David Cole

Title: Antigen-targeted soluble bispecific T cell receptor (ImmTAC®) molecules in immunotherapy

Abstract: Immunotherapies that activate patient's T cells to attack cancer cells have a potential to eradicate tumours. Although therapies using monoclonal antibodies have been proven effective, they are limited to targeting cell surface proteins. This limitation is overcome by T cell receptor (TCR) based approaches, as TCRs recognize a broad range of peptides presented in the context of human leukocyte antigens (HLAs). At Immunocore, we have developed Immune mobilizing monoclonal TCRs Against Cancer (ImmTAC® molecule) a new class of soluble bi-specific biologics comprising an affinity-enhanced TCR fused to an anti-CD3 effector domain. ImmTAC molecules recognize a specific target peptide presented by HLA on tumour cells and redirect the patient's T cells to carry out potent tumour cell killing. Development of ImmTAC® molecules is a multi-step process where safety and specificity are the key considerations. Key is affinity maturation of the TCR through mutagenesis of CDR loops. The highest-affinity mutants are further screened for specificity and cross-reactivity using a range of cellular assays. This process has been successfully applied to produce ImmTAC® molecules for a number of targets, including from pathogens and autoimmune conditions, demonstrating the robustness of the platform. As an example, IMCgp100, an ImmTAC® molecule recognizing melanoma associated protein gp100, is currently undergoing clinical trials in patients suffering from advanced malignant melanoma.

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