SIMICA

THERAPEUTIC SITE-SELECTIVE
PROTEIN-MODIFICATION CHEMISTRIES

Newsletter II

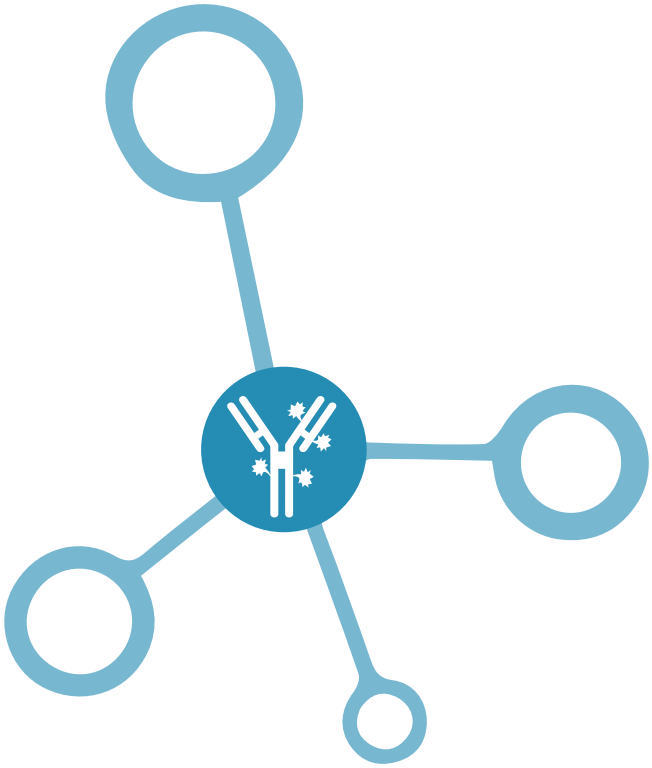
December 2020

SIMICA

THERAPEUTIC SITE-SELECTIVE PROTEIN-MODIFICATION CHEMISTRIES

OVERVIEW OF THE PROJECT

The SIMICA Project intends to place the Instituto de Medicina Molecular João Lobo Antunes within the core of a European network of laboratories that seeks to produce cutting-edge research in the field of site-selective protein modification.



Did you know that:

Novel aqueous chemistries for the selective modification of proteins have been described in recent years and chemical protein modification has become a key instrument in chemical biology (Nat. Rev. Chem. 2019, 3, 147 - 171). It is commonly agreed that these tools will provide major insight into basic biology and enable the development of novel protein conjugates to study their intrinsic properties in cells and in vivo.

Are you interested in studying a protein intercellularly?

At the core of our research, we are engineering reactions for the site-selective modification of proteins and antibodies under mild conditions (pH 7 - 8, 25 - 37 °C) with stoichiometric amounts of reagents. For example: (i) fluorescent probes can be attached to proteins for imaging and tracking; (ii) biotin tags may be installed on proteins to provide key biological insights; and (iii) toxic agents can be bioconjugated to proteins for cancer therapy (Nat. Rev. Chem. 2019, 3, 147). In our consortium we are developing reagents that targets cysteine residues on native proteins and antibodies for bioconjugation of different biophysical tags (**Figure 1**).

PROTEIN MODIFICATION

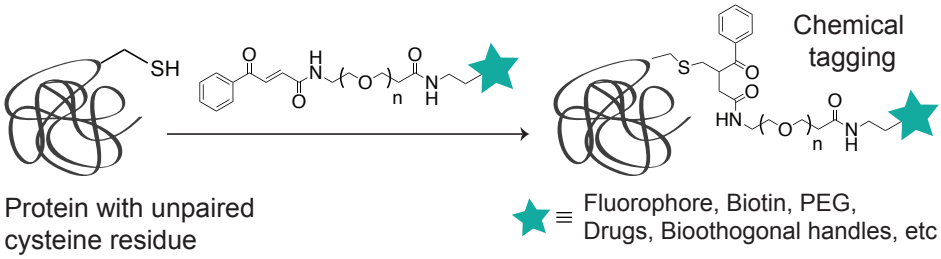


Figure 1: Chemical tagging for protein fluorescent labelling, glycosylation, lipidation, PEGylation, biotinylation, drugability, among others.

Meet the SIMICA

Dr Gonçalo Bernardes leads an interdisciplinary group working at tthe interface between chemistry and biology. It aims at developing novel aqueous, chemoselective methods and to implement their use for selective protein/ligand labelling in vitro and in vivo to understand and influence human disease. Dr Bernardes group has attracted national and internation funding including an ERC starting grant and proof of concept. He has over 130 peer-reviewed publications to/with/on his name.

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If you are interested in additional information please have a look on the following references (Nat. Protoc. 2019, 14, 86; Nat. Commun. 2016, 7, 13128) or simply send us an email.

Quick look

In body antibody making: the Pfizer-BioNTech's vaccine is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a mutant viral spike (S) protein of SARS-CoV-2. The vaccine triggers the body to make a protein that will prompt an immune response, causing the body to produce antibodies against SARS-CoV-2. If you are interested, the clinical studies of the Pfizer-BioNTech COVID-19 vaccine have been just published on The New England Journal of Medicine (N. Engl. J. Med. 2020, 383, 2603).

