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Phenotypic Models of CAR T-Cell Activation Elucidate the Pivotal Regulatory Role of CAR Downmodulation

Raanan Greenman, Yoav Pizem, Maya Haus-Cohen, Guy Horev, Galit Denkberg, Shai Shen-Orr, Jacob Rubinstein, and Yoram Reiter

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About the Cover

In this month’s cover, Dwivedi and colleagues demonstrate the binding of a single chain variable fragment (scFv) of the humanized anti-CD19 CAR with CD19 target antigen, obtained through molecular modelling. The unique composition of amino acid residues of the framework region as well as the complementary determining regions (CDRs) of the scFv resulted into the scFv interaction to the CD19 antigen with high binding affinity and with high structural flexibility. Further preclinical and ex vivo studies confirmed that the distinct structural modification in CAR design confers the novel humanized anti-CD19 CAR with a favorable balance of efficacy to toxicity. Read the article on page 846.