Lab: CR$_2$TI

Team: Team 3 iThink

Name and position of the supervisor: Fabienne Haspot, CRCN INSERM, HDR

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Candidate (if internship filled): Eléa Giraudet

Title of the internship: In depth cellular characterization and consequences of CD28H-HHLA2 interaction.

Summary of the internship proposal:

HHLA2, a new B7 family's member, can simultaneously contact its activating receptor CD28H and its inhibitory receptor KIR3DL3. CD28H is mainly expressed by naïve T lymphocytes and most of NK cells. Demonstrating KIR3DL3 protein expression on T and NK cells is challenging due to its poor to no expression on circulating T and NK cells and to difficulties in obtaining reliable antibodies because of homologies between the KIR proteins. We and other have demonstrated that the expression of HHLA2 by target cells is protective since they are less killed by NK cells than their WT counterpart. On the other hand, Zhuang and colleagues have shown an increased killing by NK cells of with other HHLA2+ target cells as compared to their WT counterparts. The nature of the HHLA2+ cells may explain this discrepancy, but it has not yet been addressed experimentally.

We propose here to transduce different cell lines with lentiviral vectors encoding either a WT-HHLA2 or truncated portions of HHLA2. These constructs will allow us to better characterize (#1) CD28H-HHAL2 and KIR3D3L-HHLA2 binding domains, (#2) and to evaluate the consequences on LT and NK cell biology upon target cells interaction.

Using time-laps microscopy, cytometry, and cellular assays, the candidate will analyze the localization of CD28H and KIR3DL3 at the cell-cell contact, the expression and/or the downmodulation of specific molecules, the biological consequences on proliferation (LT) and cytotoxicity (NK cells). This will presumably allow a better understanding of the consequences of CD28H-HHLA2 engagement regarding target cells.

Option(s) linked to the project:

☐ Clinical Research Profile (Recherche Clinique)
☐ Data Analyst Profile (Recherche et Analyse de Données Biologiques)
 X Experimental Biology Profile (Recherche Expérimentale)

Form to be sent by email to : gpi3@univ-nantes.fr