Grenoble Alliance for Integrated Structural & Cell Biology

GRAL MASTER 2 RESEARCH SCHOLARSHIP - Program 2017 - 2018

INTERNSHIP PROPOSAL

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Research project title: Characterization of the interaction between human Adenovirus of serotype 3 interactions and its Desmoglein 2 receptor

5 Keywords to describe the project: Adenovirus – Receptor – Interaction – Structure – Vectorology

Description of the project (aims, experimental techniques, recommended background):
We have identified that desmoglein 2 (DSG-2), a component of desmosomal junction was the attachment receptor for some Human Adenoviruses serotypes (Ad3, Ad7, Ad11 and Ad14) (Wang et al., 2011). DSG-2 carries four cadherin domains in its ectodomain. The goal of the project will be to express the minimal constructs of this receptor known to interact with the virus. The virus/receptor mapping has already been performed by expressing different DSG2 constructs encoding one, two or three cadherin domains in a mammalian expression system. The final goal is now to solve the structure of the adenovirus/DSG2 complex. Up to now, crystallisation is hampered by glycosilations. The goal of the M2 student will be to co-express both the DSG2 minimal domain and the adenovirus fibre in a prokaryotic system that will result in non-glycosylated complex that would diffract properly. Beside this, a set of glycosidases will be tested with the current mammalian expression system in order to get functional non-glycosilated DSG2 minimal domain.

By solving the fibre/receptor interface it would be possible: (i) to understand the mechanism of the first step of the adenovirus infection, (ii) to mutate the adenovirus fibre and thus change the natural tropism of this virus which is used as a therapeutic vector in some cancer indications.

Relevant publications of the team:

1. Desmoglein 2 is a receptor for adenovirus serotypes 3, 7, 11 and 14. Wang H, Li ZY, Liu Y, Persson J, Beyer I, Möller T, Koyuncu D, Drescher MR, Strauss R, Zhang XB, Wahl JK 3rd, Urban N, Drescher C, Hemminki A, Fender P, Lieber A. **Nat Med. 2011; 17(1):96-104**

2. Lu ZZ, Wang H, Zhang Y, Cao H, Li Z, Fender P and Lieber A. Penton-Dodecahedral Particles Trigger Opening of Intercellular Junctions and Facilitate Viral Spread during Adenovirus Serotype 3 Infection of Epithelial Cells. **PLoS Pathog. 2013 ; 9(10):e1003718**

3. Sumarheni S, Hong SS, Josserand V, Coll JL, Boulanger P, Schoehn G, Fender P. Human Full-Length Coagulation Factor X and a GLA Domain-Derived 40-mer Polypeptide Bind to Different Regions of the Adenovirus Serotype 5 Hexon Capsomer. **Hum Gene Ther. 2014 ; 25(4):339-49.**