ANNUAL REPORT 2024

VaXHub Sustainable

Cover images

(Clockwise from top centre)

Group break-out sessions at the VaxHub Sustainable Launch, December 2023
(VaxHub Sustainable)

Encapsulin nanocompartments research; Naail Kashif-Khan, Renos Savva, Stefanie Frank, Mining metagenomics data for novel bacterial nanocompartments, NAR Genomics and Bioinformatics, Volume 6, Issue 1, March 2024, lqae025
(Naail Kashif-Khan and Stefanie Frank)

Year 12 class learning in the UCL Biochemical Engineering Labs
(*Raymond Johnson, Alexandra Park School, London)*

Calcareous Arabesque, Bio-ID / Brenda Parker, Marcos Cruz, Yao Meng, Anete Salmane, Pradeep Devadass
(Marcos Cruz)

Automation work on equipment in the UCL Biochemical Engineering Labs
(VaxHub, 2018-2023)

Acknowledgements

Funding from the UK Engineering and Physical Sciences Research Council (EPSRC) for the Manufacturing Research Hub for a Sustainable Future (VaxHub Sustainable) co-directed by University College London and the University of Oxford with UK university partners is gratefully acknowledged (Grant Reference: EP/X038181/1).

VaxHub Sustainable would also like to thank all members of the research group and International Advisory Board along with our colleagues and future Hub members in companies and other institutions without whom we would not be able to achieve the aims and objectives of the Hub.

Contents

Foreword

In this first report from the VaxHub Sustainable team, it has been a pleasure to read about the progress, aims and achievements of the Hub so far. Building on the success of the first VaxHub consortium (2018-2023), the VaxHub Sustainable team are now focusing on a move to deliver manufacturing innovations that enable a transformative change towards sustainable and rapidly responsive vaccine manufacture. I was pleased to read of the Hub vision being designed to minimise environmental impact and carbon emissions, aspects which seem popular topics of debate worldwide.

In the coming year, I am looking forward to seeing progress in the Hub's vision to bring academia, industry, not-for-profit organisations and policy makers together to propose radical change in vaccine development and manufacturing technologies, building on a technological innovation culture.

This project is so important in the wider climate where the lessons learned from the Covid-19 pandemic cannot be ignored. The UK had a leading role during the pandemic and VaxHub Sustainable builds on this success to advance novel research on a broader range of technologies.

Barry Buckland, Chair, VaxHub Sustainable International Advisory Board

Introduction to VaxHub Sustainable

The Manufacturing Research Hub for a Sustainable Future (VaxHub Sustainable) aims to establish the UK as the global centre for integrated discovery through to bioprocess manufacture of next generation vaccines in preparation for the next pandemic, building on a technological innovation culture.

VaxHub Sustainable is a collaboration between UCL and the University of Oxford led by Professor Martina Micheletti, Professor of Bioprocess Fluid Dynamics at UCL, and Professor Dame Sarah Gilbert DBE FRS, Professor of Vaccinology at the University of Oxford. The University of Leeds, the University of Manchester and the London School of Hygiene and Tropical Medicine are also partners in the Hub. VaxHub Sustainable received funding for seven years with a £12 million grant from the EPSRC and started on 1st September 2023.

The Hub aims to enable the UK to be better prepared for the next pandemic. It brings together a multidisciplinary team with decades of cumulative experience in all aspects of vaccine design and manufacturing research, including synthetic biology, protein engineering, virology, vaccinology, analytics development, microscale bioprocessing and automation and bioprocess sustainability. This Hub will bring academia, industry, not-for-profit organisations and policy makers together to propose radical change in vaccine development and manufacturing technologies.

The Hub's work focuses on the development of improved vaccine platforms which can be flexible enough to be used for multiple product manufacture. The impact of this Hub will be felt internationally, as the UK reaffirms its leadership in Global Health and works to ensure that the outputs of this Hub reach the global community and the most vulnerable, especially children.

There are two Grand Challenges, each with its own aims and integrated and interconnected work packages.

> *The Hub aims to enable the UK to be better prepared for the next pandemic.*

Grand Challenge 1: to develop new tools and technologies to accelerate manufacture and enable distribution, storage and administration.

There are to be three main Work Packages in Grand Challenge 1:

WP1.1 Creation of improved platforms. This work package will focus on cell engineering tools and improving immunogenicity by optimising production and purification methods and by using novel encapsulation approaches. For virus-like particle vaccines we will use a modular platform to ensure compatibility and flexibility. Recombinant vaccines against bacterial pathogens will also be developed as an exemplar, using a novel Protein-Glycan Conjugation Technology.

WP1.2 Rapid and responsive development and manufacture. The potential for the technologies researched in WP1.1 to be exploited as platform technologies will be explored and their adaptability to new antigen targets studied. Automated microscale bioprocessing coupled with advanced laboratory automation and modelling will be used alongside engineering fundamentals to mimic the whole manufacturing process at short notice, which could be deployed to support pandemic response.

WP1.3 Needle-free and thermostable formulation. Injectable vaccines do not generate sufficient immune responses at the portals of pathogen entry and alternative routes of administration must be established that could provide faster administration with less carbon footprint impact than plastic disposables. In this work package, alternative mucosal routes of immunisation will be investigated, and formulations tailored for these sites developed for some of the Hub vaccine technologies. A range of adjuvants will also be tested.

Grand Challenge 2: to focus on tools that better support the understanding of the impact on the environment and facilitate waste re-use and facility design for (re)manufacture, to ensure that the Hub will be a sustainability leader in the sector.

To meet the vision of the Hub as a sustainability leader in the sector we will focus on tools that support better understanding of the impact on the environment and will facilitate waste re-use and facility design for (re)manufacture (GC2).

WP 2.1 (Understanding bioprocess sustainability impact) will address two key issues. Firstly, we will produce a "best practice" document to ensure that the scope and preparation of the life cycle inventory can be refined so that outputs are meaningful. This will facilitate hotspot analysis or decision-making in process design. Secondly, we will source data and boost the range of well-defined inputs to enable more precise life cycle inventories reflective of the actual materials used in bioprocesses.

WP 2.2 (Exploring industrial symbiosis and circular economy of resources) will investigate how we might plan for future facilities to be embedded within a circular economy and aims to address three key aspects around the use of waste and novel facility design: a) Identification of waste streams and location of future manufacturing. b) Biopharmaceutical waste streams as a future resource. c) Design of facilities to enable effective use of waste streams.

Another objective of VaxHub Sustainable is to achieve adoption of the technologies developed into the vaccine manufacturing and related industries and our strong and ongoing partnerships with industry are key to achieving this.

The final objective of VaxHub Sustainable is to become the national focal point of best practice, knowledge transfer and resource sharing for the sector. This will be achieved through Platform Interactions that include training, public and policy engagement activities to maximise dissemination, long term relationship building and exchanges.

Meet the team

Research Team UCL

Martina Micheletti, Co-Director

Professor Martina Micheletti is Professor of Bioprocess Fluid Dynamics at UCL and her research focuses on the fundamental engineering underpinning development and scaling challenges of upstream processing for vaccines, monoclonal antibodies and cell and gene therapy products. She has applied her expertise in the use of advanced optical and imaging techniques for the measurement and quantification of flow characteristics and mixing dynamics for bioreactors with different agitation mechanisms (rocked, stirred, shaken). She has pioneered microscale methods for rapid process development, adapting these for quasi-perfusion of monoclonal antibodies, and will apply her expertise to novel vaccine technologies within the Hub.

Duygu Dikicioglu, Co-Investigator

Dr Duygu Dikicioglu is Associate Professor in Digital Bioprocessing and Biochemical Engineering in the UCL Department of Biochemical Engineering. Duygu's main research interests include the areas of digitalisation and industrial biotechnology. Additionally, Duygu contributes to various undergraduate and postgraduate IChemE accredited degree programmes operated by the department. Duygu also leads the Smart Digitalisation Decisions in Bioprocess Development and Manufacturing MBI and contributes to the Advanced Data Analytics for Biopharmaceutical Optimisation MBI.

Daniel Bracewell, Co-Investigator

Professor Daniel G. Bracewell is Professor of Bioprocess Analysis at the UCL Department of Biochemical Engineering. His notable contributions have significantly advanced our understanding of biological product purification, often through collaborations with industry leaders. He has authored over 100 peer-reviewed journal articles, many of which involve fruitful partnerships with esteemed institutions in Thailand, India, and the USA. Currently, he oversees 15 doctoral and postdoctoral projects. One particularly impactful project led to the creation of Puridify, a nanofiber adsorption technology company now owned by Cytiva. As the academic lead for the UCL-Cytiva Centre of Excellence, Daniel is at the forefront of pioneering efforts in bioprocessing. His current focus involves the development of cell-free / enzymatic manufacturing technologies, aimed at facilitating personalised cell and gene therapies.

Stefanie Frank, Co-Investigator

Dr Stefanie Frank is Associate Professor in Engineering Biology at UCL's Department of Biochemical Engineering. She has pioneered work in bioengineering bacterial protein compartments and Virus-Like Particles (VLPs), leading to the development of novel tools and applications. Dr Frank's research focuses on creating new modular protein-based vaccine technologies, combining strategies for antigen display and cargo encapsulation using protein nanoparticles to create a versatile platform for vaccine applications. In addition to her research, Dr Frank contributes to vaccine manufacturing training as the module leader for the UCL-MIT MBI Vaccine Bioprocess Development and Commercialisation course. She supports knowledge dissemination in her roles as Co-Chair at the ECI Microbial Engineering and ECI Vaccine Technology conference series and as an active member of the Royal Society of Chemistry's (RSC) Analytical Biosciences committee.

