Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

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Host laboratory:
IBS, https://www.ibs.fr/

Host group/team:
MP: Membrane & Pathogens

Title of the M2 research internship:

Characterization of bacterial recognition by C-type lectin receptors from the antigen presenting cells

Project summary:

C-type Lectin Receptors (CLRs) present on the surface of dendritic cells, in mucosae and epithelia, constitute a class of pathogen recognition receptors (PRRs). They are dedicated to the recognition of carbohydrate-based molecular patterns associated with pathogens and participate in the modulation of the immune response. Gram negative bacteria surface is covered with carbohydrate motif belonging to the Lipopolysaccharide composing the outer membrane. These LPS are known to be amongst the best elicitors of the immune system. They are recognized by PRRs as Toll Like receptor as well as C-type lectin receptor. While recognition by TLR has been well described, the structural information and mechanism of LPS recognition by CLR are scarce. This is partly due to the difficulty to manipulate these LPS molecules that are highly hydrophobic. Moreover, the multivalency generated between cell surface exposed CLRs and the LPS at the bacterial surface is key to ensure tight interactions. To mimic this interaction context and to characterize it, within a collaboration with C. Laguri (IBS), soluble nano-objects resembling the bacterial surface to study CLRs interactions with LPS have been developed. These LPS-nanodiscs, can be generated from different Gram-negative bacteria (notably from the ESKAPE group). Combining these tools to our library of CLR, as well as ours SPR-CLRs oriented-surfaces we are able to characterize the interactions for a given couple CLR/bacterial LPS species. Combining this with structural approaches, we can even provide atomic scale models of the interactions (manuscript on preparation). In this M2, we will apply preliminary development we have initiated in recent years on bacterial recognition, towards DC-SIGN and MGL receptors, to the the study of another lectin receptor of our CLR library, Dectin2 or Mincle.

Keywords:
host-pathogen interaction, lipopolysaccharide, C-type lectin receptors

Relevant publications of the team:

Powerful avidity with a limited valency for virus-attachment blockers on DC SIGN: Combining chelation and statistical rebinding with structural plasticity of the receptor. Vanessa Porkolab, Martin Lepšík, Stefania Ordanini, Alexander St John, Aline Le Roy, Michel Thépaut, Emanuele Paci, Christine Ebel, Anna Bernardi, Franck Fieschi. ACS Central Science (2023). In press. doi.org/10.1021/acscentsci.2c01136.

Immobilization of biantennary N-glycans leads to branch specific epitope recognition by LSECtin. Bertuzzi, Sara; Peccati, Francesca; Serna, Sonia; Notova, Simona; Thépaut, Michel; Jiménez-Osés, Gonzalo; Fieschi, Franck*; Reichardt, Niels-Christian*; Jiménez-Barbero, Jesús*; Ardá, Ana*. ACS Central Science, 2022, Oct 26;8(10):1415-1423. doi.org/10.1021/acscentsci.2c00719.

DC/L-SIGN recognition of spike glycoprotein promotes SARS-CoV-2 trans-infection and can be inhibited by a glycomimetic antagonist. Thépaut M, Luczkowiak J, Vivès C, Labiod N, Bally I, Lasala F, Grimoire Y, Fenel D, Sattin S, Thielens N, Schoehn G, Bernardi A,Delgado R, Fieschi F. Plos Pathogens 2021 May 20;17(5):e1009576. doi: 10.1371/journal.ppat.1009576. (BioRxiv, 10 Aug 2020. DOI: 10.1101/2020.08.09.242917)

Development of C-type lectin-oriented surfaces for high avidity glycoconjugates: towards mimicking multivalent interactions on the cell surface. Porkolab V, Pifferi C, Sutkeviciute I, Ordanini S, Taouai M, Thépaut M, Vivès C, Benazza M, Bernardi A, Renaudet O, Fieschi F. Org Biomol Chem. 2020 Jul 1;18(25):4763-4772. doi: 10.1039/d0ob00781a.

Human Macrophage Galactose-Type Lectin (MGL) Recognizes the Outer Core of Escherichia coli Lipooligosaccharide. Maalej M, Forgione RE, Marchetti R, Bulteau F, Thépaut M, Lanzetta R, Laguri C, Simorre JP, Fieschi F, Molinaro A, Silipo A. Chembiochem. 2019 Jul 15;20(14):1778-1782. doi: 10.1002/cbic.201900087.