

SIMICA

THERAPEUTIC SITE-SELECTIVE
PROTEIN-MODIFICATION CHEMISTRIES



Newsletter VII

April 2022

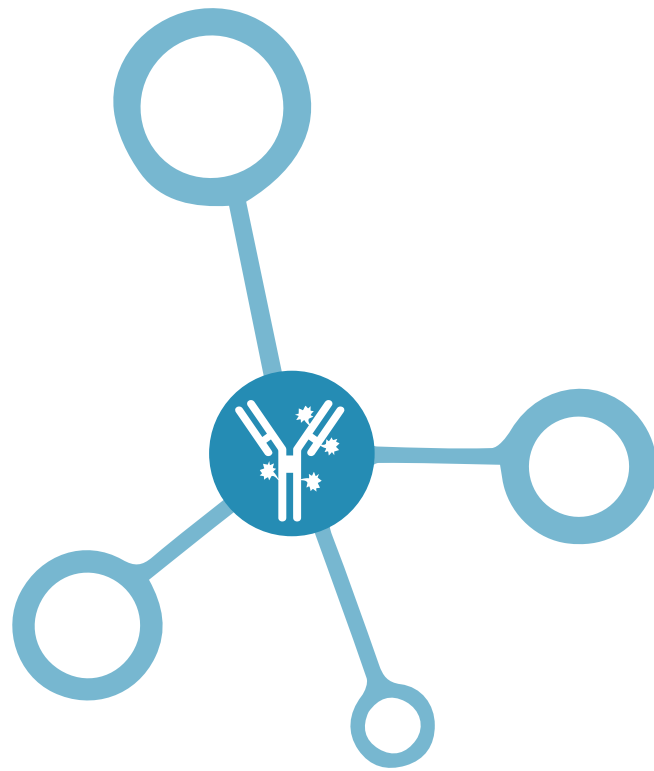


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PROTEIN-MODIFICATION CHEMISTRIES

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:

In computational biology, de novo protein structure prediction refers to an algorithmic process by which protein tertiary structure is predicted from its amino acid primary sequence.

Neoleukin's de novo proteins to improve biologics

With a platform to design proteins from scratch, Neoleukin is making a new class of biologics that resemble their endogenous protein counterparts in structure, but not in sequence.

IL-2's effects are mediated by interactions with a receptor that has three parts: alpha (CD-25), beta (CD122), and gamma (CD132). The toxicity of IL-2 is exacerbated by its interaction with CD25. For decades, protein engineers have been searching for ways to limit IL-2's interaction with CD25.

The concept behind the platform is that if a structure can be replicated de novo, it is possible to get the same function that the natural protein has but with a different sequence.

Using this platform Neoleukin

developed the first computationally-designed de novo protein targeting IL-2 that enter clinical studies.

IL-2 is a powerful immune-stimulating cytokine. Recombinant IL-2 (aldesleukin) has been used to treat cancer, but its toxicity has greatly limited clinical application.

By applying the innovative Neoleukin platform, the company have succeeded in creating a protein that potently stimulates IL-2 signaling without any binding to CD25.

Meet the SIMICA Collaborators

Daniel is a leader in the fields of protein folding, structure, dynamics, and function and is the primary architect of the Neoleukin Biotech. Prior to joining Neoleukin, he served as a Translational Investigator in the Department of Biochemistry at the University of Washington. In 2013, Daniel received a Pew Latin American postdoctoral fellowship to train with David Baker at the University of Washington, where he developed state-of-the-art de novo protein design algorithms. Daniel Silva has co-authored over 20 published research articles, including three in Science, and two in Nature. He is currently founder and CEO of Monod bio, a pioneer company in the design of de novo protein biosensors.