Michael Thomas, Co-Investigator

Dr Mike Thomas is a Lecturer in Bionanotechnology and Biochemical Engineering based at UCL's London Centre for Nanotechnology and the Department of Biochemical Engineering. Mike's main area of research is in lateral-flow biosensor technology development. Mike brings advanced engineering principles, nanomaterial synthesis and characterisation techniques to develop improved understanding of nanoparticle responses in various biosensing formats. The technologies developed within his research are then directed at both infectious disease detection, and to the development of small-scale/low-cost platform analytical tools for bionanoparticle characterisation and bioprocess monitoring.

Sudaxshina Murdan, Co-Investigator

Dr Sudaxshina Murdan is a Reader (Associate Professor) at the UCL School of Pharmacy. Sudaxshina is a pharmacist and pharmaceutical scientist. Her research is in the delivery of drugs, delivery of vaccines, pharmacy and pharmacy education. Additionally, Dr Murdan teaches on the UCL MPharm, MSc, PhD and Qualified Persons programmes.

Brenda Parker, Co-Investigator

Dr Brenda Parker is Associate Professor of Sustainable Bioprocess Design at UCL. Her current research seeks to address the need for sustainable and scalable platforms for industrial biotechnology and bio-integrated design. Brenda is an Executive Editor of the Journal Biotechnology Design (Cambridge University Press). She is an Associate Member of the Institute of Chemical Engineers and a Fellow of the Higher Education Academy.

Cheng Zhang, Post-Doctoral Research Associate

Dr Cheng Zhang combines computational and experimental skills in protein engineering and formulation. He led the freeze-drying process development for the Oxford-AstraZeneca ChAdOx vaccine for COVID-19, supported by the previous VaxHub. In his current role, Cheng develops pipelines and software routines for automated experimentation to facilitate the digitalisation of experimentation for vaccine bioprocess development.

Rita Morais, Research Assistant

Rita Morias joined the VaxHub Sustainable team in April 2024, focusing on researching opportunities for industrial symbiosis and the circular economy within the industry. Rita holds a Master of Architecture in Bio-Integrated Design from UCL's Bartlett School of Architecture, a bachelor's degree in Business from Nova SBE in Lisbon and completed a certification in business sustainability management from the University of Cambridge. Rita's interdisciplinary approach integrates nature into the design process, combining scientific exploration, computational design, and environmental simulations to create sustainable solutions.

Mohammed Yousif, Post-Doctoral Research Associate

Dr Mohamed Yousif acquired a PhD in Pharmacy from the University of Nottingham in 2018. He worked at Boots and Reckitt Benckiser pharmaceutical companies for a short period of time, then joined UCL in 2019 as a PDRA. He is currently a Research Fellow at UCL School of Pharmacy, and his research work focuses on developing vaccine formulations using different adjuvants and delivery platforms for human and veterinary use.

University of Oxford

Sarah Gilbert, Co-Director

Professor Dame Sarah Gilbert's chief research interest is the development of viral vectored vaccines that work by inducing strong and protective T and B cell responses. Professor Gilbert's work also focuses on the rapid transfer of vaccines into GMP manufacturing and first in human trials. In 2020 Professor Gilbert became the Oxford Project Leader for ChAdOx1 nCoV-19, a vaccine against the novel coronavirus SARS-CoV-2.

Catherine Green, Co-Investigator

Dr Cath Green is an Associate Professor in the Nuffield Department of Medicine at the University of Oxford. She is Co-Director of VaxHub Global, and one of the co-investigators of VaxHub Sustainable. Professor Green heads Oxford's Clinical Biomanufacturing Facility (CBF), and is a Fellow of Exeter College, Oxford. Cath is an expert in genetics and cell biology and specialises in manufacturing vaccines according to the principles of Good Manufacturing Practise (GMP) for use in clinical trials. She played an integral role as GMP-lead in the development of the Oxford Covid-19 vaccine in 2020.

Sandy Douglas, Co-Investigator

Dr Sandy Douglas is an Associate Professor at the Jenner Institute, University of Oxford. Sandy's main research interests are the development of new antibody-inducing vaccines and breaking down the barriers to translation of new biological medicines into clinical trials. Sandy leads the University's Bioprocess and Analytical Development (BiPAD) team which is concerned with bringing together clinical and bioprocess understanding to make small-scale GMP manufacturing more cost-effective, lowering the barrier to experimental medicine and early-phase clinical development of novel interventions.

Sumi Biswas, Co-Investigator

Dr Sumi Biswas is an Associate Professor of Vaccinology at the Jenner Institute, University of Oxford where she leads the Transmission Blocking Malaria Vaccine Group. She is also a co-founder, President and Chief Scientific Officer of SpyBiotech Limited, a biotech company working on developing effective vaccines. In 2017, she was named as a rising star in BioBeat's Movers and Shakers list of 50 inspirational women in the BioTech industry.

Catherine Cherry, Post-Doctoral Research Associate

Dr Catherine Cherry earned her undergraduate degree in biochemistry from the University of Oxford, Catherine pursued a PhD specialising in the mechanism of Herpes Simplex Virus-1 infection within the Virology section of the Department of Infectious Disease at Imperial College London. Following the completion of her doctoral studies, Catherine worked as a scientist with the Standards Lifecycle team at the MHRA, where she contributed to the development of WHO International Standards for viral vaccines. In October 2023 Catherine began a Senior Scientist position with Sandy Douglas at the Jenner Institute, University of Oxford.

Jacqueline Vieira, Research Associate

Jacqueline Vieira gained her master's degree at Pierre et Marie Curie University (Paris). Following that, she embarked on a successful career in the upstream bioprocessing / cell culture sector of the industry. Jacqueline began her career at Oxford Biomedica and played a crucial role in lentivirus production for CAR-T gene therapy, gaining invaluable experience with Good Manufacturing Practices (GMP). In her current role for VaxHub Sustainable, Jacqueline will be contributing to the development of a perfusion system for improved adenovirus production.

Reshma Kailath, Research Assistant

Reshma Kailath completed a BSc in Biochemistry (University of East London) and an MSc in Biomedical Science (Nottingham Trent University). She has been part of Sarah Gilbert's team as a Research Assistant for six years, where she is heavily involved in the early stages of the design of viral vectored vaccines. Reshma has recently transitioned to work on the development of vaccine platforms to improve the infectivity and immunogenicity aiming for vaccines sustainability in VaxHub Sustainable.

University of Manchester

James Winterburn, Co-Investigator

Dr James Winterburn is a Reader in Chemical Engineering at The University of Manchester, with a research focus on developing scalable, efficient manufacturing methods for biobased chemicals, including biosurfactants and biopolymers, via a bioprocessing and biochemical engineering route. He commercialised patented (WO2017220957A1) biosurfactant production and separation technology via Holiferm, spun out from the Winterburn Research Group in 2018. Additionally, he is Associate Editor of The Biochemical Engineering Journal.

Phavit Wongsirichot, Post-Doctoral Research Associate

Dr Phavit Wongsirichot is a postdoctoral researcher experienced in biorefining and industrial biotechnology. He is particularly experienced in the fractionation and valorization of agricultural byproducts for the production of bioactives, biochemical and biomaterials, including phenolics, proteins, biopolymers and biosurfactants.

University of Leeds

Nicola Stonehouse, Co-Investigator

Professor Nicola Stonehouse is Professor of Molecular Virology at the University of Leeds. Her research concerns virology and RNA biology, applying novel approaches to the study of virus replication and assembly. The focus of her research within VaxHub Sustainable is the generation and characterisation of virus-like particles.

Emma Wroblewski, Post-Doctoral Research Associate

Dr Emma Wroblewski graduated with a PhD in Molecular Biology in 2019 and now works as a PDRA in the Stonehouse group at the University of Leeds. Emma's work focuses on the development of novel virus-like particle vaccine candidates and generic vaccine scaffold systems. Additional research areas include scalable purification methods for transfer to industrial settings.

London School of Hygiene and Tropical Medicine (LSHTM)

Brendan Wren, Co-Investigator

Professor Brendan Wren is a co-investigator in both VaxHub Sustainable and VaxHub Global. He is Professor of Microbial Diseases at LSHTM and Co-Director of the LSHTM Vaccine Centre. His current research focuses on glycosylation in bacterial pathogens and developing a "glycotoolbox" for glycoengineering.

Management and Engagement Team

Stephen Morris, Outreach and Public Engagement Manager, UCL

Dr Stephen A Morris has worked in academic institutions in the UK, Germany and USA, and spent a number of years developing VLP based vaccines in the UK Biotech industry. Stephen initially joined the original VaxHub as Research Fellow specialising in the use of high throughput methodologies for vaccine bioprocess development and analytics, with an emphasis on the transfer of these technologies for use in Low- and Middle-Income Countries (LMICs).

Sean Elias, Public Engagement with Research Lead, University of Oxford

Dr Sean Elias is the VaxHub Sustainable Public Engagement with Research Lead based at the University of Oxford. Sean was formally a laboratory-based immunologist and has more than a decade of experience working on vaccines and clinical trials. The Covid-19 pandemic provided Sean with the opportunity to switch careers to another interest, public engagement and outreach. Through collaborations with schools, science festivals and science museums Sean has been working on novel ways to take the science of designing and manufacturing vaccines from the laboratory into public spaces.

Ludovica Vaiarelli, Partners Relations Manager, UCL

Ludovica Vaiarelli holds a BSc in Bioprocessing of New Medicines with Business and Management and an MSc in Bioscience Entrepreneurship from UCL. She served as Outreach Coordinator in VaxHub 1, facilitating the public dissemination of research outcomes through webinars, two YouTube series, training in vaccine development and production, and as co-lead of an outreach programme in schools. As Partners Relations Manager , she is responsible for cultivating and strengthening collaborative relationships with key partners, identifying potential strategic alliances, discussing synergies, and ensuring engagement and effective communication between the core research group and its partners.

Anca Tacu, Policy Advisor, UCL

Anca Tacu is based in UCL Engineering's Policy Impact Unit, she is currently working closely with researchers within the hub to facilitate and enhance the policy impact of their work. Anca previously held roles in UCL in the Institute for Innovation and Public Purpose (IIPP) and the UCL School of Pharmacy. Anca's background includes a particular emphasis on the Sustainable Development Goals (SDGs). She was the founding network manager of the Sustainable Development Solutions Network UK, growing this into a thriving collaborative space for UK HEIs to contribute actionable research to policy making.

Lalintip Hocharoen, Programme Manager, University of Oxford

Dr Lalintip Hocharoen is a Programme Manager based at the University of Oxford. Lalintip brings extensive experience in biopharmaceutical and vaccine manufacturing processes, gained from her previous role as a bioprocess scientist at King Mongkut's University of Technology Thonburi, Thailand. She looks forward to contributing her diverse background and expertise to drive advancement in the VaxHub initiatives.

Michael Sulu, Equality, Diversity and Inclusion Lead, UCL

Dr Mike Sulu is a Lecturer in Biochemical Engineering. Alongside this substantive role he is also the UCL Race Equality Envoy, a Mental Health First Aider, UCL Dignity Advisor, UCL Fair recruitment specialist and the PI for two concurrent grants that aim to improve access to doctoral education for underrepresented groups in HE. Outside of this he remains active in the areas of communication, mentoring, access and widening participation, and supports Further Education as a school governor.

Jane Doogan, Project Manager, UCL

Jane Doogan is a project manager within VaxHub Sustainable. Jane joined the original VaxHub in 2019 and has more than 20 years' experience of working in management and public affairs roles within education and healthcare.

Emily Petch, Project Manager, UCL

Emily Petch is an experienced project manager within the VaxHub Sustainable team based at UCL. Emily joined the original VaxHub team as a project manager in April 2019. Prior to joining UCL, Emily's experience includes working in the not-for-profit and healthcare sectors.

International Advisory Board

Barry Buckland, Chair

Barry Buckland is an experienced international expert for the development of biologic products with a special focus on vaccines and therapeutic proteins and for many years was head of the Merck Research Laboratories Bioprocess R&D group. Barry has received numerous awards recognising his contributions towards developing many important vaccines throughout his career and is a member of the prestigious USA National Academy of Engineering (NAE).

Ingrid Kromann, Member

Ingrid Kromann is the Acting Executive Director of Vaccine Manufacturing and Supply Chain Division at CEPI. She joined CEPI in 2020 as Head of CMC in CEPI's Vaccine R&D Department and has also performed the role of Director of Manufacturing and Quality Control Development. Ingrid has a background as a chemical engineer and has over 30 years of experience in vaccine development, including working at Statens Serum Institut (Denmark) as Director of Vaccine Development.

Günter Jagschies, Member

Günter Jagschies has been active in the biopharmaceutical manufacturing market since 1985. Günter has been an ambassador for GE Healthcare Life Sciences (now Cytiva) globally advising biopharma companies on manufacturing strategies and economics and as an active member in the biopharma community and its conferences. His main contribution to the science and education in this field is "Biopharmaceutical Processing" a comprehensive textbook on development, design, and implementation of manufacturing processes, which he published in 2018 with support from 100 industrial and academic co-authors. He is now the Principal Consultant in his own consulting firm Gemini BioProcessing.

David Pollard, Member

David Pollard has 30 years' experience of diverse industrial bioprocess development for a range of therapeutics including novel mAbs, peptides, anti infectives, biocatalysts and more recently cell therapies. Between 1995 to 2017 David led process development teams for early and late stage CMC pipeline teams and provided contributions to multiple IND's & BLA's for Biologics & Vaccines development at Merck & Co. Inc. David has experience of Kite Pharma, Tessera Tx and now heads an arm of Sartorius corporate research for advancements in bioprocessing.

Marianne Ellis, Member

Marianne Ellis, BEng, PhD, CEng, MIChemE, is Professor of BioProcess and Tissue Engineering at the University of Bath, UK. Her research is focused on bioprocess design for tissue engineering applications. Marianne is Director of 'CARMA' (Cellular Agriculture Manufacturing Hub), the EPSRC Sustainable Manufacturing Hub. She started her career focused on the scale up of regenerative medicine and cell therapies, moved into non-animal technologies for in vitro models, and is now focused on cellular agriculture and in particular cultured meat. Marianne is also co-founder and CTO of Cellular Agriculture Ltd.

A representative of the funders, the Engineering & Physical Sciences Research Council (EPSRC), also sits on the board as a member.

Grand Challenge Research

GC1 Improved tools and technologies to speed up manufacture and mass administration

WP 1.1 Improved Platforms

Microbial pathogens engineering

Led by Brendan Wren (LSHTM), Catherine Green (University of Oxford)

Two new recombinant vaccines against bacterial pathogens will be developed using a novel Protein-Glycan Conjugation Technology (PGCT) and produced as an exemplar in collaboration with the Oxford CBF. These vaccines will protect against Francisella tularensis (biothreat, protein coupled to lipopolysaccharides) and Streptococcus pneumoniae serotype 1 (multi-antibiotic resistance threat, protein coupled to capsule).

Year one deliverables:

- 🕒 Provide clear protocols towards producing a Strep pneumo serotype 1 vaccine to GMP- ongoing- new funding has been granted (£12.3m BBSRC GlycoCell Engineering Biology Mission Hub) where Professor Wren is Co-Principal Investigator. Research will be used to clone all 100 Strep pneumo serotypes and has been used to improve the production of the Strep pneumo serotype 1 vaccine in E. coli cells. Protocols for upscaling and GMP with this new approach for a Strep pneumo serotype 1 vaccine are in progress.
- 🕒 Discuss the provision of a logistical pathway to facilitate the production of PGCT-derived glycoconjugate vaccines to GMP- Ongoing- multiple discussions have taken place regarding the production of PGCT-derived glycoconjugate vaccines to GMP. These include starting materials, cell banks, bill of materials, equipment lists, process descriptions, validation plans, critical process parameters, risk assessments, waste management, critical quality attributes, toxicology, adjuvants and an assay validation plan. It is proposed that the prototype Francisella glycoconjugate vaccine will initially be attempted to GMP followed by the Strep pneumo serotype 1 vaccine.

A pathway for upscaling and downstream processing of PGCT-derived glycoconjugate vaccines has been established.

Novel platform development

Led by Nicola Stonehouse (University of Leeds)

This work-package will focus on a platform antigen display technology by the University of Leeds, VelcroVax. This technology will be used where the capsid/core of hepatitis B virus is used as a scaffold in order to 'present' antigens. This system compliments other two-component VLP vaccine delivery platforms using technologies in which a small peptide spontaneously forms a covalent (isopeptide) bond with its partner protein (e.g. Spytag/Spycatcher). However, VelcroVax employs non-covalent interactions, which is potentially more compatible with the recognition and presentation of oligomeric structures such as trimeric viral glycoproteins.

Year one deliverables:

- ✓ Produce and characterise picornavirus VLPs in yeast - polio types 1,2 and 3 VLPs (PV1 PV2 and PV3) have been supplied to collaborators.
- ✓ VLPs for EVA71 B2 and C4 strains have been generated and EVD68 work is in progress.
- 🕒 Develop the VelcroVax system (in yeast and E. coli) for modular antigen display – ongoing.

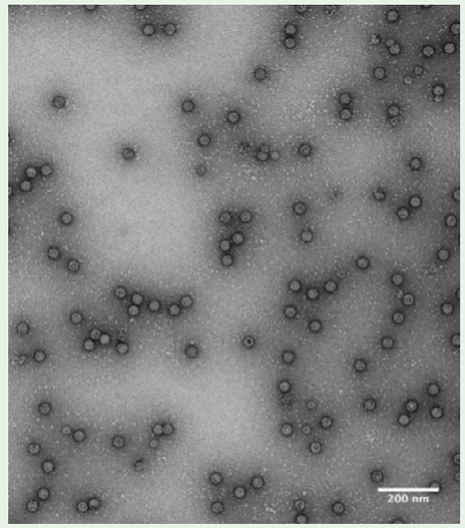


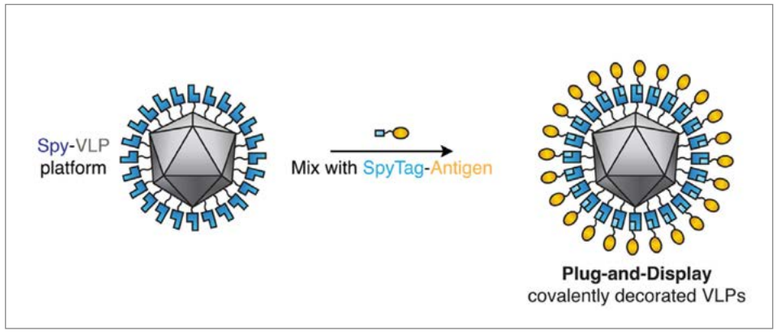
Fig 1.: TEM (negative stained) of poliovirus VLPs produced in Pichia pastoris.

Strategies to enhance immunogenicity

Led by Sandy Douglas and Sumi Biswas (University of Oxford)

This work-package will focus on strategies to develop a platform approach to vaccine manufacturing that will be centred around pandemic preparedness. A Virus Like Particle (VLP) based vaccine platform will use a carrier VLP with a SpyCatcher molecule. The manufacturing of the VLP is independent of antigen-specific processes and therefore suitable for a rapid response platform. The carrier VLP can easily be conjugated by the formation of an isopeptide bond with a recombinant antigen from the pathogen of interest, when the antigen is expressed with the Tag molecule attached. This platform will be optimised for resource efficient rapid manufacturing and increased stability of thermostable formulations.

