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Contribution of galectin-9 to tumor immune escape: Investigations on a pre-clinical model and characterization of neutralizing antibodies

Pierre Busson

CNRS, Gustave Roussy, France

Extra-cellular *galectin-9* (*gal-9*) is suspected to be a major immunosuppressive factor in several types of human malignancies, including melanomas, renal, pancreatic and lung carcinomas. There are clues about its contribution to secondary resistance to immune checkpoint inhibitors. It is produced either by malignant or stromal cells. The mechanisms of *gal-9* immune suppression are diverse and not fully understood. There is a need for an *in vivo*, integrated experimental approach. Our general aim is to build a syngeneic murine tumor model in order to investigate which factors regulate *gal-9* production from tumor and stromal cells and what is its impact on various target cells (T-effs, T-regs, TAMs, and MDSCs). We have found that it is possible to address these questions in the CT26 tumor model using, among other tools, CT26 clones KO for *gal-9* and neutralizing antibodies. Invalidation of *gal-9* by gene editing results in a mild decrease of CT26 tumor growth in nude mice and its dramatic reduction in syngeneic Balb-C mice. The modifications of the lymphoid and myeloid infiltrate resulting from *gal-9* suppression are currently under investigation. Control knock-in clones are in preparation. In parallel, we have shown that in some experimental conditions systemic administration of anti-*gal-9* antibodies has an impact on CT26 tumor growth. Current investigations aim to maximize these effects and to investigate the underlying modifications occurring in the tumor microenvironment. On a longer term, the aim is to assess the therapeutic potential of these antibodies for immune restoration, in human malignancies.

Biography

Pierre Busson, after being trained as MD and PhD in Paris, did his Post-doctorate at the University of North Carolina (Chapel Hill, USA). He was recruited by the CNRS (French National Center for Scientific Research) and established his group at Gustave Roussy (Villejuif, France). He has published over 95 articles in peer-reviewed scientific journals. He is academic Editor for *Plos One*.

Pierre.BUSSON@gustaveroussy.fr

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