

# 9<sup>TH</sup> EUROPEAN IMMUNOLOGY CONFERENCE ASSOCIATED WITH ANTIBODY ENGINEERING MEETING

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## Developing the next generation of antibody-like therapeutic proteins with immune functions for cancer

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Despite substantial clinical progress with targeted therapies, current antibody-based approaches have limited efficacy at controlling HER2/neu-positive breast cancers, especially in the absence of chemotherapies. Previously we showed that the combination of IFN- $\gamma$  and anti-HER2/neu antibody synergistically reduces tumor growth in an *in vivo* implanted mammary tumor model. Here, we report a recombinant approach to produce an HER2 AbZED-IFN- $\gamma$  fusion protein, which contains anti-HER2 scFv, an engineered effector domain (EED) scaffold, and IFN- $\gamma$ , as a novel way to treat HER2+ tumors. HER2 AbZED-IFN- $\gamma$  induces *in vitro* apoptosis in an IFN- $\gamma$  receptor dependent manner. In the *in vivo* xenografted tumor model, HER2 AbZED-IFN- $\gamma$  at a very low dose demonstrates superior activity over the anti-HER2/neu antibody on the growth of HER2+ tumors. In the CT26-HER2 tumor model, which is resistant to anti-HER2 antibody trastuzumab, HER2 AbZED-IFN- $\gamma$  remains to show activity to inhibit tumor growth. Examination of tumor infiltrated macrophages and lymphocytes reveals that the fusion protein can induce changes in tumor microenvironment to support immune reactivity against tumors. Furthermore, we have humanized the EED domain to minimize immunogenicity of the therapeutic protein. Our studies have defined a targeted immunotherapy approach for the treatment of cancers.

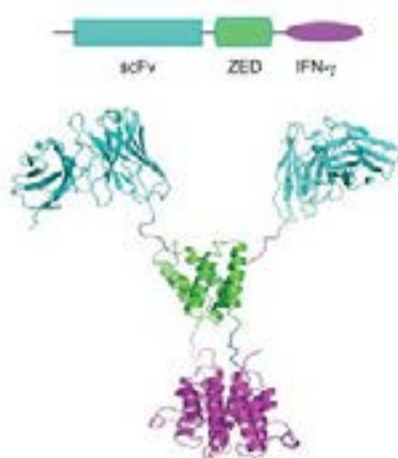


Figure 1. Diagram of the HER2 AbZED-IFN $\gamma$  construct.

### Biography

Hongtao Zhang is a Research Associate Professor in the Department of Pathology and Laboratory Medicine at the University of Pennsylvania, Perelman School of Medicine. Currently his research focus is in the receptor- targeted therapies using antibodies, antibody-like proteins, and small molecules. The research projects in his lab are relevant to understand the functions of cytokines in the regulation of immune cells in tumor microenvironments, including the polarization of tumor associated macrophages. He is also devoted to the identification of serum biomarkers that can help the diagnosis and therapeutic guidance for breast cancer and melanoma. He has published more than 70 articles in journals including Nature Medicine and Nature Biotechnology. He is listed as inventors in 17 approved patents and some other pending patents. He serves as an Editorial Board Member for several journals.

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