Fig 2. Spy-VLP platform



Year one deliverables:

- Select primary upstream antigen-production approaches- ongoing- The polyclonal stable pool strategy has been chosen as the benchmark for CHO-K1 cell line development and antigen production optimisation. Work has also begun on optimising transient expression as an alternative approach. The overarching goal for antigen production is to optimise yield while minimising input materials and resources, ensuring a time and cost-effective and scalable production strategy.
- Select exemplar antigen- ongoing- The performance of most CHO cell lines are evaluated by cell specific productivity (picograms of product per cell per day), often using a model IgG. In addition to candidate vaccine antigens, we have therefore selected Trastuzumab as a widely used IgG1 mAb to optimise recombinant protein production, allowing comparison of the performance to published benchmarks.
- Develop analytics to support future studies of dried formulations- ongoing- studies have been conducted on the stability of Ag-VLP particles in various formulation buffers. HPLC-SEC was utilised to examine the ratio of Ag-VLP conjugated particles and free antigen through successive freeze thaws. These stability indicating assays will be valid for a wide range of antigens produced in the course of the project. The implementation of thermostable dried formulations in vaccine production will allow an improved global supply system by avoiding the requirement for a cold chain.

Modular antigen display on nanoparticles

Led by Stefanie Frank and Michael Thomas (UCL)

This work package will focus on a novel modular protein nanoparticle platform that facilitates oriented attachment of one or more type(s) of antigens onto versatile protein nanoparticles. Proof of concept studies show that such mosaic particles have potential in protection against SARS-CoV-2 and other pathogens. Promising display designs will be efficacy-tested in cell-based assays and/or small animal studies and have the potential to be combined with WP1.3 designs.

Year one deliverables:

- Recruitment of PDRA who will work across WP1.1 and WP1.3 – ongoing scheduled for year 2 to align with a current project.
- First insights into stability of protein nanoparticle-based vaccine candidate designed previously – work not yet started.

Strategies to enhance immunogenicity

Led by Sarah Gilbert (University of Oxford)

Adenoviruses enter cells by binding to the Coxsackie Adenovirus Receptor via the fibre protein on the virus capsid. However, during Adenovirus vector vaccine preparation the fibre protein can be sheared off the viral particle rendering these particles non-infectious even though they still have the capacity to express the transgene if delivered into cells. The aim is to increase the infectivity and immunogenicity of the viral vectored vaccines by encapsulating these non- infectious adenoviruses inside lipid nanoparticles.

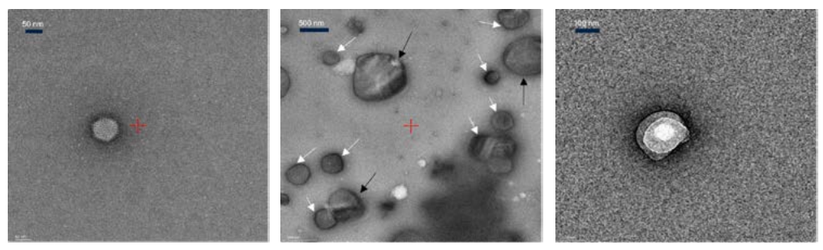
Various lipid formulations have been developed and tested that contain cationic lipids (DOTAP) and ionisable lipids. As DOTAP has been proven to be toxic to cells, there has been a focus on a particular formulation, that contains ionisable lipid, and used analysis techniques such as dot blot analysis for determining the encapsulation efficiency, dynamic light scattering for size measurement and flow cytometry for level of transgene expression to confirm the success of this formulation. These formulations have also been analysed via negative stain electron microscopy and encapsulation of adenoviruses has been confirmed (Fig 3). However, these techniques were not providing data to determine the encapsulation efficiency. Therefore, the team are currently looking at finding a biophysical analysis toolbox to determine the encapsulation efficiency through which we will be able to separate encapsulated adenoviruses and non-encapsulated adenoviruses. In parallel there is a focus on looking at transduction of different cell lines which are or are not permissive to adenovirus infection this includes looking at blocking the CAR receptor on the same cell line which can give better comparison results for transduction studies.

In the coming year, the aim is to focus on developing and modifying a formulation containing modified cationic lipids that assist as a delivery system and increase transfection, infectivity, and immunogenicity. Once all these have been determined, the aim is to perform in vivo testing of these formulations.

Year one deliverables:

- Data on encapsulation of adenoviruses with different formulations - ongoing works and trying out new formulations as increased infectivity not observed.
- Data on in vitro infectivity of encapsulated adenovirus in different cell lines - ongoing- achieving data with the current formulation that is being tested.
- Written plan for in vivo immunogenicity experiments and sourcing of reagents required - ongoing work.

Figure 3: Analysis of adenovirus and LNPs by negative stain electron microscopy. 9a) ChAdOx1 (100 to 110nm) (b) Empty liposomes (150 to 170nm) with white arrows indicating particles of the mentioned sizes and black arrows indicating sizes ≤500nm (c) Encapsulated ChAdOx1 (180nm to 210nm) The sizes given are based on DLS analysis, and this was used as a guide to determine particles in electron microscopy analysis.



A *B* *C*

WP 1.2 Rapid development and manufacture

Process intensification and distributed manufacture and Digitalised automated workflow

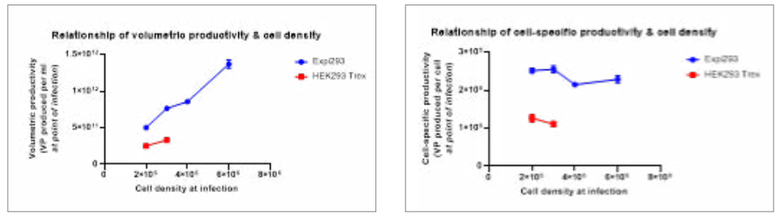
Led by Sandy Douglas and Catherine Green (University of Oxford)

This work package will focus on process intensification and purity improvement. A higher-productivity process for making adenovirus will allow production in smaller facilities, with less waste, and more quickly.

Year one deliverables:

- Cell line selection- ongoing- a cell line has been selected due to higher productivity. Moving from HEKTrex to Expi293F inducible cell line. An agreement has been reached between ThermoFisher for the usage of these cells as GMP starting material for adenovirus production.
- Create a cell banking strategy- ongoing- In order to reduce waste and improve the timeline, a high cell density cryopreservation is currently being evaluated.

Fig 4: Volumetric productivity and Cell productivity according to the cell density in HEKTrex (in red) and Expi293F inducible (in blue) cell lines.



Process intensification and distributed manufacture and Digitalised automated workflow

Led by Duygu Dikicioglu and Martina Micheletti (UCL)

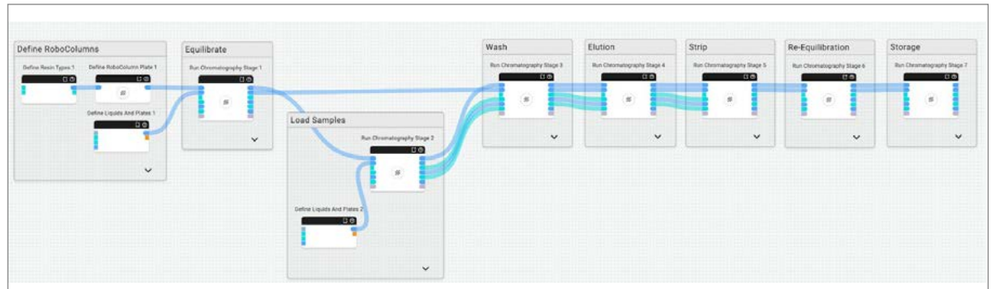
This work package will focus on developing a first-of-its-kind platform, unlike others optimised for the execution of a specific type of task, or those that bear extensive entry-barriers associated with a steep learning curve for the end user. Such a platform will enable any researcher to execute their non-standard, out-of-the-box process development operation for any vaccine system yielding high quality, error-free data, and with minimal training requirements as well as minimal use of resources (consumables and laboratory man-hours). We will also facilitate remote operation of the platform, removing the across-institution barriers and demonstrate how operation can be maintained in the face of laboratory shutdown due to unforeseen circumstances. The platform will also facilitate cloud data sharing across institutions, thus avoiding unintended replication of experiments and yielding maximal digital efficiency.

Year one deliverables:

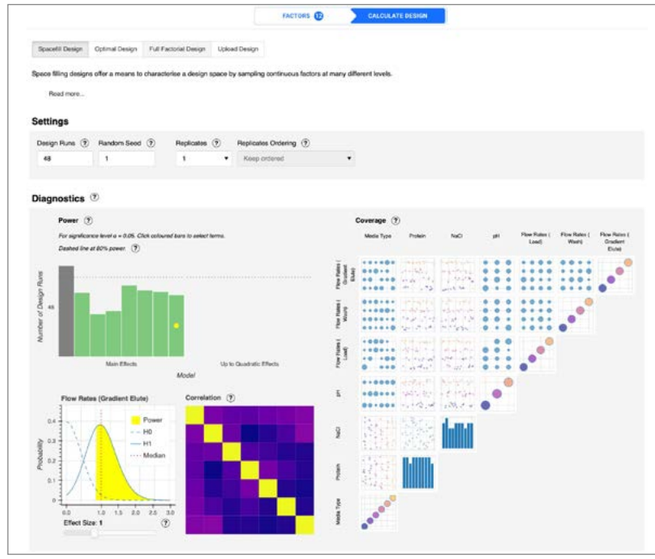
- ✓ Successful recruitment of a PDRA with automation expertise- Cheng Zang recruited and started in April 2024.
- 🕒 Setting up the Synthace system- ongoing.
- 🕒 PDRA to receive Synthace elements and Tecan training- ongoing to be completed by end of June 2024.
- 🕒 Set up operation of the Tecan platform and carry out professional maintenance- ongoing to be completed by end of June 2024.
- 🕒 To start establishing the first Synthace workflow of a test case of miniaturised upstream bioprocess operation described in (Samaras et al (2021)- ongoing-planned for Summer 2024.

