LABEX IGO – 2024 INTERNAL CALL FOR PROJECTS FOR YOUNG INVESTIGATORS

Evaluating the effect of Virus-Like Particles derived from M13 bacteriophages on tumorassociated macrophages

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Cancers with a poor prognosis, in particular malignant pleural mesothelioma (MPM), represent a major challenge due to limited therapeutic options. MPM, a highly aggressive cancer associated with asbestos exposure, is known for its short median survival compared to other malignancies. Although there is growing hope for immunotherapy in MPM, unfortunately too many patients do not respond to this therapy. The development of new therapies is then necessary. In the field of cancer treatment, there is growing interest in 'nanovectors' to improve the delivery of therapeutic agents, their solubility, their precise targeting of tumors and the reduction of adverse effects. Viral-like particles (VLPs) derived from a variety of viruses, including the filamentous bacteriophage M13, have emerged as promising nanovectors, as they are non-replicating, non-integrating and present a safe profile in clinical trials. These VLPs are also particularly suitable for the delivery of cDNAs encoding therapeutic proteins. The team designed non-replicative VLPs derived from bacteriophage M13 to target MPM cells by fusing an anti-mesothelin nanobody (MSLN). MSLN is a tumor antigen overexpressed in various cancers, including MPM, and targeted in several therapeutic strategies. After successfully creating these VLPs, they confirmed their structure and size by transmission electron microscopy, and demonstrated their ability to target MPM cells expressing MSLN and to deliver a reporter gene encoding luciferase (patent application pending). The viral origin of VLPs could also have a beneficial effect on the immunogenicity of the tumor microenvironment (TEM) by reducing immunosuppression. The aim of this project is therefore to study this property through the impact of VLPs on the phenotype of macrophages, a major component of this TEM involved in immunosuppression.