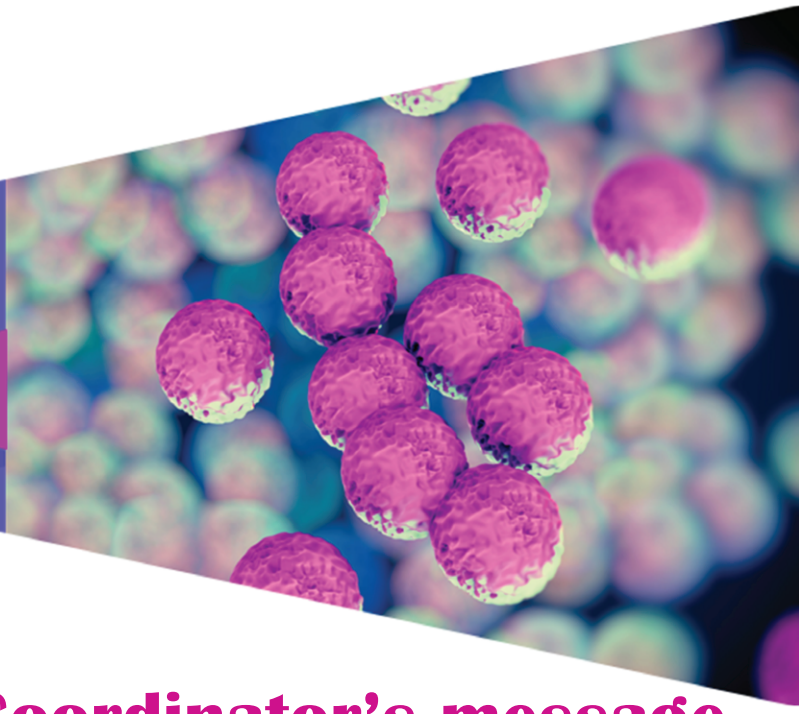
News Letter

Issue 2 I June 2020



In this issue

Coordinator's message

It gives me great pleasure to welcome all our new Early Stage Researchers to the BactiVax project. These ESRs are the heart and soul of any Innovative Training Network and we are very fortunate to have such a range of enthusiastic talented scientists join the BactiVax training programme since the beginning of the year.

They hail from all over Europe including Spain, Germany, Hungary, Italy, Poland, France, the Netherlands, Bosnia and beyond (Costa Rica, the Philippines, Malaysia, USA). Over the next 3 to 4 years they will carry out world class research as they progress to their PhD awards. Due to COVID-19, not all of them have reached their host labs yet, but despite this, they have been busy writing blogs, getting involved in public engagement and writing review manuscripts on their chosen research project. We anticipate that they will all arrive in their host labs to start their lab-based experiments by September and I am looking forward to seeing how their research develops.

Their research projects include identifying new vaccine antigens for problematic infections; understanding the immune response required to beat these infections; optimising the immune response with adjuvants which will improve the potency of vaccines. Outside the lab they will support our efforts to promote the benefits of vaccination. In BactiVax we are unanimous in our view that vaccines are the most effective medical intervention ever introduced.

Assoc. Prof. Siobhán McClean
BactiVax Coordinator

Meet our Early Stage Researchers!

ESR 1

Irene Jurado

University College Dublin (Ireland)

Exploiting a novel proteomic approach for *P. aeruginosa* vaccine antigen identification

ESR 2

Paulina Zarodkiewicz

Queen's University Belfast (Northern Ireland)

Novel glycoprotein vaccines to fight *Burkholderia* infections globally

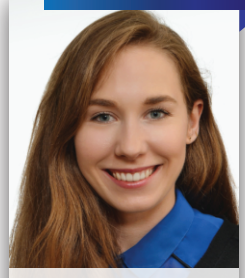
ESR 3

Océane Sadones

Ludwig Maximilian University of Munich (Germany)

Vaccine antigen identification against systemic infections

ESR 4



Eliza Kramarska

CNR Institute of Biostructures and Bioimaging (Italy)

