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Bispecific antibodies in breast cancer immunotherapy

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Over the past 15 years, mounting evidence of the key contribution of NK cells in immunity against cancer has boosted the investigations into NK cell-based therapies. Among these strategies, antibody-based therapeutics is currently the fastest growing segment of the drug and biological market. However, tumor-targeting antibodies often have to face up an exhausted tumor environment responsible for their suboptimal effectiveness. Our objective is to manipulate NK cell functions and tumor targets using an original format of nanobody-based bispecific antibodies (bsFab) to revert the dampened immune response for treating breast cancer. Treatment and outcomes of HER2-amplified breast cancers have been revolutionized by the approval of trastuzumab. However, significant proportions of HER2 positive breast cancer are or become resistant due to de novo or acquired resistances. As well, triple negative breast cancers (TNBC) are intrinsically insensitive to most of the current targeted therapies such as hormonotherapy or trastuzumab. These cancers of poor prognosis remain a clinical challenge despite therapeutic innovations. We generate bispecific formats that display a unique, specific and high affinity for FcγRIII on NK cells and a moderate affinity for two tumor associated antigens: HER2 and mesothelin overexpressed in a large proportion of TNBC. NK antitumor effects driven by trastuzumab and bsFabs, alone or in combination, were investigated on different 2D and 3D breast cancer models. Our data underline the potential of these bsFabs to enlarge the number of patients eligible for breast cancer immunotherapy and prompt to consider combination strategies.

Biography

Joanie Del Bano is a Pharmacist Resident and also pursuing PhD in Immuno-Oncology at the University of Aix-Marseille in the team "Therapeutic Antibodies and Immuno-targeting" led by Drs Daniel Baty and Patrick Chames. She is pursuing Pharmacy Residency Program at Marseille Public University Hospital. She is working on the development of bispecific antibodies for breast cancer immunotherapy.

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