Claims

1. Agonistic monoclonal antibody, or an antigen-binding fragment thereof, that specifically binds to the human CD40 receptor and is capable of inducing CD40 signaling independent of Fcγ mediated CD40 receptor crosslinking, wherein the antibody comprises
   a) a VH region comprising a CDRH1 region of SEQ ID NO: 29, a CDR2H region of SEQ ID NO: 43 and a CDR3H region of SEQ ID NO: 57, and
   b) a VL region comprising a CDR1L region of SEQ ID NO: 71, a CDR2L region of SEQ ID NO: 85 and a CDR3L region of SEQ ID NO: 99.

2. Antibody according to claim 1, wherein the antibody is a humanized IgG1LALA antibody comprising at least amino acid substitutions at L234A and L235A of the human IgG1 Fc region.

3. Antibody according to claim 1, wherein the antibody comprises at least amino acid substitutions at S228P and L235E of the human IgG4 Fc region.

4. Antibody according to any of the preceding claims, wherein the antibody binds to an epitope that is overlapping with the CD40L binding site.

5. Antibody according to any of the preceding claims, wherein the antibody activates human antigen-presenting cells (APCs).

6. Antibody according to any of the preceding claims, wherein the antibody activates cells selected from the group comprising dendritic cells (DCs), B-cells, monocytes, and myeloid cells.

7. Antibody according to any of the preceding claims, wherein said antibody has an indirect immune cell-mediated cytotoxic effect on tumor cells.

~~8. Antibody according to any of the preceding claims, which has at least one of the further characteristics~~

~~(a) no binding to the Fcγ Receptor;~~
~~(b) having a CD40 cell binding affinity with a EC50 value of equal or less than 49,5 ng/ml;~~
~~(c) having KD values of equal or less than 15,7 nM;~~

~~(d) being cross reactive to cynomolgus monkey CD40 with a KD value equal or less than 10,3 nM;~~

~~(e) inhibiting CD40L by binding to CD40;~~

~~(f) prevent synergistic and additive effects of CD40L-mediated functions;~~

~~(g) inducing maturation of antigen presenting cells as determined by IL12p70 release with an EC50 value of equal or less than 208 ng/ml~~

~~and/or as determined by the induction of CD86 on dendritic cells by at least 7,5-fold and with an EC50 of equal or less than 148 ng/ml; and/or~~

~~(h) reducing the level of CD40 on the cell surface by less than 50%.~~

~~9.~~8. Antibody or antigen-binding fragment according to any of the previous claims, wherein the antibody comprises a heavy chain variable (VH) region is at least 85 % identical to a VH region of SEQ ID NO: 1.

~~10.~~9. Antibody according to any of the previous claims, wherein the antibody comprises a light chain variable (VL) region that is at least 85 % identical to a VL of SEQ ID NO: 15.

~~11.~~10. Antibody according to any of the previous claims for use in the treatment of patients suffering from cancer.

~~12.~~11. Use of the antibody according to any one of claims 1-~~10~~ 9 in the manufacture of a medicament for treating cancer.

~~13.~~12. The use according to claim ~~12~~11, wherein the cancer is a solid tumor.

~~14.~~13. The use according to claim ~~12~~11, wherein the cancer is selected from the group comprising pancreas cancer, advanced pancreatic carcinoma lung cancer, non-small cell lung (NSCL) cancer, bronchioloalviolar cell lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, gastric cancer, colon cancer, breast cancer, kidney cancer, Hodgkin's lymphoma, liver cancer, Gall bladder cancer, bladder cancer, prostate cancer, Thyroid cancer, salivary gland cancer, or uterine cancer.

~~15.~~14. The use according to any of claims ~~12~~ 11 to ~~14~~13, wherein the antibody is to be used in combination with cytotoxic or cytostatic agents, radiotherapy, targeted therapy, immunotherapy or surgery.

~~16.~~15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the antibody according to any of claims 1-~~10~~9.