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Single doman antibodies against immune checkpoint targets PD-1 and PD-L1

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Several monoclonal antibodies (mAbs) against immune checkpoint targets have been approved by the FDA for diagnostic or therapeutic applications in advanced cancer. An increasing number of mAbs has been developed against PD-1, PD-L1, CTLA-4, and other immune checkpoint proteins. Here we report a new type of mAb, single domain antibodies (sdAbs) derived from llama, against PD-1 and PD-L1. Immunization of llama with recombinant PD-1 or PD-L1 ectodomain generated a strong humoral immune response. Phage display libraries were constructed from PBMCs of immunized animals and screened against the immunogens after a single round panning. Genes encoding antigen specific sdAbs were isolated and sequence analyses indicated they belong to several families. The isolated sdAbs bound to PD-1 or PD-L1 at low nanomolar affinity in ELISA. sdAbs also bound to PD-L1 transfected cells as detected by flow cytometry and immunocytochemistry. None of the sdAbs bound denatured proteins in Western blot, in contrast to murine mAbs against the same target. We also analyzed binding epitopes using a peptide ELISA scan. These results indicated that the sdAbs prefer conformational epitopes. In summary, with the unique features of sdAbs including their small size (~15 kDa), stability under extreme conditions, enhanced tissues penetration, and accessibility to the epitopes that conventional antibodies can't bind, these high affinity sdAbs may have unique applications for research, diagnosis and therapy.

Biography

Yu Geng has completed his MD. from The Fourth Military Medical University in China and postdoctoral studies from University California San Diego and The Scripps Research Institute. He is the Founder, CEO and CSO of ProSci Incorporated, an antibody-focused private company. He has published more than 30 papers in reputed journals and has been receiving multiple SBIR awards for HIV vaccine research and development as well as cancer biomarker discovery.

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