Synthace

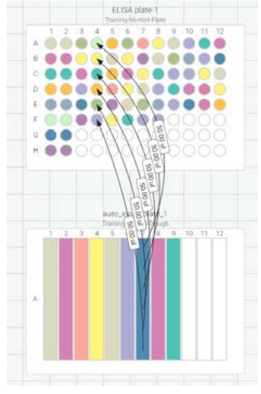
Fig 5. Example Synthace workflow.



The figure illustrates a detailed workflow for a chromatography process, starting with the definition of RoboColumns and progresses through several stages from equilibration to final storage.



The figure shows the power analysis, effect sizes, and factor coverage for a 48-run, space-filling experimental design, highlighting the ability to detect effects and the relationships between factors.



The figure illustrates the transfer of specific volumes from multiple troughs to a 96-well ELISA plate, showing the mapping and pipetting volumes for each well.

Microscale processing and robust scaling strategies

Led by Martina Micheletti (UCL)

This work package will focus on microscale processing, scale-down tools and knowledge of scaling fundamentals will be employed for experimental data collection on different vaccine technologies (from WP1.1) for validation and scalability purposes. Recruitment of a researcher for this work package is ongoing.

Year one deliverables:

- Scoping literature exercise to inform publication of an overview of scaling strategies to better define and understand gaps- ongoing.
- Familiarisation and knowledge transfer with other researchers to map out challenges to inform miniaturisation strategies- ongoing.

Product impurities and separation

Led by Dan Bracewell (UCL)

This work package will focus on downstream processing opportunities by investigating the potential of a polishing chromatography step based on affinity chromatography using both commercial and novel ligands.

Year one deliverables:

- Identifying potential new cell based analytics for critical quality attributes of adenovirus based on the receptor the virus uses to gain entry into cells. – ongoing.
- Identifying which critical quality attributes / features of adenovirus might be suitable for the development of separations to reduce product heterogeneity. – ongoing.
- From points 1 and 2 define improved objectives and an associated job description to hire a suitable PDRA by October 2024. – ongoing.
- Research discussions initiated with collaborators in Oxford. – ongoing.

WP 1.3 Mucosal and thermostable formulations

Bio-based excipients and adjuvants

Led by James Winterburn (University of Manchester)

This work package will focus on fermentation processes for the production of novel materials for vaccine formulation and delivery, e.g. biosurfactants, that will be engineered to be robust, scalable and with consideration of both technical feasibility and economic viability. Materials produced will be tested within the Hub. Our initial focus will be on sustainable formulations, investigating how squalene in water emulsions can be stabilised with a variety of biosurfactants.

Year one deliverables:

- Recruit PDRA –successfully recruited. Expected start date: June 2024.
- Literature review to identify specific application areas of biosurfactants and biopolymers in formulations and potential for use in drug delivery and as excipients and adjuvants – in progress, scope for two reviews 1) An updated review on recent advances in the use of these biopolymers as adjuvants 2) Lab-scale production and scale-up of potential biopolymer adjuvant. Target journals Carbohydrate Polymers. (IF 11.2), Nature Chemical Engineering.
- Initial production of molecules of interest, characterisation – to be started once PDRA is in post.
- Provision of fully characterised bio-based materials to others in VaxHub Sustainable– ongoing working with Sudaxshina Murdan (UCL) and Croda on bio-based formulation.

Fig 6 – Polyhydroxyalkanoate (biopolymer) film.

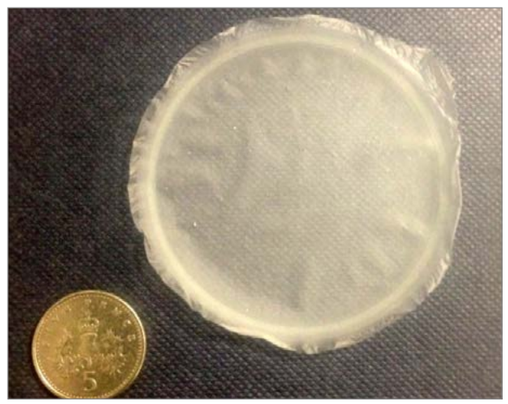
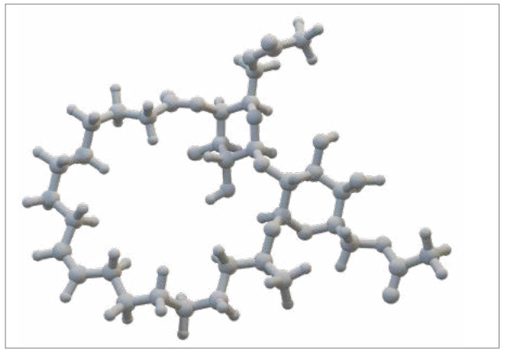


Fig 7 – Sophorolipid biosurfactant 3D structure.



Enhancing mRNA stability by novel encapsulation strategies

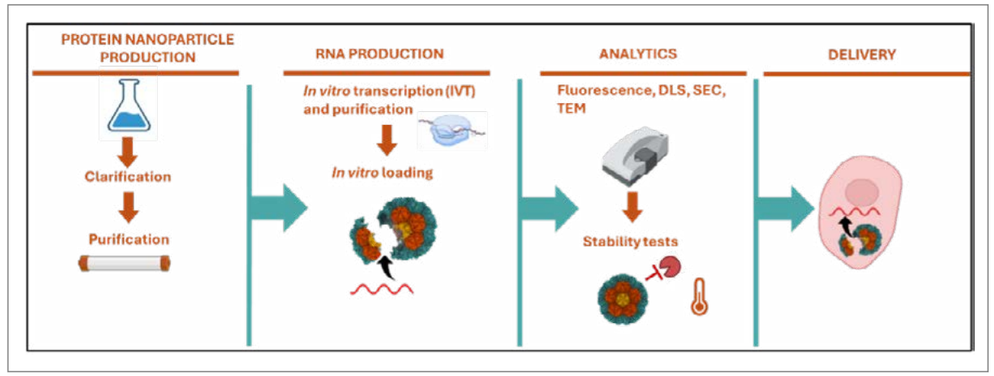
Led by Stefanie Frank and Michael Thomas (UCL)

This work package will focus on exploring novel encapsulation strategies which will be explored for mRNA vaccines using self-assembling protein nanoparticles to improve stability, storage and administration. Engineering biology approaches will be employed to develop loading strategies for mRNA molecules of varying designs for encapsulation into cages with desirable properties. Capacity and stability analysis including cell-based assays will be carried out to test particle delivery.

Year one deliverables:

- ✓ Design for RNA loading strategies – completed as part of an associated EngD project.
- 🕒 In vitro loading adapted from protocol in our group (Van de Steen et. al. 2024, accepted in ACS Applied Biomaterials) – in progress, optimisation of disassembly and reassembly of particles required.

Fig 8: Workflow for encapsulation strategy into protein nanoparticles.



Mucosal vaccination strategies and Platform sublingual formulations

Led by Sudaxshina Murdan (UCL) and Nicola Stonehouse (University of Leeds)

Progress of mucosal vaccination has been hampered by the limited number of mucosal vaccine adjuvants and of vaccine formulations. This work package will focus on investigating the sublingual mucosal route of immunisation. Two to three sublingual platform formulations will be developed, using two to three types of antigens. Up to ten substances will be investigated for their potential to act as sublingual vaccine adjuvants. Experiments will be conducted in vitro and in vivo. To produce dry vaccine formulations (which are more thermostable than liquid ones), freeze-drying and spray-drying will be investigated and conditions that retain the immunogenicity of vaccine formulations will be identified.

Year one deliverables:

- 🕒 Continue collaboration between Leeds and UCL re sublingual delivery, initially with PV1- ongoing.
- 🕒 Explore needle-free approaches to immunisation.- ongoing.
- ✓ In vivo testing of new vaccine adjuvants by the sublingual route.- (achieved - several adjuvants have been tested).

GC2 Sector-specific tools for environmental assessment and facility design

This Grand Challenge will address sustainability in a holistic manner, examining our internal activities as a Hub, the current opportunities for regenerative design, and how to plan for facilities of the future. We aim to establish clear frameworks for assessing our current environmental footprint along the entire manufacturing and production supply chain and use these as departure points for intervention.

WP 2.1 Understanding bioprocess sustainability impact

LCA methodology for hotspot analysis and decision-making and Development of a comprehensive inventory for biotechnological manufacture

Led by Brenda Parker (UCL)

WP2.1 will address two key issues, while learning from recognized sustainability Project Partners. Firstly, the current framework for LCA methodology (ISO standard) provides a general template, however producing life cycle assessments that are comparable is challenging. We will produce a "best practice" document to ensure that the scope and preparation of the life cycle inventory can be refined so that outputs are meaningful. This will facilitate hotspot analysis or decision-making in process design. Secondly, the current EcoInvent database is not comprehensive in regard to the types of inputs relevant to biotechnological manufacture e.g. media formulation, single-use equipment. We will source data and boost the range of well-defined inputs to enable more precise life cycle inventories reflective of the actual materials used in bioprocesses. The study will examine the process and environment using a cradle-to-gate approach, including an inventory analysis, a detailed impact assessment followed by an interpretation and process review stage. Linking with the work in GC1, we can then assess the environmental benefit of thermostable formulations and other advances in upstream processes.

