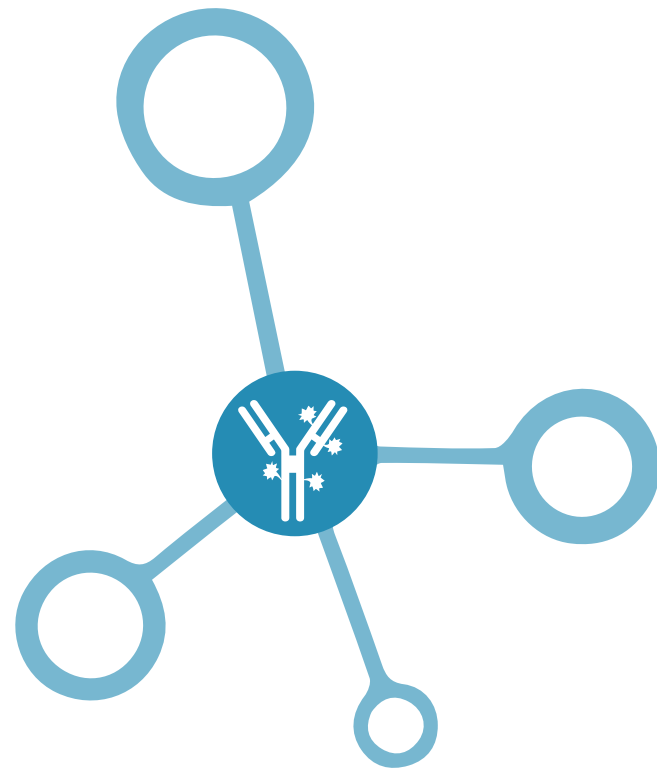


# SIMICA

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.

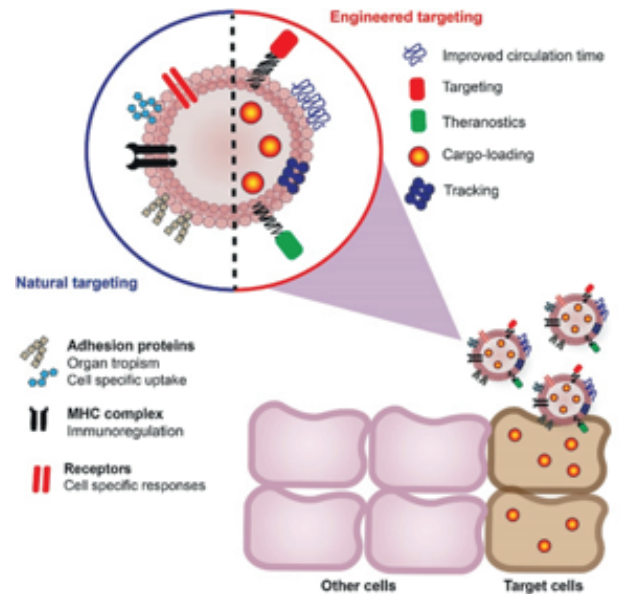


### Did you know that:

Extracellular vesicles (EVs) are small lipid bilayer-delimited particles released by most of our cells and can be obtained from different body fluids such as urine, blood, milk and cerebrospinal fluids. These vesicles have an important role in the intercellular communication and transport of biomolecules, providing a unique source of biological information. Depending on their cellular origin EVs can be provided with specific adhesion proteins, immunoregulatory molecules, genetic material and receptors. This is interesting from a therapeutic point of view as some of these molecules for example,

## BIOLOGICAL FUNCTIONS OF EVs

provide EVs with the capacity to avoid immune system recognition, pass through biological barriers and accumulate in defined sites. Scientists have also discovered that some EVs can also produce cellular specific responses such as modulating the immune system, promoting cell regeneration, cardioprotection and anti-cancer effects.



**Figure 1:** Extracellular vesicles as targeting vectors for biological applications.

## Meet the SIMICA

Dr Alan Chan leads a team of specialists at PERC, who are experts in small animal molecular imaging, probe development and acquisition and analysis of imaging data. The team consists of technicians, statisticians, bioinformatics experts, PhD students and experienced postdocs to mentor and support IMM's scientists. All staff members of PERC will fully support the incoming visiting IMM employees transferring their respective knowledge as part of the staff exchange activities. Furthermore, the SME aspect of the staff exchange will prove invaluable in bringing new skills to all levels of personnel at IMM.

