Ecole Doctorale	Sciences Chimiques et Biologiques pour la Santé
Titre	Un nouveau type d'anticorps bi-spécifiques avec une pénétration tumorale améliorée combinée à une activité de déplétion de facteurs solubles protumoraux du microenvironnement tumoral pour la thérapie du cancer
Titre	A new type of bi-specific antibodies combining improved tumor penetration and pro-tumoral intratumoral soluble factor depletion for cancer treatment
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Mots clés	cancer, immunothérapie, ingénierie des anticorps
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Bispecific antibodies are new promising therapeutic molecules that co-target two antigens. In cancerology, the rational for using them instead of native monospecific antibodies is to increase selectivity and intrinsic toxic effect for tumor cells (i.e anti EGFR/HER2 bispecific antibodies) and/or to enhance target cell immune effector killing (i.e. anti-EpCAM/CD3 bispecific antibodies) [1].
The goal of the thesis project is to design and test a new type of bispecific antibodies combining binding to a internalizing tumor specific receptor and (2) and binding of tumor microenvironment soluble factors implicated in tumor growth (immunosuppressive or inflammatory cytokines, growth factors). We have characterized an antagonistic internalizing anti-tumor antibody that exerts an inhibitory effect on cancer cells in various cancer models .

We anticipate that the simultaneous targeting of a soluble molecule of the tumor micro-environment and this receptor with this specific internalizing antibody wil be highly effective to deplete the tumor environment of the soluble molecule targeted by inducing its intracellular degradation, based on a mechanism similar to the one of soluble antigen "sweeping" antibodies designed against IL6 soluble receptor [2]. may both display high tumor penetration compared to anti-tumor antigen antibodies used in the clinic [2]. Additionnally, due to the properties of these specific antibody and tumor antigen, we expect improved tumor penetration [3]. These hypothesis will be tested in a cancer model, in vitro and in vivo (for more details, marie-alix.poul-pearson@umontpellier.fr).

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