Background: OX40 is a costimulatory TNFR-superfamily receptor expressed almost exclusively on activated T lymphocytes and not on naïve or resting memory cells. OX40 signaling can enhance proliferation, survival and effector functions of T cells with a more pronounced effect on late, chronic and memory responses. Many studies have indicated that OX40 may play a central role in various T-cell mediated pathological immune responses, thus implying a therapeutic potential for antagonistic antibodies targeting OX40. However to date no antagonistic antibodies targeting OX40 have been published.

Conclusion: Generation of OX40 targeting mAbs devoid of agonism is difficult but possible. GBR 830 suppressed acute xenogeneic reactions in a GvHD model. Targeting OX40 suppressed memory-T cell reactivation, more efficiently than targeting CD28. Finally GBR 830 displayed a potent therapeutic anti-psoriatic activity. These results highlight the therapeutic potential of targeting OX40 in T cell-mediated inflammatory and autoimmune diseases and warrant further clinical studies with GBR 830.