WP 2.2 Exploring industrial symbiosis and circular economy of resources

Investigation of waste streams as future resource and Design for (re)manufacture

Led by Brenda Parker (UCL)

WP2.2 looks for novel intervention points and innovation. This work answers the fundamental question of how we might plan for future facilities to be embedded within a circular economy and aims to address three key aspects around the use of waste and novel facility design: a) Identification of waste streams and location of future manufacturing. Linking with GC1, we will use LCA as a tool to calculate the potential sustainability gains through sharing waste utilities and recycling of water. b) Biopharmaceutical waste streams as a future resource. We will experiment with source-segregated waste streams and develop a sector-specific classification system (organic, inorganic, mixed) to identify opportunities for recycling or remanufacture. c) Design of facilities to enable effective use of waste streams. Aligned to the CBF expansion and ongoing initiatives at our partner companies, we will evaluate new bio-integrated technologies that respond to environmental needs (e.g. carbon dioxide capture, heat loads, wastewater reuse) and support building design, which facilitate a wider circular economy network.

Year one deliverables:

- ✓ Recruitment of the RA position - completed: Rita Morais joined the VaxHub Sustainable team as a Research Assistant for Sustainable Bioprocess Design in April 2024, focusing on researching opportunities for industrial symbiosis and the circular economy within the industry.
- 🕒 Advertisement for the PDRA position for LCA- ongoing.
- ✓ Initial meetings with 2-3 industry partners to scope sustainability topics and priorities for LCA research - We have met with members of the AstraZeneca team online, and following Sartorius' visit to UCL Biochemical Engineering on April 23, 2024, where the team presented their overall sustainability goals, we have begun to build a SharePoint structure to be able to capture information about industry priorities to enable us to assess common themes, as well as track progress.
- ✓ Public engagement activity on water recycling and remediation (Water Pressure Exhibition, Hamburg – opening March 2024). An output of this public engagement activity is the Augmented Polycultures installation, featured in the Water Pressure exhibition at the Museum of Arts and Crafts in Hamburg. This installation represents a decentralised approach to bioremediation of greywater and surface run-off for future buildings, through the use of algae biofilms inoculated in 3D printed ceramic tiles.

Research spotlights

Sandy Douglas

I am one of the Co-Investigators of VaxHub Sustainable and an associate professor at the Jenner Institute, University of Oxford. My main research interests are the development of new antibody-inducing vaccines and breaking down the barriers to translation of new biological medicines into clinical trials. I lead the University's Bioprocess and Analytical Development (BiPAD) team, which is concerned with bringing together clinical and bioprocess understanding to make small-scale GMP manufacturing more cost-effective, lowering the barrier to experimental medicine and early-phase clinical development of novel interventions.

Experience

Clinical

- GMC Specialist Register Pharmaceutical Medicine
- Chief Investigator of Phase I/II trials of adenovirus-vectored rabies vaccine candidate and intranasal administration of Ox/AZ COVID-vaccine

CMC

- Previous: Developed large-scale process and distributed manufacturing strategy for Ox/AZ COVID-19 vaccine
- Now: Established University of Oxford Bioprocess & Analytical Development team

Pre-clinical

- Previous: Development of malaria and rabies candidates now in Phase I/II
- Now: Wellcome Trust prize fellowship – EBV vaccine development

Research interests and projects

My main interests are the development of new antibody-inducing vaccines and breaking down the barriers to translation of new biological medicines into clinical trials and onward to real-world impact. This includes making GMP-compliant manufacturing more cost-effective and accessible to clinical academics.

I previously led the development of the large-scale manufacturing process for the Oxford-AstraZeneca COVID-19 vaccine, which has resulted in over three billion doses being manufactured. I am Chief Investigator on three early phase clinical trials of vaccines, one on using intranasal administration of the Oxford-AstraZeneca COVID-19 vaccine, and two on rabies (one in the UK and the other in Tanzania).

I am working on improving the translation of scientific discoveries to patient impact and continuing work on manufacturing processes for Adenovirus-vectored vaccines, in collaboration with partners such as Sartorius, Pall and CEPI. I'm also working on the development of monoclonal antibodies targeting several pathogens. Finally, I am working on the pre-clinical development of vaccines against EBV using non-Adenovirus platforms, including the use of structural immunology to guide the development of optimal immunogens.

Meet the team

I have recruited two researchers to work on VaxHub Sustainable work-packages. Catherine Cherry is the VaxHub Sustainable Senior Scientist focusing on VLP (Virus-like Particles) vaccine platform development and she started in October 2023. Jacqueline Vieira started at the same time and is focusing on Upstream Process Development.

My VaxHub Sustainable research team will also include Shawkat Hussain who will supervise both Catherine and Jacqueline.

Shawkat Hussain

I am a chartered biochemical engineer by trade and I work with Sandy as senior Scientist with BiPAD, supervising Jacqueline and Catherine across their respective projects. My current interests are vaccine CMC development and enabling lower cost of early-phase GMP for all, which includes developing and making available low cost open-access vaccine production platforms, as well as low-cost approaches to minimise regulatory hurdles for early phase work.

Work in the Hub

I will lead some of the work on the creation of improved platforms in work-package (WP 1.1). In collaboration with my Co-Investigator Dr Sumi Biswas, our work in this area will focus on strategies to develop a platform approach to vaccine manufacturing that will be centred around pandemic preparedness. I will also lead some research in WP 1.2 with Dr Cath Green which will focus on process intensification and purity improvement.

More information

- Sandy Douglas' LinkedIn
- BiPAD website

Brenda Parker

I am one of the Co-Investigators of VaxHub Sustainable and I am an Associate Professor of Sustainable Bioprocess Design within the UCL Department of Biochemical Engineering. My current research seeks to address the need for sustainable and scalable platforms for industrial biotechnology and bio-integrated design. My doctoral work investigated directed evolution of proteins for green chemistry processes, but I moved to a different shade of "green" when I joined the Algal Biotechnology Consortium at the University of Cambridge for my postdoctoral work. Prior to joining UCL in 2015 I worked on a number of EU projects focusing on the scale up of plant and algae-based processes.

Meet the team

I will be working with Rita Morais who is the VaxHub Sustainable Research Assistant (RA) on sustainability. With her group project Urban MYCOskin, developed during her studies in Bio-ID, Rita participated in several exhibitions and conferences. Recently, the project won the New European Bauhaus Prize in the "Shaping a Circular Industrial Ecosystem and Supporting Lifecycle Thinking." category.

Work in the Hub

I will lead the work to meet the Hub's vision to become a sustainability leader in the sector and focus on tools that support better understanding of the impact on the environment and facilitate waste re-use and facility design for (re)manufacture.

An important aspect of the work that Rita and I will do in the Hub will involve bridging the domains of research and built work. We will do this by producing "demonstrator" installations that examine topics of relevance to the field, such as resource management or carbon mitigation, and enable co-design with our stakeholders to iterate these ideas further.

Research interests and projects

My current interdisciplinary research aims to develop sustainable and scalable platforms for industrial biotechnology and bio-integrated design. This allowed me to dip a toe in the world of vaccine manufacture when I led a previous BBSRC grant on the production of edible vaccines in microalgal hosts. While this looked at making material for use in aquaculture, it enabled me to connect my research on photosynthetic host organisms with the complexities of delivering vaccines.

In 2018, I co-founded the Bio-Integrated Design Lab with Professor Marcos Cruz from the Bartlett School of Architecture. Bio-integrated design brings together two essential elements: biology as the core structure of life, and humanity, which through our worldwide presence and constructed environments, has profoundly altered our planet. We are interested in working with nature as a medium: creating new materials, scaffolds and systems for our built environment. The integration of biotechnology within our building fabric relies on many of the core skills of biochemical engineering that help us navigate scaling up. The work of Bio-ID has been showcased internationally at venues such as the Centre Pompidou, the London Design Festival, and the Venice Biennale. An algal bioremediation project, INDUS, developed within the Bio-ID Lab, won the Water Futures Design Challenge in 2019 and was shortlisted for Beazley Designs of the Year.

Other projects I am involved in include an international research collaboration with "Building with Blue Biomass," an international network that connects local knowledge and shares solutions among countries rich in regenerative marine resources, aiming to identify future pathways to reduce the environmental impact of the building industry. Additionally, I am a Co-I on the cross-institutional ELEMENTAL Mission Hub in Engineering Biology, looking at the recovery of technology-relevant metals using biological mechanisms. This Mission Hub collaborates with ongoing projects related to mineral extraction, urban mining, industrial waste, and nuclear waste, and I am going to be contributing some of our approaches from Bio-ID by embedding robotics and additive manufacturing techniques to translate lab scale processes. Finally, I have also joined the editorial board of Biotechnology Design, a publication by Cambridge University Press, exploring the cross-disciplinary and emergent nature of this iterative research field.

Outside the Bioscope pavilion at St Andrews Botanic Garden.

Photo credit: *James Robertson.*

Our first output is the Augmented Polycultures installation, featured in the Water Pressure exhibition at the Museum of Arts and Crafts in Hamburg. We are presenting a decentralised approach to bioremediating greywater and surface run-off for future buildings. This project utilises consortia of algae and bacteria, forming stable biofilms that play crucial roles in nutrient cycles and pollutant remediation. The installation integrates ceramic systems with controlled porosity, morphology, and glazing to direct microbial growth, supported by advanced computational design and manufacturing techniques that create efficient water recirculation mechanisms.

The installation's main bioremediation structure comprises of ceramic tile-bricks with a three-dimensional infolding geometry, designed to increase water residency time and optimise conditions for algae consortia growth. A cistern with a submerged pump and a geometrically patterned top surface slows down water run-off, enhancing the bioremediation process. This collaborative project involves contributions from experts in various fields across UCL. We hope that this installation exemplifies our unique approach in the integration of design and science for the development of sustainable water treatment solutions – a topic that we know is important to the Hub.

Right, top:
Augmented Polycultures with circulating water and algae in exhibition at the Museum of Arts and Crafts (MK&G), Hamburg.

Right:
Augmented Polycultures opening, from L-R: Jingyuan Meng (BSA B-MADE); Brenda Parker; Jane Withers (Curator, Water Pressure exhibition)

Bio-Integrated Design team at the Bioscope, St Andrews Botanic Garden. Installation of engineered living materials derived from cyanobacteria and biohybrid panels embedded with melanin and violacein. L-R: Prantar Tamuli, Brenda Parker, Ella Hetherington, Marcos Cruz.

