [5], ADDomer is now delivering novel COVID19 vaccine candidates that confer protection against multiple SARS-CoV-2 variants from a single vaccine preparation.

4. In 2019, Perriman developed a new cell membrane modification methodology where the inherent heart tissue homing properties of the infectious bacteria *Streptococcus gordonii* are transferred to human stem cells [6]. This was achieved *via* the rational design of a chimeric protein–polymer surfactant cell membrane binding construct, comprising the cardiac fibronectin (Fn) binding domain of the bacterial adhesin protein CshA fused to an artificial membrane binding protein. This discovery formed the basis of the spin-out company Cytoseek, who are exploiting this artificial membrane binding protein technology to address challenges faced by cell therapies targeting solid tumours.

3. References to the research

1. Thomson AR, Wood CW, Burton AJ, Bartlett, Sessions RB, Brady RL, **Woolfson DN**. (2014). Computational design of water-soluble α -helical barrels. *Science*, 345: 485-488. DOI:[10.1126/science.1257452](https://doi.org/10.1126/science.1257452)
2. Byrne MJ, Lees NR, Han LC, van der Kamp MW, Mulholland AJ, Stach JE, Willis CL, **Race PR**. (2016). The Catalytic Mechanism of a Natural Diels-Alderase Revealed in Molecular Detail. *Journal of the American Chemical Society*, 138(19): 6095-8. DOI:[10.1021/jacs.6b00232](https://doi.org/10.1021/jacs.6b00232)
3. Marsh CO, Lees NR, Han L-C, Byrne MJ, Mbatha SZ, Maschio L, Pagden-Ratcliffe S, Duke PW, Stach JEM, Curnow P, Willis CL, **Race PR**. (2019). A Natural Diels-Alder Biocatalyst Enables Efficient [4 + 2] Cycloaddition Under Harsh Reaction Conditions. *ChemCatChem*, 18: 5027-5031. DOI:[10.1002/cctc.201901285](https://doi.org/10.1002/cctc.201901285)
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5. Toelzer C, Gupta K, Yadav SKN, Borucu U, Davidson AD, Kavanagh Williamson M, Shoemark DK, Garzoni F, Staufer O, Milligan R, Capin J, Mulholland AJ, Spatz J, Fitzgerald D, **Berger I**, Schaffitzel C. (2020). Free fatty acid binding pocket in the locked structure of SARS-CoV-2 spike protein. *Science*, 370(6517): 725-730 DOI:[10.1126/science.abd3255](https://doi.org/10.1126/science.abd3255)
6. Xiao W, Green T, Xiaowen Liang, Perry G, Cuahtecontzi-Delint R, Roberts M, le Vay K, Back CR, Ascione R, Wang H, **Race PR**, **Perriman AW**. (2019). Designer artificial membrane binding proteins direct stem cells to the myocardium. *Chemical Science*, 10: 7610-7618. DOI:[10.1039/C9SC02650A](https://doi.org/10.1039/C9SC02650A)

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Grant Funding:

- i. **Woolfson DN, Race PR, et al.**, [BrisSynBio: Bristol Centre for Synthetic Biology](#), BBSRC/EPSRC, 2014 – 2021, GBP13,528,180

4. Details of the impact

Synthetic Biology (SynBio) is an emerging field of research that seeks to apply the principles and practices of engineering to the design of biological parts, devices, and systems, or to redesign systems already found in nature. Although this technology is still in its infancy, members of the Bristol SynBio community have already achieved major successes in commercialising their research in this area.

Commercialisation of new synthetic biology technologies

i. Zentraxa - novel biopolymers for security, medical and defence industries

Zentraxa was established in 2017 to commercialise and exploit an enzyme-based polymer crosslinking technology developed within UoB [2,3]. Since incorporation, the company has attracted >GBP500,000 of investment and has successfully delivered >GBP200,000 of research contracts to the UK Ministry of Defence (MoD), through the development of bio-adhesives for use across a range of applications [Bi]. They were recently awarded a further GBP150,000 contract from the MoD in partnership with the multinational defence technology company QinetiQ, to apply their biodesign approach to develop disbondable adhesives for the attachment of sensor devices to unmanned vehicles [Bii]. Zentraxa currently employs eight staff and had a turnover of >GBP600,000 in 2020. The success of Zentraxa is directly attributable to the underpinning research conducted within BrisSynBio [2, 3]. The Zentraxa CSO states that, *“the fundamental research was funded by BBSRC, so without that there would be...no Zentraxa”* [C].