Behind the success of mRNA vaccines there are many previous breakthroughs. For example, ordinary mRNA produces only low levels of proteins, and the molecule degrades too quickly inside the body to make it suitable as a therapeutic. On the other hand, RNA can trigger an immune response that's independent of the response to the protein it encodes. A few key technological advances discovered by Katalin Karikó and Drew Weissman have contributed to the success of the SARS-CoV-2 vaccines (Nat. Rev. Drug Discov. 2018, 17, 261). In 2005 they reported that the use of synthetic nucleosides could both increase protein production from the mRNA and drastically suppress the immune system's reaction to the mRNA molecules themselves (Immunity 2005, 23, 165). The use of lipid nanoparticles to protect the mRNA molecule and enhance its delivery into cells has been also detrimental for the success of the vaccine (Ther Deliv. 2016, 7, 319).

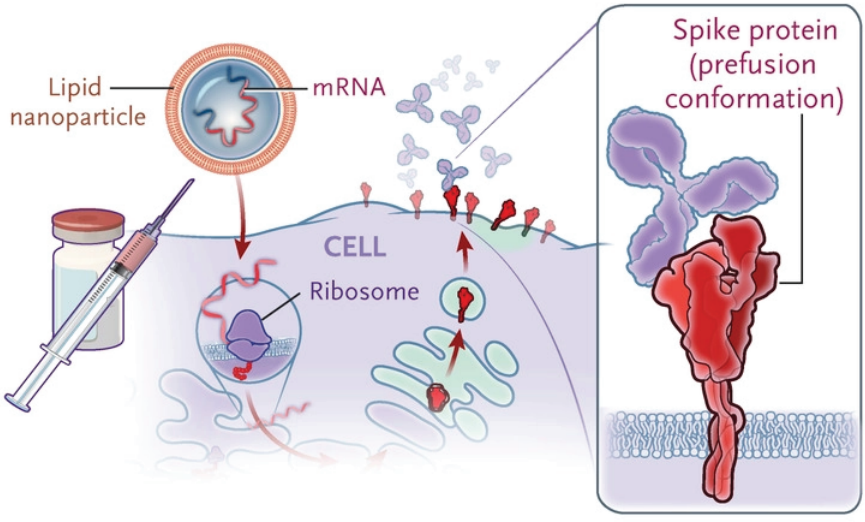

Figure 2: How the Pfizer-BioNTech vaccine works (N. Engl. J. Med. 2020, 383, 2603).

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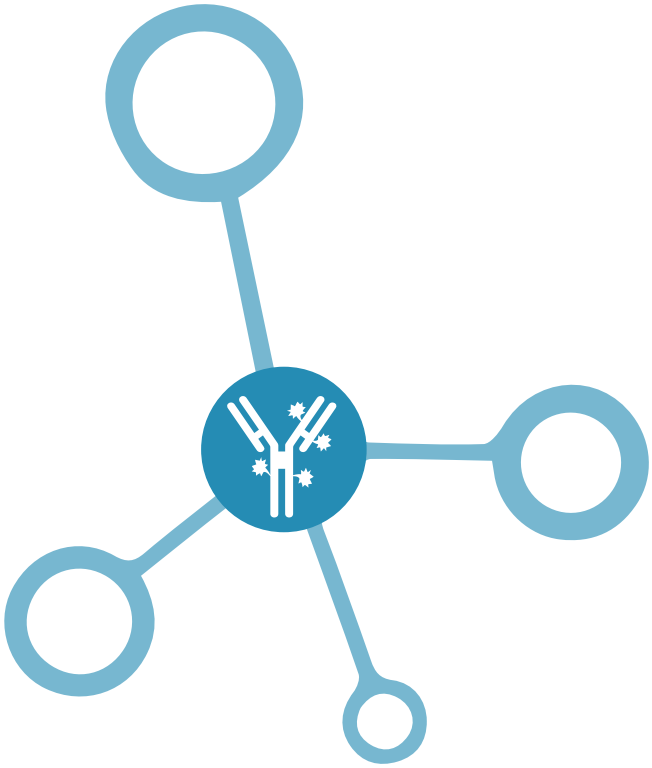

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SIMICA news

On the January we will launch the "Simica Mentorship Programme". This programme is intended to stimulate new intersectorial mentorship activities at IMM by adding the experience of the twinning partners. It is meant for IMM young research staff that work in the field of medicinal chemistry, chemical biology, antibody research and related disciplines. For more information, please contact: anamguerreiro@medicina.ulisboa.pt

We are looking for a partner to organize a workshop about antibody production and purification. If you have any suggestion please contact us.

Our coordinator Bruno Oliveira has been admitted as a Member of the Royal Society of Chemistry. As part of the RSC, new opportunities for collaboration and networking are created to enhance innovation on the field of antibody bioconjugation.

Congratulations to Gonçalo Bernardes for being one of 4 young scientists selected by the ICBS@ChemBioSociety to receive the 2020 Young Chemical Biologist award.

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