Getting hands on with a soil bioremediation project at Barking Riverside, London.

Impact Activities

Outreach and Public Engagement

The Hub is developing an active outreach programme with the aim of promoting public understanding and confidence in vaccines, with a particular focus on vaccine manufacture.

Our strategy will focus on three areas:

Increasing vaccine manufacturing transparency by better describing:

- Physical processes
- Ingredients
- Risks vs benefits
- Profitability
- Trust

Increased understanding of vaccines including:

- Among healthcare workers and community leaders
- Vaccine delivery – what do people want?
- Policy maker involvement

Supporting VaxHub members in public engagement activities by:

- Providing new tools
- Training researchers
- Addressing reluctance to engage
- Improving impact measures

The Hub's public engagement and outreach work is led by Dr Stephen Morris (UCL) and Dr Sean Elias (Oxford). To date, Dr Morris has led on structured outreach programmes with secondary schools, with a focus on GCSE and A level aged students, whilst Dr Elias has focused on opportunistic engagement with school aged children as well as engagement through science centres, festivals, and collaborations with museums.

Above: A group of year 12 students using lab equipment in the UCL Biochemical Engineering labs.

In the initial phase of VaxHub Sustainable, we have embedded some examples of best practice in outreach and engagement achieved in the original VaxHub. Examples include:

- Partner recruitment over summer 2023, in the form of the second running of a three-day CPD training for secondary school teachers and participation in the London STEM Teachers Conference, resulting in the program network being extended to include five additional educational institutions, bringing the total of actively engaged partners to eight.
- Between September 2023 and April 2024, 24 events and activities have been run, totalling over 100 hours of engagement with over 1,000 students, covering age groups 14 – 18 studying GCSE, A-level, BTEC and T-Level courses. These include a mixture of talks, interactive workshops, long-term theoretical research projects by the students and practical laboratory sessions.
- Dr Elias has developed and tested a set of activities and resources focused on explaining the upstream and downstream processes required in the manufacturing of vaccines. These activities were designed to be age range flexible, easy to replicate, affordable and transportable. The Hub now has versions of these activities at both Oxford and UCL and has already utilised them at a number of events. Some of these resources have also recently been adapted to form part of an exhibit in the History of Science Museum in Oxford.

Above, from top: VaxHub Sustainable researcher, Catherine Cherry, at the stand at the 'Oxford Brookes Science Bazaar,' 3rd February 2024; Stand at the 'Oxford Brookes Science Bazaar,' 3rd February 2024; VaxHub Senior Outreach and Public Engagement Manager, Steve Morris, speaking to a group of year 10 students.

In the coming year, we plan to expand the reach of our public engagement and outreach work in addition to developing resources and activities focused on new core projects. We hope to expand our audiences beyond Oxford and London and to bring in other UK based university partners, for example, to reach areas such as south Wales and the north of England. In addition, we plan to develop projects with industry partners. We think that there are significant opportunities to learn from partners with existing outreach and engagement programmes and to support others to develop new projects.

Above and left: 'The Future of UK Manufacturing' event, April 2024.

Right: Photo taken at the launch of VaxHub Sustainable, 8th December 2023.

Policy Engagement

Policy engagement capacity was embedded in the plans for VaxHub Sustainable from the outset through the funding of a dedicated Policy Adviser role to support the Hub in translating its research outputs into real world effects and to inform and shape policy that will address current and future national and global health challenges.

The hub's Policy Adviser, Anca Tacu, joined the VaxHub Sustainable team in February 2024. She is based in the Policy Impact Unit at UCL where she is part of a team of policy engagement specialists who work at the interface between academic and policymaking with the aim of increasing the use of research-based evidence in the policymaking process.

The focus of our policy engagement work to date has been on scoping key areas and activities to build the Hub's policy engagement plan for the next 12-18 months whilst remaining responsive to new engagement opportunities.

Initial policy engagement activities have included:

- A written submission to the call for evidence on engineering biology as part of a House of Lords Science and Technology Committee inquiry scrutinising the UK government's plans for engineering biology. Our response to this call for evidence aims to share a unique perspective on engineering biology with policymakers that comes from bringing together research expertise in vaccine design and manufacturing technologies, and bio-integrated design.
- Attendance at 'The Future of UK Manufacturing' event organised by the EPSRC together with the High Value

Manufacturing Catapult and Institute for Manufacturing at the University of Cambridge. The event brought together the manufacturing and research communities as well as policymakers to review the current UK manufacturing landscape and to look ahead to future research and innovation priorities and opportunities. We published a blog article sharing key reflections on the fundamental role of manufacturing in building a thriving and resilient UK economy.

Future plans
We will be delivering a talk on 'Why we need engineers in vaccine manufacturing?' at the Institution of Engineering and Technology in June, which will explore the essential role of engineers in large scale vaccine manufacture from a research, public engagement, and policy perspective.

Above: Photo of the materials workshop at the launch of VaxHub Sustainable, 8th December 2023.

We are currently organising a workshop themed around future pandemic preparedness. This will be a knowledge exchange event taking place in mid-July during the UCL Festival of Engineering that will bring together researchers, policymakers and our industry members to showcase how the research being undertaken within the Hub is responding to challenges related to future pandemic preparedness. This will provide a timely opportunity to engage with policymakers in the context of the ongoing international negotiations to develop the WHO Pandemic Prevention, Preparedness and Response Accord.

Future workshops beyond July are likely to focus on areas such as challenges and opportunities in relation to sustainability in vaccine manufacturing, and the regulatory implications of rapid developments for vaccine technologies.

Events

Past events

VaxHub Sustainable Launch
VaxHub Sustainable was launched at a hybrid event held in London on 8th December 2023. With almost 100 delegates in attendance, the audience were able to hear from leading Hub academics about the overall aims and vision of the Hub as well as the research plans relating to each work package.

In addition, delegates were given the opportunity to learn about how industry is tackling the challenges presented by the need for improved manufacturing sustainability with presentations from AstraZeneca, Croda and Synthace.

During the day, delegates also enjoyed two dynamic opportunities for networking with a very lively quiz competition and a stimulating materials workshop.

The day concluded with an interesting keynote from Paul Newton, Professor of Tropical Medicine, University of Oxford on "The epidemiology of substandard and falsified vaccines and innovation for their detection in supply chains".

Event in numbers:

- Almost 100 attendees
- Average satisfaction score: 4.58/5
- ¾ of those who gave feedback identified areas of collaboration at the event
- 11 speakers

Future events

Joint VaxHub Sustainable and VaxHub Global Symposium
The first VaxHub Sustainable and VaxHub Global Joint Symposium will take place from 19th – 20th September 2024 in Oxford.

This landmark event will be conducted in a hybrid format, allowing for both in-person and virtual participation.

This symposium marks the first occasion on which our expansive global network will come together, showcasing the full breadth of our ambitions and collaborative efforts. The event aims to foster a comprehensive understanding of our goals and to highlight the significant strides we are making in the fields of sustainable vaccine development for pandemic preparedness and enhanced vaccine manufacturing for Low- and Middle-Income Countries (LMICs). Delegates will have multiple opportunities to benefit from:

- Networking: Connect with leading experts from industry and academia, policy makers, UK and international VaxHub members
- Insightful Presentations: Gain insights from a series of keynote speeches, panel discussions, and presentations that cover a wide range of topics related to vaccine innovation and global health challenges.

Below: St Anne's College, University of Oxford.

- Collaborative Platforms: Engage in meaningful discussions and collaborations that aim to drive forward the agenda of sustainable and rapid responsive vaccine manufacture.

Event Highlights

- Dates: 19th - 20th September 2024
- Venue: Tsuzuki Lecture Theatre, St Anne's College, University of Oxford
- Format: Hybrid (In-person and virtual)

Industry engagement

Industry engagement in VaxHub Sustainable is critical to the realisation of our vision to deliver manufacturing innovations that enable a transformative change towards sustainable and rapidly responsive vaccine manufacture.

Establishing our network
We aim to establish and secure strategic partnerships with companies initially through one-to-one meetings that clarify priorities and to formalise these relationships via our research collaboration agreement, which all members are required to sign. To date, our industry relations team has engaged with over 25 prospective industry partners, ranging from large vaccine manufacturers to SMEs involved in upstream and downstream vaccine processing, as well as formulation and innovative sustainable packaging and delivery solutions.

In line with funder expectations, member companies are required to make an annual cash and/or in-kind contribution to the Hub, dependent on their organisation type and size. These fees enable members to participate in Hub meetings and access platform funding opportunities and support the Hub's networking and knowledge transfer activities. In-kind contributions might be derived from staff participation in Hub meetings or dissemination activities, involvement in feasibility studies or provision of materials /access to facilities.

Overview of member benefits
Joining the Hub gives members access to a range of benefits including:

- Exposure to Hub-funded research complementary to their priorities
- Opportunities to co-defined projects aligned to their company's priorities and industrial challenges
- Access to translational research and opportunities for technology transfer
- Staff training opportunities
- Access to world-leading experts and scientific innovations

Engagement mechanisms
Funded project calls, open only to members, are planned for early 2025. These include 'open calls' for small projects or 'feasibility studies' for larger projects up to £100,000, aimed at testing new vaccine platforms, optimising existing technologies, and improving manufacturing processes. Please see "Funded Project Calls" for further details.

User Group meetings bring our network of stakeholders together to present updates on Hub research, share technology developments, gain an insight into the priorities of member companies, hear about industry trends and sector news from invited speakers and give feedback on Hub operational and dissemination activities to ensure that we remain a valuable resource.

