AAP SIRIC 2018
Recherche translationnelle et SHS en oncologie

Identification du Projet	
Titre	Caractérisation et valeur pronostique de la sous-population de lymphocytes T circulants CD8+/PD-1+/TIGIT+ chez les patients porteurs de mélanome traités par anti-PD-1
Axe thématique du SIRIC	Etude de la résistance tumorale et ses paramètres
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Résumé du Projet

The definition of an early marker correlated with the efficacy of anti-PD-1 therapy is a crucial issue for anti-tumor immunotherapy. It is now accepted that anti-PD-1 immunotherapies modify the pre-existing anti-tumor T repertoire. We previously documented that, within an antigen-specific peripheral $CD8^+$ T cell repertoire, the emergence of T cells with high functional avidity, identifiable by the co-expression of PD-1 and TIGIT molecules, was associated with clinical responses in melanoma patients under anti-PD-1 therapy (*Cancer Res 2017*).

Based on these results, we hypothesized that tumor-specific T lymphocytes amplified upon PD-1 blockade could recirculate and be identified in the periphery within this $PD\text{-}1^+/TIGIT^+$ fraction. We already obtained promising preliminary results on 5 melanoma patients undergoing anti-PD-1 treatment, supporting this hypothesis that we now want to confirm on a larger number of patients (treated either with anti-PD-1 in monotherapy (until n=12), or with a treatment combining anti-PD-1 and anti-CTLA-4 (n=5)).

This project thus proposes to deeply characterize this particular subpopulation of circulating $PD1^{pos}/TIGIT^{pos}$ CD8 T lymphocytes, before and at different time-points during the the treatment. We will compare this subpopulation to 3 other CD8 T cell populations from the same blood sample: $PD\text{-}1^{neg}/TIGIT^{neg}$; $PD\text{-}1^{pos}/TIGIT^{neg}$; and $PD\text{-}1^{neg}/TIGIT^{pos}$, in terms of phenotype, T cell repertoire, RNAseq and anti-tumor specificity. These results will be analyzed in light of clinical results, 6 months after the initiation of the therapy.

The aim of this program will be to define an early immune marker, from peripheral blood, associated with clinical efficacy of anti-PD-1 therapy.

Keywords: Immunotherapy, anti-PD-1, melanoma, biomarker, T cells