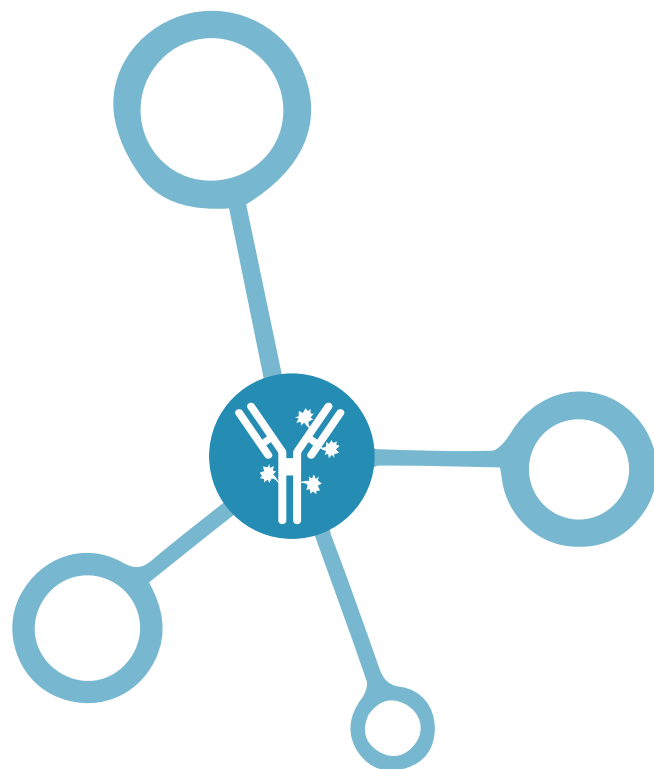


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### Cargo loading into EVs

EVs have a great potential for drug delivery due to their exceptional properties and versatility. In order to utilize EVs as drug carriers, a prerequisite is to find a strategy for efficient cargo loading. Different techniques have been employed for exogenous loading of EVs, including electroporation, simple incubation, sonication, extrusion and freeze-thawing, with variable degrees of success. EVs can also be loaded endogenously, by exploiting the sorting machinery of cells for the production and loading of biomolecules into vesicles. (Adv Drug Deliv Rev 2020;159:332-343)

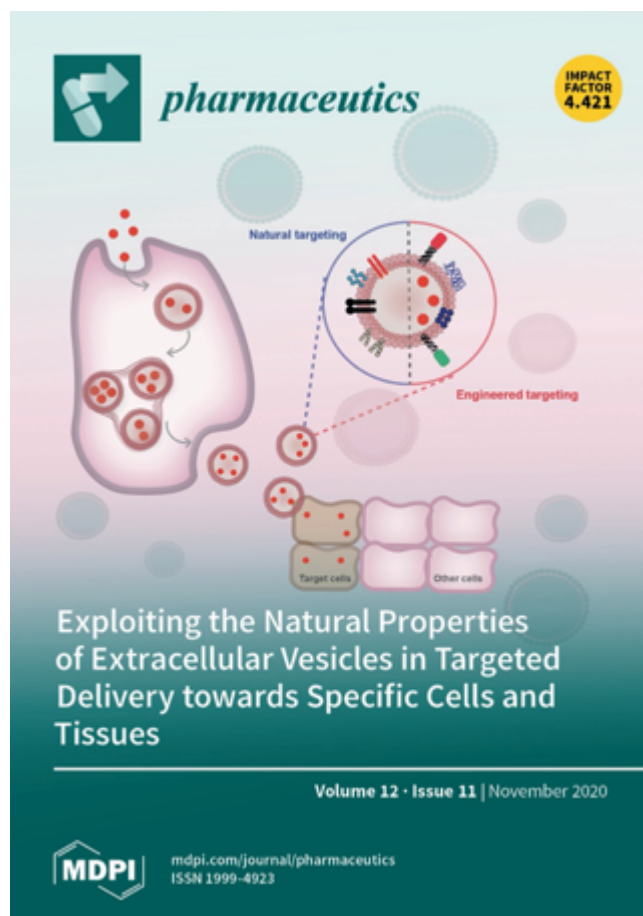
### Surface functionalization strategies of EVs

