

CLAIMS

1. A combination comprising:
 - one or more mRNA molecules encoding all of the functional immunostimulatory proteins CD40L, CD70 and caTLR4 (constitutive active TLR4);
 - one or more mRNA molecules encoding a target-specific antigen; and
 - a PD-1 pathway inhibitor selected from the list comprising: a nanobody directed against PD-1, an antagonistic antibody directed against PD-1; a nanobody directed against PDL1, an antagonistic antibody directed against PDL1;~~or a derivative thereof~~; and
 wherein said one or more mRNA molecules are protected mRNA molecules which are in the form of an intravenous formulation.
2. The combination as defined in claim 1; wherein said PD-1 pathway inhibitor is in the form of mRNA encoding said PD-1 pathway inhibitor.
3. The combination as defined in claim 1; wherein said antagonistic antibody directed against PD-1 is selected from the list comprising: nivolumab (BMS-936558/MDX1106), pidilizumab (CT-011), pembrolizumab (MK-3475).
4. The combination as defined in any_one of claims 1 to 3, wherein said target-specific antigen is a marker specific to tumor, bacterial and fungal cells, or viral proteins or viral structures.
5. The combination as define in any_one of claims 1 to 4, wherein the target-specific antigen is a tumor-associated antigen.
6. The combination as defined in any_one of claims 1-5; wherein said mRNA molecules are formulated for intravenous administration, and encompassed in nanoparticles.
7. The combination as defined in claim 6, wherein said nanoparticles are lipid nanoparticles.
8. The combination as defined in claim 7, wherein said lipid nanoparticles comprise a combination of an ionizable lipid, a phospholipid, a sterol and a PEG lipid.
9. The combination as defined in any_one of claims 1-8; wherein said PD-1 pathway inhibitor is formulated for parenteral administration.
10. The combination as defined in any one of claims 1-8, wherein said PD-1 pathway inhibitor is formulated; ~~more in particular~~ for intravenous, intratumoral, intradermal, subcutaneous, intraperitoneal, intramuscular or intranodal administration.

~~10~~11. A vaccine comprising the combination as defined in any_one of claims 1-~~9~~10.

~~11~~12. The vaccine as defined in claim ~~10~~11; wherein said vaccine is formulated for ~~parenteral~~ administration; ~~more in particular for intravenous, intratumoral, intradermal, subcutaneous, intraperitoneal, intramuscular or intranodal~~ administration.

~~12~~13. The combination as defined in any_one of claims 1-~~9~~10 or the vaccine as defined in any_one of claims ~~10-11~~11-12 for use in combination therapy in human or veterinary medicine.

~~13~~14. The combination as defined in any_one of claims 1-~~9~~10 or the vaccine as defined in anyone of claims ~~10-11~~11-12 for use in combination therapy to prevent~~the prevention and/or treatment~~ treat of cell proliferative disorders of cancer.

~~14~~15. The combination as defined in any_one of claims 1-~~9~~10 or the vaccine as defined in any_one of claims ~~10-11~~11-12 for use in combination therapy in eliciting an immune response towards a tumor in a subject.

16. Use of the combination as defined in any one of claims 1-10 or the vaccine as defined in any one of claims 11-12 in the manufacture of a medicament for treating cancer in a subject.