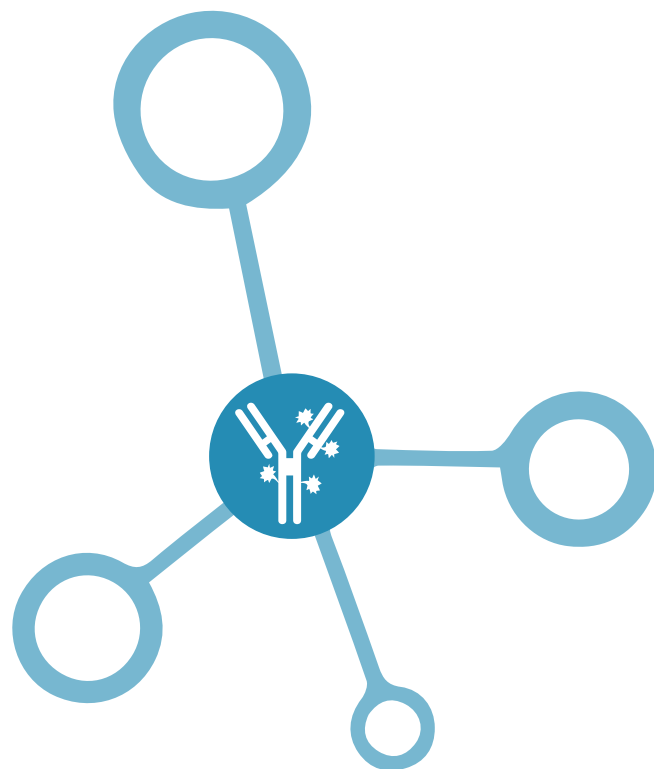


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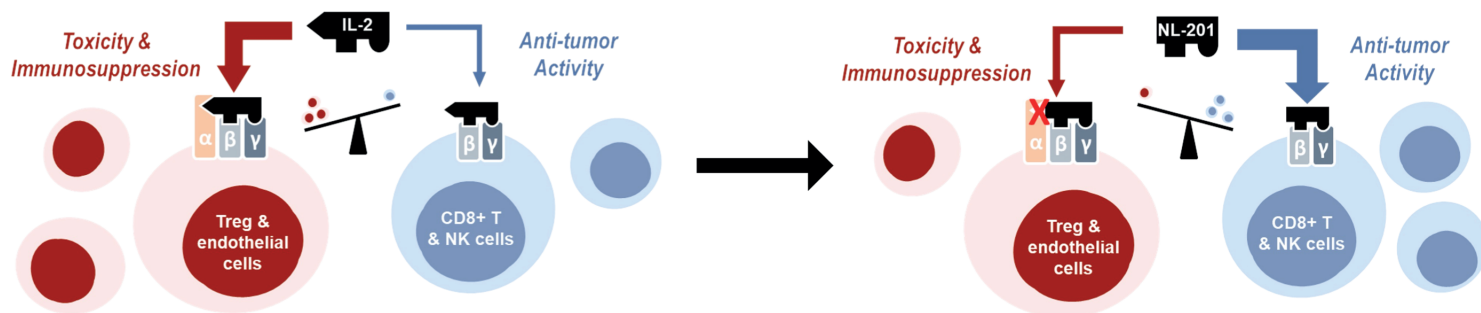
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By applying the innovative Neoleukin Platform, the company have succeeded in creating a protein that potently stimulates IL-2 signaling without any binding to CD25. This protein, NL-201, interacts exclusively with the beta and gamma chains of the IL-2 receptor to selectively expand anti-tumor effector T-cells. NL-201 showed improved therapeutic effect in multiple preclinical models and was until recently being tested in clinical trials. Detailed technical information about this program is available in “De novo design of potent and selective mimics of IL-2 and IL-15” published in Nature (2019). SIMICA is excited to be partnering with Neoleukin to evaluate the efficacy of de novo therapeutic proteins against SARS-CoV-2 using animal models of disease currently implemented at IMM. This research agreement is hopefully the first of many others.



SIMICA news:

- Gonçalo Bernardes was named as finalist of the 2022@BlavatnikAwards for Young Scientists in the UK.
- Our publication describing arylethynyltrifluoroborate dienophiles for chemically triggered IEDDA reactions is now on open access.
- Xurxo García-Otero, a PhD student from the University of Santiago de Compostela doing a internship at IMM with the SIMICA coordinator Bruno Oliveira is being mentored by Luis Cruz from LUMC on nanomaterials.
- Bruno Oliveira hosted the PhD students of the Lisbon BioMed program to talk about the SIMICA project.
- Larissa Dornelles, a MD student from the Faculty of Medicine, started her mentoring program with Bruno Oliveira.
- Results of the 3rd Scholarship to attend international meetings were released.