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**A PROMISING CANCER IMMUNOTHERAPY TARGET:
NOVEL FULLY HUMAN AGONIST ANTIBODIES AGAINST
THE HUMAN T-CELL COSTIMULATORY RECEPTOR CD27**

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Background CD27 is a member of the TNF receptor superfamily and plays a critical role in T-cell activation by providing a costimulatory signal. CD27 signaling enhances T-cell proliferation, activation and differentiation of effector and memory T cells and therefore promotes cytotoxic T cell (CTL)-based anti-tumor immunity.¹ Agonistic stimulation of CD27 is a promising cancer immunotherapy approach to boost specific T cell driven anti-tumor responses.

Methods In this study, we generated a series of 147 fully human monoclonal anti-CD27 antibodies and tested their agonist properties to stimulate T cell activation.

Results Using a NF- κ B reporter Jurkat cell line, we evaluated in vitro the ability of anti-CD27 antibodies to induce CD27 receptor activation. With this assay, five antibodies have been selected for their agonist properties. When combined with suboptimal T cell receptor (TCR) stimulation, agonist antibodies induced CD27 receptor activation with an EC50 of 1–5 μ g/mL. We also used human peripheral blood T cells to characterize the CD27-mediated costimulatory effects of agonist antibodies in combination with TCR stimulation. Our anti-CD27 monoclonal antibodies boosted T cell proliferation and induced IL-2 and TNF α secretion only in a presence of TCR engagement. Moreover, CD27 agonists induce strong T cell proliferation in a Mixed Lymphocyte Reaction. CD27 antibodies were shown to bind human and cynomolgus monkey CD27 with a KD value of 5–20 nM as determined by BioLayer Interferometry, but do not bind to mouse CD27. In vivo experiments are currently ongoing to demonstrate the efficient anti-tumor activity of the selected CD27 agonist antibodies in different mice tumor models.

Conclusions In conclusion, we have developed and successfully selected efficient fully human immuno-stimulatory agonist CD27 mAbs as a promising cancer immunotherapy.

REFERENCE

1. Hendriks J, Xiao Y, Borst J. CD27 promotes survival of activated T cells and complements CD28 in generation and establishment of the effector T cell pool. *J Exp Med* 2003; **Volume 198**, Number 9:1369–1380.

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