EVs have innate functionality due to cellular origin. To further add desired functionality to these natural vesicles, different surface functionalization strategies have been explored which apply chemical methods, among others. On these methods the presence of an amine/carboxylic terminated phospholipid or transmembrane protein moiety can be directly functionalized with different functional groups such as EDC/NHS chemistry and thiol-maleimide chemistry. (J Mater Chem B 2020;8(21):4552-4569)

### What can we do with this?

The natural properties of EVs can be combined with multiple therapeutic compounds to increase therapeutic efficacy. In SIMICA we aim to functionalize EVs with antibodies to specifically target cancer cells, as well as allowing the tracking of the EV-complex in the body. This will allow to increase drug selectivity and reduce undesirable secondary effects.

## EVs FOR DRUG DELIVERY



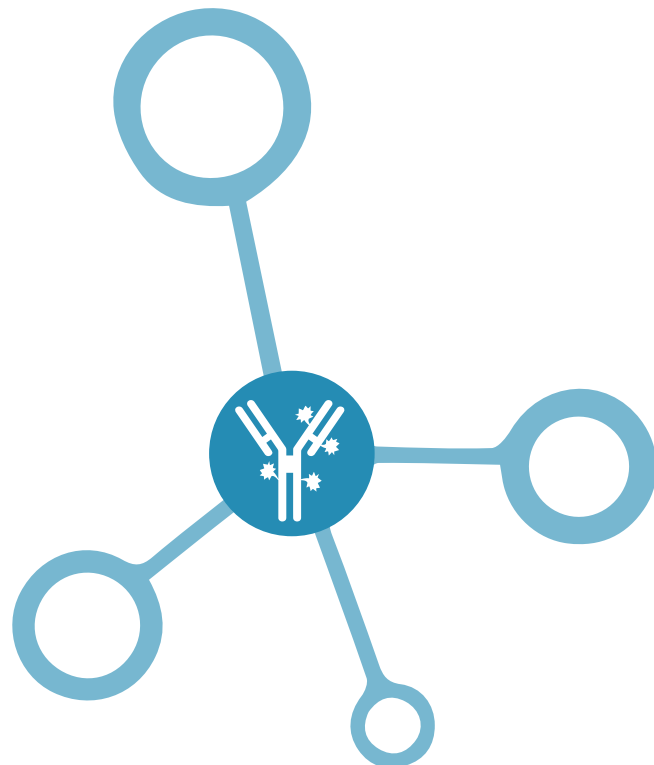
**Figure 2:** Want to learn more about EVs. Please check the SIMICA's publication *Pharmaceutics* 2020;12(11):1022)

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## SIMICA news

On July we will launch the 3rd “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](mailto:anamguerreiro@medicina.ulisboa.pt)

Let’s travel again!! The SIMICA Scholarship to attend international meetings will be

opened on September. Don’t miss the chance to attend an international scientific conference in 2021 and get the registration fee, traveling, accommodation and daily subsistence expenses covered.

Our work is highlighted in a Bioconjugate Chemistry virtual issue on “Bioorthogonal Chemistry and Bioconjugation”. We hope you enjoy the issue, which can be found here, <https://pubs.acs.org/page/bcches/vi/bioorthogonal-chemistry-and-bioconjugation>.

May 26, save the date. The UCAM partner Mar Cabeza-Cabrerizo will be presenting at the oncobiology club

of IMM (her work about “Development of multiparameter medical imaging tools for cancer diagnosis”).

Pablo Lara recently presented his work on extracellular vesicles for drug delivery at IMM. If you missed it you can watch it here (<https://bit.ly/3D9rbPP>).

Don’t miss also the opportunity to watch Michele Vendruscolo’s talk on “Rational Design of Conformation-Specific Antibodies Targeting Protein Aggregates”. Follow the link to access the full lecture online (<https://bit.ly/3B8Hfk9>).

## Follow us

- <https://simica.imm.medicina.ulisboa.pt/#home>
- [https://twitter.com/SIMICA\\_IMM](https://twitter.com/SIMICA_IMM)
- <https://www.linkedin.com/in/simica-twinning-project-at-imm/>

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