Structural and functional characterisation of novel vaccine antigens

ESR 5

Unai Atxabal

CIC bioGUNE (Spain)

NMR molecular recognition of antigen by key receptors

ESR 6

Yi Ni Ong

University of Milano Bicocca (Italy)

Development of TLR-directed adjuvants and incorporation in novel vaccine formulations

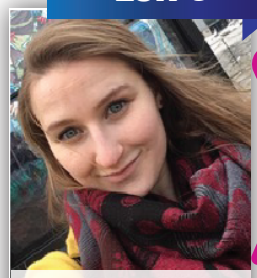
ESR 7

Samuel Pasco

CIC bioGUNE (Spain)

Elucidation of the host response to facilitate more effective vaccines

ESR 9

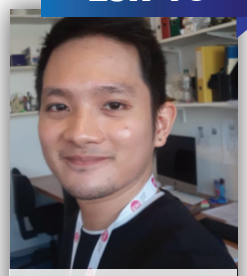


Franziska Pieper

Imperial College London (UK)

Optimisation of host response and T-cell targeting

ESR 10

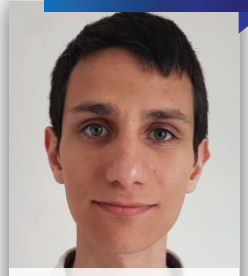


Emil Vergara

St. George's University of London (UK)

Post-exposure vaccination against multi-drug resistant tuberculosis

ESR 11



Zsolt Bognár

EPFL (Switzerland)

Byciclic peptide vaccine antigens

ESR 12

Maite Sainz

University College Dublin (Ireland)

Optimisation of adjuvants for therapeutic vaccinations against respiratory infections

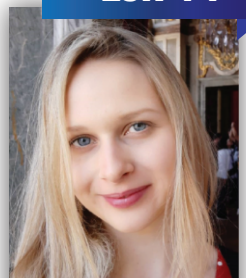
ESR 13

Chiara Bellini

Eötvös Loránd University (Hungary)

Nanocapsulated peptide-based immuno-therapeutics

ESR 14



Enisa Smlatic

Ludwig Maximilian University of Munich (Germany)

Development of a therapeutic vaccine against *P. aeruginosa*

ESR 15

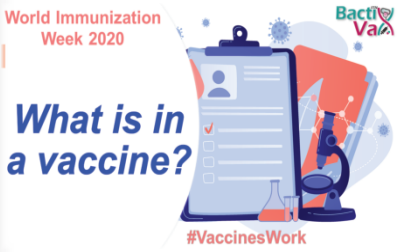
Lorenzo Bossi

ImmunXperts (Belgium)

Development of *in vitro* monitoring for candidate vaccines and identification of correlates of protection

Vaccine advocacy

Celebrated in the last week of April, World Immunization Week aims to promote immunisation to protect people of all ages against vaccine-preventable diseases. Vaccination saves millions of lives every year and is recognised as one of the most successful public health interventions. This year was the first celebration of World Immunization Week for the BactiVax team, and to mark it accordingly, we ran a well-received, two-week information campaign on social media and our website (www.bactivax.eu).



Our campaign aimed at informing the public about a few key aspects such as how vaccination eradicated or significantly decreased disease incidence, or which are the benefits of immunisation for individuals and the community. As we are an international group and so is our audience, we translated our infographics into all the languages spoken by our Early Stage Researchers: French, Italian, Spanish, Chinese, German, Polish and Dutch. Our ESRs led the campaign by sharing the information through their personal accounts, reaching a wider public and various age groups. For more reliable and accessible information on vaccines, make sure to follow BactiVax on social media and read our monthly blog posts!

Training activities

Even though our Early Stage Researchers have only recently joined the BactiVax programme and have mostly worked remotely, they already completed their first training activity! Held by UCD's Data Manager, Jenny O'Neill, the first training session focused on introducing the principles of Open Science and the best practices to make scientific data findable, accessible, interoperable and reusable (FAIR). Our ESRs also learned how to effectively manage their day-to-day research data and how to document their approach in a Data Management Plan.

