Development of an anti-TAM antibody for anticancer therapies

J Bordenave (1), M Tosolini (1), F Pont (1), O Zaki (1), S Péricard (1,2), F Lopez (1) P Brousset (1,2) P Rochaix (1,2), C Laurent (1,2), JJ Fournié (1), L Ysebaert (1,2), M Poupot (1)
(1) CRCT U1037, ERL5294 CNRS, Univ Toulouse III, Toulouse, France; (2) IUCT-Oncopole, Toulouse, France.
mary.poupot@inserm.fr; ysebaert.loic@iuct-oncopole.fr

Purpose: Tumor microenvironment (TEM) is highly involved in the tumor development and chemoresistance. Among cellular components of the TEM, tumor associated macrophages (TAM) are modified macrophages educated by the tumor to favour its development. Numerous studies aim to target TAM which are present in most cancers. Being able to eliminate or deactivate these cells is a challenge today in anticancer therapies.

We recently produced a new antibody specifically directed against TAM. We chose the chronic lymphocytic leukaemia (CLL) as model which is a malignant hemopathy with only 50% of complete remission and a deleterious effect of the treatment on the immune system of the patients (Ysebaert 2010). The resistance of the residual disease is due to the intrinsic properties of cancer cells but also to their close contact in lymph nodes with nurse like cells (NLC). We defined these cells as CLL’s TAM, infiltrating the lymph nodes and associated with the aggressiveness of the disease in a contact dependant manner (Ysebaert 2011, Boissard 2016a and 2016b). Target these cells would be a new therapeutic insight in cancer.

Experimental Design and results: NLC are easily produced in vitro by the culture of PBMC from CLL patients by the differentiation of monocytes in contact with CLL cells. After a mouse immunization with these NLC, we selected one antibody specifically targeting NLC (patent Inserm). This antibody called 6-25 don’t bind leukemic cells or healthy B and T lymphocytes and monocytes. Moreover, this antibody can target different TAM from different tumors revealed by immunohistochemistry and immunofluorescence. We found by immunoprecipitation and mass spectrometry analysis its molecular target which was checked by western blot analysis with the corresponding recombinant protein.

Conclusion: The anti-CD115 antibody is today the only one anti-TAM antibody used in clinical trials. The advantage of our anti-TAM antibody is the specificity of targeting. Indeed, the CD115 receptor being expressed on TAM but also on monocytes, M2 macrophages and on microglia, could have negative effects on inflammatory processes, bone turnover and on immune responses in central nervous system. Here, we developed an antibody specifically directed against TAM with a promising future in anticancer therapies.

References: