**Interdisciplinary PhD Project in Plant and Cancer Biology**

## Development of a multi-functionalized, plant-virus-derived nanoparticle that targets cancers and kills tumor cells through restoration of anti-tumor immunity

**Major Aim:** Generate *Tobacco mosaic virus*-based compound coat protein nanoparticles with integrated engineered functions to FIND and KILL tumor cells, to INHIBIT immune suppression by the tumor microenvironment, and to boost immune checkpoint therapy.

With its small size and self-assembly, the coat protein (CP) of Tobacco mosaic virus (TMV) is an ideal nanoparticle carrier for the delivery of small molecules into tissues. We recently generated a CP-based nanoparticle able to target neuropilin-1 and showing biological activity in vitro (Gamper et al., 2019, Cancers).

Now we plan to use a similar strategy to target crucial molecules of the tumor microenvironment that we have recently shown to regulate the immune suppressive properties of tumors (Spenlé et al., accepted in Cancer Immun Res). By assembly of different CP-peptide fusions we plan to generate nanoparticles with multiple functions, namely to find and kill the tumor cells and to repress the immune suppressive properties of the TME. In a first step, single CP-peptide fusions will be generated to find (tenascin-C) the tumor cells. In the next step, CP will be fused with peptides that target chemokine receptors downstream of tenascin-C and restore anti-tumor immune-surveillance. We have recently shown that blocking these chemokine receptors enhanced anti-tumor immune-surveillance, thereby causing reduced tumor growth and reduced metastasis.
High yields of CP-peptide fusion molecules will be produced by molecular farming in plants. The CP-peptide fusion molecules and assembled particles will be tested in immune competent tumor models to determine their impact on tumor growth, metastasis and immune cell infiltration. In addition, we will determine whether immune checkpoint therapy, that usually is effective in only a small percentage of patients, can be boosted by our novel nanoparticles.

This project will be supervised by M. Heinlein (IBMP, Strasbourg) and co-supervised by G. Orend (INSERM U1109, Strasbourg).

Applications are invited **until 10 July 2020** to: manfred.heinlein@ibmp-cnrs.unistra.fr and gertraud-orend@inserm.fr