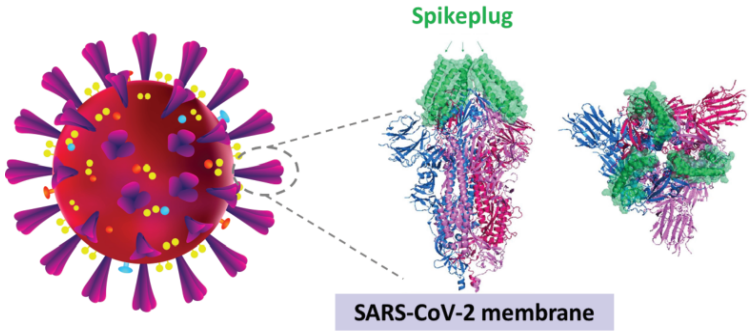
The ESRs were introduced to the Open Research Data Pilot in Horizon 2020 and received lots of useful tips on how to maximise access to research data generated by EU-funded projects. All participants found the workshop very useful and have already started to draft their data management plans!

Research updates

An engineered stable mini-protein to block SARS-CoV-2 virulence

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the type of coronavirus that causes the COVID-19 illness, responsible for the current pandemic. Like other coronaviruses previously studied, this new virus relies on a Spike protein located on its surface to bind human cell receptors. These receptors are called angiotensin-converting enzyme 2 (ACE2) and represent the entry point for the virus to infect a wide range of human cells. Therefore, molecular species capable of interfering with the recognition of SARS-CoV-2 Spike proteins by ACE2 receptors could represent promising treatments or post-exposure vaccine candidates.

Dr. Rita Berisio's research team at the National Research Council, Institute of Biostructures and Bioimaging in Naples, Italy, have designed and investigated a mini-protein with the aim of creating a soluble and stable Spike interactor. This recombinant mini-protein (Spikeplug), which was produced in high yields, has a stable conformation and resembles the structure of the human ACE2 receptor. Spikeplug recognizes the receptor binding domain on the viral protein and binds with similar affinity to the one of ACE2 receptors on human cells. The team at CNR-IBB are currently designing additional variants to further improve binding affinity to the Spike protein.



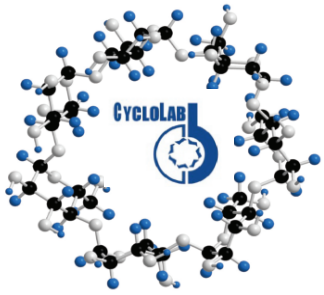
SARS-CoV-2 structure

Cartoon representation of a plugged Spike protein. The structure of the viral unit is shown in magenta, prune and blue, while plug molecules, that bind to and block the Spike, are shown is green.

This approach is very promising as a therapeutic strategy, not only for the current strain of coronavirus, but for potential future ones, that use the ACE2 receptor to infect cells. Additionally, due to the almost complete identity to the correspondent domains of the endogenous human ACE2, Spikeplug is expected to be very well tolerated.

Romano M, Ruggiero A, Squeglia F, Berisio R. An engineered stable mini-protein to plug SARS-Cov-2 Spikes. Preprint bioRxiv (2020). doi: doi.org/10.1101/2020.04.29.067728

Funding news



BactiVax team members from Cyclolab, in collaboration with UC Berkeley and Excivion, recently secured funding from the National Institutes of Health (NIH) in the US, to evaluate a wide range of cyclodextrins as a potential treatment against SARS-CoV-2 (the agent of COVID-19). Cyclodextrins are widely recognised for their medical use as excipients in anticancer and antiviral therapeutics. Only recently it was hypothesized that cyclodextrin derivatives could have significant potential and versatility to act as drugs in formulations. According to Dr. Tamás Sohajda, R&D Director of Cyclolab, "while certain cyclodextrin derivatives are known to have antiviral activity (against HIV, herpes, RSV, influenza, etc.), so far no study has sought to understand their mechanism(s) of action and optimize the cyclodextrin structure to exploit the highest possible antiviral and anti-disease potency." Having initially focused on flavivirus research under the original grant, the consortium applied for supplementary NIH funding specifically for SARS-CoV-2. The recently approved grant will support research on defining pathogenic mechanisms of SARS-CoV-2-triggered pulmonary dysfunction and will fund the development of therapies targeting SARS-CoV-2 infection.


