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Tumor associated Tie2^{+} macrophages: Novel targets and effectors of anti-breast cancer therapies

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While advances in treatment and screening have greatly improved outcomes for most breast cancer patients, major unmet needs remain for treatment of patients with metastatic disease. Breast cancer has not benefitted to the same extent as other cancers from the recent introduction of immunotherapies due to poor inherent immunogenicity of breast tumors associated with a highly immunosuppressive microenvironment. New strategies are needed to overcome these limitations. We identified and characterized a subpopulation of pro-tumoral macrophages: The Tie2-expressing monocytes/macrophages (TEMs) endowed with pro-angiogenic and immunosuppressive activities, both involving signaling through the ANG2/TIE2 pathway. Indeed we demonstrated that blocking the ANG2/TIE2 pathway disables the pro-angiogenic activity of TEMs resulting in inhibition of tumor angiogenesis, growth and metastasis in mouse models of breast carcinogenesis. We are now investigating whether the *in vivo* blockade of ANG2 is not only inhibiting the pro-angiogenic activity of TEMs, but also reverting their immunosuppressive activity, thus providing a strong rational for the development and testing of new combination therapies. Moreover, by exploiting the tumor homing ability of TEMs we turned them into an efficient vehicle for the tumor-targeted delivery of a potent immune-stimulatory molecule: Interferon-alpha (IFNα). We think that the multiple activities of type I IFNs in the complex network of cell interactions that lead to activation and deployment of immune responses may represent a valid strategy to promote and improve the outcome of cancer immunotherapy for the treatment of advanced breast cancer including lung and bone metastasis.

Biography

Roberta Mazzieri has obtained her PhD in Genetic Science from the University of Pavia, Italy and subsequently undertook one Post-doctoral position at the New York University, USA and two at the San Raffaele Scientific Institute in Milan, Italy. In 2012, she was nominated by the Young Ambassadors from the Metastasis Research Society (MRS) to speak at MRS meeting in recognition of her potential to launch independent research and contribute to high-quality publications. The same year she was recruited by the University of Queensland, Brisbane to establish her own research group to continue her work on targeting pro-tumoral macrophages.

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