CD27 is a member of TNFR superfamily. It is constitutively expressed on the majority of T cells and a subset of NK cells, playing key roles in T cell activation and survival and in NK cell proliferation and cytokine production in response to ligand CD70. Some antibodies to mouse CD27 have been reported that display agonistic and anti-tumor activities while other mAbs had less anti-tumor activity and were depotent. We hypothesized that differences in these antibodies may be due to Fc receptor engagement, as has recently been shown for the agonistic and anti-tumor activities of agonistic CD40 mAbs, which is also member of TNFR superfamily. We have determined the CD27 transgenic mouse model (K2D7-Tg) to explore the therapeutic potential of targeting CD27. In this study, we examined the effect of modifying the constant region of the Fc mAbs on its ability to enhance antigen-specific T cell responses. With the original 1F5 hG1 as template, a panel of 1F5 variants was made including 1F5 mG1, 1F5 mG2a, 1F5-CD27 transgenic mouse model (hCD27-Tg) to explore the therapeutic potential of targeting CD27. In vivo CD27 stimulation with its ligand (CD70) promotes strong CD27 activation well-regulated by CD70; ligand is generally only transiently expressed by Thymoma cells and imply that engagement of the inhibitory FcγRIIb binding by Biacore analysis. The effect of recombinant 1F5 mAb and Fc mutants on anti-tumor activity in huCD27 transgenic mice is currently being investigated. The 1F5-CD27 Tg mice were fully backcrossed to C57B16/Hu. Binding to CD27-expressing human CCRF-CEM cells

CD27 Background

- Member of the tumor necrosis factor (TNF) receptor superfamily
- Constitutively expressed on the majority of mature T cells, memory B cells, and a portion of natural killer (NK) cells
- CD27/CD70 Co-stimulatory Pathway
  - CD27 activation well-regulated by CD70; ligand is generally only transiently expressed on activated T cells, B cells, and dendritic cells
  - On T cells: causes activation, proliferation, survival, and maturation of effector capacity and memory
  - On B cells: activates and promotes the generation of plasma cells, proliferation, and the production of immunoglobulin
  - On NK cells: induces cytolytic activity
- In vivo CD27 stimulation with its ligand (CD70) promotes strong primary and secondary CD8 T cell responses and expression of CD70 on dendritic cells improves immunity of dendritic cell vaccines (Rowley TF and Ali-Shamkhani A. J Immunol. 2004; Kaller AM et al. Immunology 2008)
- Agonist anti-CD27 mAbs can induce potent anti-tumor immunity through T cell activation (Freisch, RR et al. Blood 2007; Sakashita, T. et al. BBRC 2010; Roberts, DJ et al. J Immunotherapy 2010)

Abstract

CD27 mAb and Fc mutants

1F5 human anti-CD27 mAb
- Generated from human Ig-expressing mice
- High specificity and efficacy for human and mouse CD27
- Agonist activity of T cell activation and proliferation in vitro when combined with TCR stimulation

1F5-CD27 transgenic mouse model (K2D7-Tg) to explore the therapeutic potential of targeting CD27. In this study, we examined the effect of modifying the constant region of the Fc mAbs on its ability to enhance antigen-specific T cell responses. With the original 1F5 hG1 as template, a panel of 1F5 variants was made including 1F5 mG1, 1F5 mG2a, 1F5-CD27 transgenic mouse model (hCD27-Tg) to explore the therapeutic potential of targeting CD27. In vivo CD27 stimulation with its ligand (CD70) promotes strong CD27 activation well-regulated by CD70; ligand is generally only transiently expressed by Thymoma cells and imply that engagement of the inhibitory FcγRIIb binding by Biacore analysis. The effect of recombinant 1F5 mAb and Fc mutants on anti-tumor activity in huCD27 transgenic mice is currently being investigated. The 1F5-CD27 Tg mice were fully backcrossed to C57B16/Hu. Binding to CD27-expressing human CCRF-CEM cells

CD27 Background

- Member of the tumor necrosis factor (TNF) receptor superfamily
- Constitutively expressed on the majority of mature T cells, memory B cells, and a portion of natural killer (NK) cells
- CD27/CD70 Co-stimulatory Pathway
  - CD27 activation well-regulated by CD70; ligand is generally only transiently expressed on activated T cells, B cells, and dendritic cells
  - On T cells: causes activation, proliferation, survival, and maturation of effector capacity and memory
  - On B cells: activates and promotes the generation of plasma cells, proliferation, and the production of immunoglobulin
  - On NK cells: induces cytolytic activity
- In vivo CD27 stimulation with its ligand (CD70) promotes strong primary and secondary CD8 T cell responses and expression of CD70 on dendritic cells improves immunity of dendritic cell vaccines (Rowley TF and Ali-Shamkhani A. J Immunol. 2004; Kaller AM et al. Immunology 2008)
- Agonist anti-CD27 mAbs can induce potent anti-tumor immunity through T cell activation (Freisch, RR et al. Blood 2007; Sakashita, T. et al. BBRC 2010; Roberts, DJ et al. J Immunotherapy 2010)