Prof. Jesús Jiménez-Barbero

CIC bioGUNE
CENTER FOR COOPERATIVE RESEARCH IN BIOSCIENCES

Congratulations to the Chemical Glycobiology team at CIC bioGUNE, led by BactiVax Principal Investigator Prof. Jesús Jiménez-Barbero, who has just been awarded a prestigious Marie Skłodowska-Curie grant! The successful project is part of the Glytunes European Training Network, which seeks to tackle new therapeutic strategies against autoimmune diseases and cancer. Specifically, the objective of the consortium is to understand, on a molecular scale, how aberrant interactions between protein immunomodulators known as siglecs and their ligands, sialic acid-containing sugars, contribute to the etiology of immune diseases. The ultimate goal is to develop glycobiotechnological therapeutic approaches for the development of molecules that modulate these interactions. The Glytunes programme, coordinated by University of Naples Federico II, was awarded €3.74 million and consists of 7 research institutions and 4 biotechnology companies in Europe. At CIC bioGUNE, Glytunes is chaired by June Ereño Orbea, Ikerbasque research fellow in the Chemical Glycobiology group.

COVID-19 vaccine candidates in clinical trials

Over the last few months, scientists worldwide have made formidable progress in developing vaccines against the new coronavirus. As of 24th June 2020, 16 vaccine candidates have entered clinical trials (see table below), including Phase II trials, and three developers, namely Astra Zeneca/University of Oxford, Sinopharm/Wuhan Institute and The Murdoch Children's Research Institute (the latter with the BCG vaccine as potentially protective), have progressed to Phase III clinical trials. The endpoints of Phase III trials is to safely and effectively prevent symptomatic COVID-19 disease, as well as severe COVID-19 and SARS-CoV-2 infection. In Europe, the European Medicines Agency has been in discussion with developers of 34 potential COVID-19 vaccines. However, based on previous experience, regulatory agencies estimate that it might take at least a year before a vaccine against COVID-19 is ready for approval and produced in sufficient quantities to facilitate broad use.

Platform	Vaccine Candidate	Developer	Clinical Evaluation Stage
RNA	Lipid nanoparticle-encapsulated mRNA	Moderna & The National Institute of Allergy and Infectious Diseases	Phase II
	Three lipid nanoparticle-encapsulated mRNA formulations	BioNTech & Pfizer & Fosun Pharma	Phase Ib/II
	Lipid nanoparticle-encapsulated-nCoVsaRNA	Imperial College London	Phase I
	mRNA	Curevac	Phase I
Non-replicating viral vector	Adenovirus vaccine	Astra Zeneca & The University of Oxford	Phase III
	Adenovirus vaccine	CanSino Biologics & Beijing Institute of Biotechnology	Phase II
	Adeno-based vaccine	Gamaleya Research Institute	Phase I
Inactivated virus	Unnamed	Wuhan Institute of Biological Products & Sinopharm	Phase III
	Unnamed	Beijing Institute of Biological Products & Sinopharm	Phase I/II
	Inactivated + alum adjuvant, PiCoVacc	Sinovac	Phase I/II
	Unnamed	Institute of Medical Biology, Chinese Academy of Sciences	Phase I
DNA	DNA plasmid vaccine with electroporation	Inovio Pharmaceuticals	Phase I
	GX-19	Genexine Consortium	Phase I
Protein subunit	Full length recombinant SARS CoV-2 Glycoprotein nanoparticle vaccine adjuvanted with Matrix M	Novavax	Phase I/II
	Adjuvanted recombinant protein	Anhui Zhifei Longcom & IChinese Academy of Sciences	Phase I
	Native-like trimeric subunit Spike protein vaccine	Clover Biopharmaceuticals & GSK & Dynavax	Phase I
BCG vaccine	Bacillus-Calmette Guerin vaccine (anti TB)	The Murdoch Children's Research Institute in Australia	Phase III