Specialist Working Groups (SWGs) provide dedicated space and time for in depth discussion of selected research themes. Each SWG will be led by a Hub PI with relevant expertise and will provide a forum to share related work and researchers' findings. To date, proposed areas of focus include RNA vaccine stability, understanding adjuvants properties and mechanism of action, and digitalisation in vaccines manufacturing.

Hub events and dissemination activities
Members are strongly encouraged to participate in our meetings and dissemination activities to:

- Hear about the latest vaccine and engineering technology developments
- Share research news and collaborate on future funding opportunities
- Influence policymaking
- Find out about and access training and workshops on priority areas including research topics, sustainability, EDI, public and policy engagement

Contact us
For further information, please contact
vaxhub@ucl.ac.uk

Funded Project Calls

VaxHub Sustainable will use various forms of member engagement to enable the extension of research, knowledge transfer and the translation of results. Funded Project Calls will be the main mechanism for industry-Hub interactions and an opportunity to widen the proposed research programme with industrially relevant projects. All Hub members will be eligible to apply for two types of calls:

Feasibility Studies (£1m).
Feasibility Studies are awards worth up to £100k with a project duration to range from six months to one year. The aim is for these collaborative projects to explore early technologies from the core research and they could be used to help generate pilot data for follow-on funding, test feasibility with key stakeholders, test new vaccine platforms, optimise existing technologies or improve manufacturing processes.

Successful applicants will need to:

- Align with and contribute to the Hub Grand Challenge research
- Show they will interact with the Hub
- Show how the funding will benefit business in the long term
- Enable applications for follow-on initiatives
- Match contributions
- Funds could be used for researcher salaries/supervision, Co-I time, consumables, travel or other research expenses

Open Calls (£1m)
The Open Call scheme will award funds on-demand and provide the flexibility required to better meet the needs of researchers and collaborating industrial/company members.

While members applying to the feasibility studies call will need to match contributions, this will not be required for the open call projects in order to facilitate collaboration with new companies or those that wouldn't have otherwise been possible.

Priority will be given to project proposals that:

- Align to the Hub Equality, Diversity and Inclusion (EDI) priorities
- Deliver sustainability objectives within the company that could be applied to the wider sector
- Support employees' development and upskilling (e.g. funds for training or company-based doctoral degrees)

When: We expect the first call for project proposals to launch in early 2025 and encourage members and prospective members to think about possible collaborative projects.

Equality, Diversity and Inclusion Activities

The Equality, Diversity and Inclusion (EDI) vision of this Hub is 2-fold. It aims to both implement and beacon best practice across the sector. This includes both Higher Education/Research institutes and industrial partners.

The practicalities of embedding EDI within the Hub have been constantly reviewed. There has been a focus on ensuring our EDI practice is combined with responsible research and innovation, to create equity within (and out with) the hub in these areas:

- Implementation
- Beaconing
- Stakeholder engagement
- Knowledge sharing
- Advocacy
- Mentoring
- Policy advice
- Public engagement

This has led to specific work that has already begun in the implementation of more inclusive recruitment practices, beaconing and knowledge sharing in the area of EDI within research through the VaxHub Sustainable network and by steering the EDI elements of external grant applications, such as the potential creation of a network of research hub EDI Leads for upcoming EPSRC EDI hub bids.

Internally the Hub has focussed on science communication, outreach and public engagement by ensuring that this work is done in spaces and ways that will enable us to reach traditionally underrepresented communities, and in doing so we have also helped other research groups learn from our findings to improve the way they interact with a wider group of stakeholders.

The plan is to expand on the work already completed by widening our focus internally and externally to the creation or adaptation of training and mentoring programmes that will be available to our early career staff on a preferential basis, to help them to succeed in their chosen career path.

Associated Projects

VaxHub Global

The Vaccines Manufacturing Hub for LMICs (VaxHub Global), aims to deliver flexible, easily transferable multi-product platforms and simplified engineering solutions that enable the development of low-cost, effective and globally deployable vaccines to Low- and Middle-Income Countries (LMICs). It was launched on 1st September 2023 and has received funding for four and a half years via a £10 million grant from the Department of Health and Social Care (DHSC) and the Engineering and Physical Sciences Research Council (EPSRC).

VaxHub Global is co-directed by Martina Micheletti, Professor of Bioprocess Fluid Dynamics at University College London (UCL) and Cath Green OBE, Head of the Nuffield Department of Medicine's Clinical Biomanufacturing Facility (CBF) and Associate Professor at the Wellcome Centre for Human Genetics at the University of Oxford. Under this collaboration, they lead a team of academics, researchers and other professionals from their own institutions in addition to colleagues from the University of Cardiff, the London School of Hygiene and Tropical Medicine and the University of Leeds.

Communicable disease epidemics remain an on-going threat to public health and present a particular risk for LMICs. It is envisioned that the Hub will provide easily transferrable multi-product platforms and simplified engineering solutions that will facilitate the development of low-cost, effective and globally deployable vaccines to LMICs.

The Hub will strengthen future vaccine manufacturing through: (i) a focus on translational manufacture, including continuous improvements of existing vaccines, for ease, speed and lowering costs; (ii) simplified manufacturing and delivery solutions, while prioritising sustainable innovations; (iii) enhancing single-dose, multivalency, stability and injection-free administration routes so that they become a reality within the lifetime of the Hub;

Members of the VaxHub Global team at the Launch event, 24th April 2024.

(iv) leveraging advances in microfluidics to build low-cost integrated engineering platforms for rapid production; (v) championing training programmes supporting the creation and development of regional Centres of Excellence to realise the delocalised manufacturing model; (vi) developing policy initiatives and best practice sharing schemes intended to smooth the path for early phase trials of novel products in disease-affected countries.

Research on adenovirus has been built on as a cost-effective platform for LMICs. The work will not be limited to viral diseases as bacterial pathogens are a constant global threat to human and animal health. For most bacterial pathogens there are no currently licensed vaccines, and this represents an unmet health need, especially in Low Income Countries (LICs) and given the likelihood of new pathogens emerging due to climate change.

The Hub will address the three themes of ease, speed and cost with three research work packages:

- WP1. Towards flexible, easily transferable multi-product technologies.
- WP2. Towards integrated engineering platforms to automate manufacturing.
- WP3. Towards simplified regimens, extended shelf-life and delivery at reduced waste.

The work of the Hub will move current development practices towards better supporting the needs of LMICs and this will achieve the greatest global impact.

CARMA: Cellular Agriculture Manufacturing Hub

Meet the team

- Professor Marianne Ellis, University of Bath
- Professor Gary Lye, University College London
- Professor Davide Mattia, University of Bath
- Dr Hannah Leese, University of Bath
- Dr Ming Xie, University of Bath
- Professor Chris Chuck, University of Bath
- Professor Linda Newnes, University of Bath
- Professor Marcelle McManus, University of Bath
- Professor Brian Squire, University of Bristol
- Dr Petra Hanga, University College London
- Dr Neil Stephens, University of Birmingham
- Dr Ruth Wonfor, Aberystwyth University
- Professor Tom MacMillan, Royal Agricultural University

The EPSRC-funded Cellular Agriculture Manufacturing Hub 'CARMA' is working to transform food production. Cellular agriculture is the production of food and other consumables, traditionally grown on the land/in the sea, in a bioprocess by utilising cells. Led by the University of Bath, CARMA is working to establish sustainable manufacturing technologies, starting with cultured meat and palm oil substitute products.

Our vision is for a just transition to environmentally, economically, and socially sustainable food systems.

Our mission is the integration of transdisciplinary responsible approaches for novel cellular agriculture tools and technologies, into current food systems, to deliver sustainable food manufacturing in the UK and beyond.

The CARMA Director is Professor Marianne Ellis, Professor of BioProcess and Tissue Engineering at the University of Bath. She leads a transdisciplinary team of academics, researchers and other professionals based at leading universities in the UK. There are two Grand Challenges, each with its own aims, and six integrated and interconnected Work Packages through which those objectives are being delivered by the team.

Grand challenge 1: to design and deliver a template for an integrated UK circular cellular agriculture manufacturing value chain. Objectives:

- Embed whole-life value analysis for decision making when addressing operational and technical bottlenecks for Cell Ag manufacturing, ensuring responsible innovation for sustainable and ethical integration with the wider industrial system
- Inform the strategy to move Cell Ag from laboratory to shopping basket through direct engagement with stakeholders and the public
- Inform investment and policy to realise the goal for the UK to be the world-leading and net exporter of Cell Ag products and manufacturing technologies

Grand challenge 2: to create the novel, underpinning manufacturing technologies to achieve the necessary process intensities in cost effective, sustainable and ethical ways for world class Cell Ag manufacturing. Objectives:

- Design and deliver a template for a UK circular Cell Ag manufacturing value chain from the outset, informing leading-edge manufacturing technologies, people and processes
- Establish the value chain from raw materials to large-scale production that makes Cell Ag financially, ethically, and sustainably viable as part of UK Trade and Industry
- Create the novel, underpinning technologies that will achieve the necessary process intensities at scale, in cost-effective and sustainable ways

CARMA is funded for seven years with a £12m EPSRC Sustainable Manufacturing Hub grant, and with contributions from industrial and university partners. The funding structure uses a hub and spoke model for academic partners with the University of Bath being the 'hub'. The other universities, Aberystwyth University, University of Birmingham, the Royal Agricultural University and UCL being the 'spokes'. A competitive selection process will select three to six additional 'spokes' midway through the project.

There are opportunities for new industry partners to join. The benefits of industry membership include early access to research developments and world leading experts across the sector, and opportunities for industry-academic projects for new partnerships.

How to contact CARMA for further information:

- Carma-hub@bath.ac.uk
- CARMA website

The CARMA Academic team connecting with our founding Industry partners in Bath.

VaxHub Sustainable

Manufacturing Research Hub for a Sustainable Future
(VaxHub Sustainable)