ii. Imophoron – rapid next-generation vaccines overcome supply chain limitations and reduce side effects

Imophoron’s core platform technology and know-how enable the rapid production of next-generation vaccines based on the ADDomer, a multivalent synthetic protein scaffold [4]. ADDomer overcomes limitations in the production, storage, transport and deployment of vaccines, and negates the requirement for a ‘cold-chain’, which is currently the major cause of loss of vaccine doses from manufacturing to point-of-care. This technology is the basis of Imophoron’s first-in-class vaccine for Chikungunya virus [Di] and is now being applied to develop vaccines for both Zika and Gumboro viruses. High resolution structural studies of the SARS-CoV-2 spike protein [5], have allowed Imophoron to enter preclinical trials with multiple SARS-CoV-2 vaccine candidates developed using the ADDomer platform and listed on the World Health Organisation COVID-19 candidate vaccine tracker [Dii]. In contrast to other approaches, the ADDomer system enables presentation of specific regions of the viral spike protein, reducing the risk of hyperimmune responses which could worsen the disease [Diii]. This work is also unlocking significant life science market opportunities for Imophoron’s partner company, the multinational computer technology corporation Oracle [E].

iii. Cytoseek – enhanced immuno-oncology therapies for solid tumours

Cytoseek has attracted >GBP1.1 million of investment since incorporation in 2019, and currently employs six staff [Fi]. Its cell membrane modification methodology [6] is being refined to develop a suite of proteins that will add enhanced homing and solid tumour invasion capacity to immuno-oncology therapies. Cytoseek’s portfolio includes candidate cell therapies which use functional payload molecules to improve targeting and retention, reduce hypoxia, and mitigate

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immunosuppression at the tumour site. Their proprietary cell type agnostic artificial membrane binding proteins can be deployed to coat CAR-T cells, TILs, natural killer cells, or any other cell with an external lipid membrane. Cytoseek's lead candidate therapeutic CYT101 is currently undergoing pre-clinical evaluation [Fii].

iv. Rosa Biotech – solving biosensing challenges in medical and industrial diagnostics

Rosa Biotech was established in 2019. The company's unique sensing platform, which mimics the olfactory systems of mammals [1], is enabling previously intractable challenges in early disease diagnosis and industrial biotechnology to be addressed accurately and at scale. Having raised GBP760,000 of angel investment, they are applying their sensing technology to enable consistent improvements in the yield rates of biologics production for pharmaceutical manufacturers [G]. Rosa's solution delivers bottom-line improvements to this high-cost process, enabling significant savings in manufacturing costs and increased product yield.

Economic growth and job creation in the South West

UoB research in Synthetic Biology has generated 9 successful start-up companies, acting as an "engine of growth" both regionally and nationally [Hi, Hii]; these are Zentraxa, Rosa Biotech, Cytoseek, Imophoron, Glaiia, Vitamica, Fluoretiq, Lazarus Biotechnology and LettUsGrow. This has transformed the biotechnology industry within South West England, which prior to the establishment of BrisSynBio, was one of the most poorly performing regions of the UK in this sector [A]. These SMEs have attracted >GBP10 million of investment, and received numerous national and international commercial innovation awards including: the 2018 Linksum SATT Out-of-Lab challenge and 2019 Great West Global Good Award to Imophoron; the 2019 Royal Society of Chemistry Emerging Technologies Award and 2019 Launch Great West "Ones to Watch Award" to Rosa Biotech; the 2019 Launch Great West Rising Star Award to CytoSeek; and the 2017 BioStart Prize for the South West's leading Engineering Biology company to Zentraxa.

A 2019 UK Synthetic Biology Startup Survey notes that recent SynBio start-up activity in Bristol 'has driven the share of companies in the South West to 6%, the highest level in England outside the Golden Triangle' [I]. Since 2017 BrisSynBio SMEs have contributed [text removed for publication] to the local economy through laboratory occupancy and facilities access at the UnitDX incubator facility [Ji] and have created >30 high skill jobs within the city of Bristol.