1. Mullard A. COVID-19 vaccine development pipeline gears up. The Lancet, 395 (10239): P1751-1752. 2. European Medicines Agency, Treatments and Vaccines for COVID-19. 3. Corum J, Grady D, Wee SL, Zimmer C. Coronavirus Vaccine Tracker. The New York Times. 4. World Health Organization, Draft landscape of COVID-19 candidate vaccines.

VACCINE TRIVIA

Learn the vax

The MMR (measles, mumps and rubella) vaccine autism controversy was started by a British researcher. The study was severely flawed: false data was just one of the major issues of the report, together with small number of patients and lack of controls. Many other groups tried to repeat the British researcher's experiments, but were unable to do so, making the study irreproducible. The study was subsequently retracted and the British researcher discredited.

Smallpox, a serious and often deadly infectious disease caused by the variola virus, is currently the only disease to be eradicated from the world by a vaccine. Public health efforts are underway to add polio to the list of eradicated diseases. Only few countries have reported wild poliovirus infections over the last few years.

While most vaccines are not given to pregnant women, two exceptions from this rule are represented by the influenza and pertussis vaccines. The influenza vaccine is recommended for pregnant women because they have a higher risk of suffering complications if infected with influenza during pregnancy. They are also advised to receive a dose of Tdap (tetanus, diphtheria and pertussis) vaccine between 27 and 36 weeks, to protect themselves and their newborns from pertussis (whooping cough).

Vaccines can have minor side effects, like any other medication: pain, swelling, or redness where the shot was given, mild fever, feeling tired, headache, or muscle and joint aches being amongst the most common of them. These mild side effects are only temporary and a sign that your body is starting to build immunity (protection) against a disease.

Adjuvants are components in vaccines that allow them to generate protective immunity while allowing for the use of smaller quantities of active ingredients (antigens) and in some cases, fewer doses. Adjuvants can act as antigen carriers, allowing the slow release of antigen in the blood over time, which stimulates the immune system to produce high-titre antibodies and long-lasting immunity.

Stabilisers are used in vaccines to protect the integrity of the active ingredients during manufacture, storage and transport. Gelatin, sugar and polysorbate 80 are some of the most common vaccine stabilisers and can also be found in various foods (polysorbate 80 is added to ice cream to make it smoother).

Did you know that the first vaccine to prevent a known cause of cancer was the Hepatitis B vaccine? Hepatitis B is a viral disease that attacks the liver and is a major cause of liver cancer. Therefore, whe the vaccine was developed, it was the first one to prevent a known cause of cancer. Today, two routinely administered vaccines prevent cancer — the hepatitis B vaccine and the HPV vaccine.

***Source:* The Children's Hospital of Philadelphia Vaccine Education Center - for more information about vaccines: vaccine.chop.edu/trivia.**

The BactiVax consortium

Beneficiaries

UCD Dublin; Consiglio Nazionale delle Ricerche; Istituto di Biostrutture e Bioimmagini; LMU Ludwig Maximilians Universität München; Università degli Studi di Milano Bicocca; Queen's University Belfast; Imperial College London; Eötvös Loránd University; EPFL École Polytechnique Fédérale de Lausanne; CIC bioGUNE Center for Cooperative Research in Biosciences; St George's University of London; Lionex Diagnostics and Therapeutics; ImmunXperts

Partners

CycloLab; nibrt National Institute for Bioprocessing Research and Training; Pfizer; Universidad del País Vasco Euskal Herriko Unibertsitatea; Pepscan shaping peptides to perfection; ULB Université Libre de Bruxelles; Yatlas molecular pharma

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