The establishment and growth of Bristol's SynBio SME ecosystem has been highlighted as an exemplar of UK translational research in the life sciences by the UK government. During a visit to these companies, the Rt Hon Lord Henley, Parliamentary Under Secretary of State at the Department for Business, Energy and Industrial Strategy said, "*Bristol's innovative businesses and academics are applying science and engineering to seize the biggest opportunities and tackle the greatest challenges of our time*" [Jii].

The importance of the work conducted by UoB academics in accelerating the growth of this sector is highlighted by the Director of the Bristol based UnitDX incubator, who notes, "*One cannot understate the significance of the underpinning research performed by Bristol academics under the auspices of BrisSynBio. It has driven, and is continuing to drive, exponential growth of the South West biotechnology ecosystem. Since 2014, and fuelled by the outputs of BrisSynBio, Bristol has grown into a leading centre of excellence in the commercialisation of synthetic biology research, delivering significant economic and associated impact*" [Ji].

Training and capacity building

UoB has taken a proactive role in commercialising its science. Since 2017 BrisSynBio's 4-day MBA has trained 35 postgraduates, postdoctoral staff, academics and industrialists in SynBio research commercialisation and entrepreneurship, including individuals from across the UK and Europe [Ki]. This activity has led directly to the formation of Cytoseek [Kii]. In addition, support and mentorship provided by the BrisSynBio Biodesign Enterprise Fellowship scheme enabled Fellows to establish a further three of the new SynBio start-ups in the city [Ki]. BrisSynBio spinouts have hosted ten innovation placement PhD students, of which five have been recruited to permanent positions by their host SMEs.

BrisSynBio's annual Connect industry networking events, which showcase translational research from BrisSynBio academics and SMEs alongside cutting-edge synthetic biology products and applications from leading UK industrialists, have attracted >250 delegates, including industrialists, venture capitalists, angel investors and members of the public from across the UK and Europe [Ki]. BrisSynBio's Royal Society Entrepreneur in Residence has provided support, training and mentorship to >50 members of the Bristol SynBio community, including assisting BrisSynBio SMEs to identify market opportunities and forging new commercial partnerships [Ki].

These collaborative approaches are now embedded within operation of the BrisSynBio research groups, the start-up cluster and the UnitDX incubator.

5. Sources to corroborate the impact

- [A] HM Government (2014). [Strength and Opportunity 2014 – The landscape of the medical technology and biopharmaceutical sectors in the UK](#)
- [B] GOV.UK – Defence and Security Accelerator funded contracts:
 i) [1 April 2017 to 31 March 2018](#)
 ii) [1 April 2019 to 31 March 2020](#)
- [C] BBSRC (2019). [Bio-engineering creates new peptide-based materials using bacteria](#)
- [D] i) ContagionLive (2019). News: [New Synthetic Vaccine Targets Chikungunya Virus](#)
 ii) WHO (2021). [Draft landscape and tracker of COVID-19 candidate vaccines \(p.12\)](#).
 iii) Insider Media (2020). [Bristol start-up puts forward Covid-19 vaccine candidates](#)
- [E] THE (2020). [Blue-sky thinking about vaccine development](#)
- [F] i) Business Leader (2019). [Cytoseek raises £1.1m for new cell therapies](#)
 ii) Cytoseek (2021). [Pipeline](#)
- [G] Rosa Biotech press release (2019). [Rosa Biotech raise £760,000 to develop groundbreaking biosensing platform](#)
- [H] i) UK BiIndustry Association (BIA) (2019). Blog: [Life sciences South West - going for growth](#)
 ii) West of England Combined Authority (WECA) (2019). [Local Industrial Strategy | Evidence base report](#)
- [I] Stephen Chambers (2019). [UK Synthetic Biology Startup Survey 2019](#)
- [J] i) UnitDX (2021). Supporting letter - Director of Science Creates Incubators & Centre Director
 ii) UoB (2018). News: [Business Minister visits Bristol BioDesign Institute and Unit DX](#)
- [K] i) BrisSynBio (2021). Supporting letter – Former BrisSynBio Innovation Manager
 ii) UoB (2017). [Two new start-up plans win BrisSynBio's first synthetic biology entrepreneurship competition](#)