CLAIMS

1. A polyplex of a double stranded RNA (dsRNA) and a polymeric conjugate, wherein said polymeric conjugate consists of a linear polyethyleneimine (LPEI) covalently linked to one or more polyethylene glycol (PEG) moieties, each PEG moiety being conjugated via a linker to a targeting moiety capable of binding to a cancer antigen, wherein said cancer antigen is prostate surface membrane antigen (PSMA), provided that the targeting moiety is not mouse EGF or the peptide of the sequence YHWYGYTPQNVI (GE11) (SEQ ID NO: 1).

2. The polyplex of claim 1, wherein said targeting moiety is $HOOC(CH_2)_2$-CH(COOH)-NH-CO-NH-CH(COOH)-$(CH_2)_2$-CO- (DUPA residue).

3. A polyplex of a double stranded RNA (dsRNA) and a polymeric conjugate, wherein said polymeric conjugate consists of a linear polyethyleneimine (LPEI) covalently linked to one or more polyethylene glycol (PEG) moieties, each PEG moiety being conjugated via a linker to a targeting moiety capable of binding to a cancer antigen, wherein said targeting moiety is $HOOC(CH_2)_2$-CH(COOH)-NH-CO-NH-CH(COOH)-$(CH_2)_2$-CO- (DUPA residue).

4. The polyplex of claim 3, wherein said cancer antigen is prostate surface membrane antigen (PSMA).

5. The polyplex of any one of the preceding claims, wherein the dsRNA is polyinosinic-polycytidylic acid double stranded RNA (poly I:C).

6. The polyplex of any one of the preceding claims, wherein the polymeric conjugate consists of LPEI covalently linked to one PEG moiety (LPEI-PEG 1:1) or to three PEG moieties (LPEI-PEG 1:3).

7. The polyplex of any one of the preceding claims, wherein said one or more PEG moieties each independently forms a bond selected from -NH-CO-, -CO-NH-, -S-C-, -S-S-, -O-CO- or -

CO-O- with said linker, and wherein said linker forms an -S-S-, NH-CO-, -CO-NH-, -S-C-, O-CO-, -CO-O- or urea (-NH-CO-NH) bond with said targeting moiety.

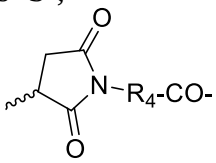
8. The polyplex of any one of the preceding claims, wherein said linker is a peptide moiety consisting of 3 to 7 amino acid residues.

9. The polyplex of claim 8, wherein said peptide moiety is -(NH-$(CH_2)_7$-CO)-Phe-Gly-Trp-Trp-Gly-Cys- (SEQ ID NO: 2) or -(NH-$(CH_2)_7$-CO)-Phe-Phe-(NH-CH_2-CH(NH_2)-CO)-Asp-Cys- (SEQ ID NO: 3), linked via its mercapto group to said targeting moiety.

10. The polyplex of any one the claims 1 to 7, wherein said linker is selected from -CO-R_2-R_x-R_3, wherein

R_2 is selected from (C_1-C_8)alkylene, (C_2-C_8)alkenylene, (C_2-C_8) alkynylene, (C_6-C_{10})arylene-diyl, or heteroarylenediyl, wherein preferably R_2 is selected from (C_1-C_8)alkylene, further preferably (C_1-C_4)alkylene;

R_x is absent or -S-, preferably R_x is -S-;

R_3 is absent or of the formula 

;

R_4 is selected from (C_1-C_8)alkylene, (C_2-C_8)alkenylene, (C_2-C_8) alkynylene, (C_1-C_8)alkylene-(C_3-C_8)cycloalkylene, (C_2-C_8)alkenylene-(C_3-C_8)cycloalkylene, (C_2-C_8) alkynylene-(C_3-C_8)cycloalkylene, (C_6-C_{10})arylene-diyl, heteroarylenediyl, (C_1-C_8)alkylene-(C_6-C_{10})arylene-diyl, or (C_1-C_8)alkylene-heteroarylenediyl, wherein preferably R_4 is (C_1-C_8)alkylene-(C_3-C_8)cycloalkylene, preferably (C_1-C_4)alkylene-(C_5-C_6)cycloalkylene;

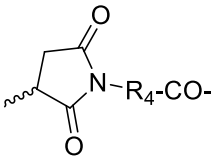
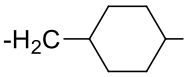
wherein each one of said (C_1-C_8)alkylene, (C_2-C_8)alkenylene, or (C_2-C_8) alkynylene is optionally substituted by one or more groups each independently selected from halogen, -COR_5, -$COOR_5$, -$OCOOR_5$, -$OCON(R_5)_2$, -CN, -NO_2, -SR_5, -OR_5, -$N(R_5)_2$, -$CON(R_5)_2$, -SO_2R_5, -SO_3H, -$S(=O)R_5$, (C_6-C_{10})aryl, (C_1-C_4)alkylene-(C_6-C_{10})aryl, heteroaryl, or (C_1-C_4)alkylene-heteroaryl, and further optionally interrupted by one or more identical or different heteroatoms selected from S, O or N, and/or at least one group each independently selected from -NH-CO-, -CO-NH-, -$N(R_5)$-, -N(C_6-C_{10}aryl)-, (C_6-C_{10})arylene-diyl, or heteroarylenediyl; and

R_5 is H or (C_1-C_8)alkyl.

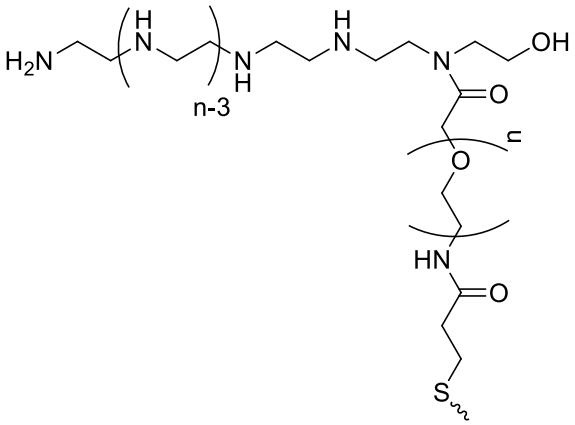
11. The polyplex of claim 10, wherein

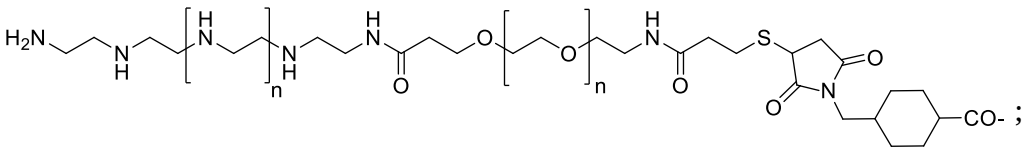
R_2 is -CH_2-CH_2-;

R_x is -S-; and

R_3 is absent or , wherein R_4 is .

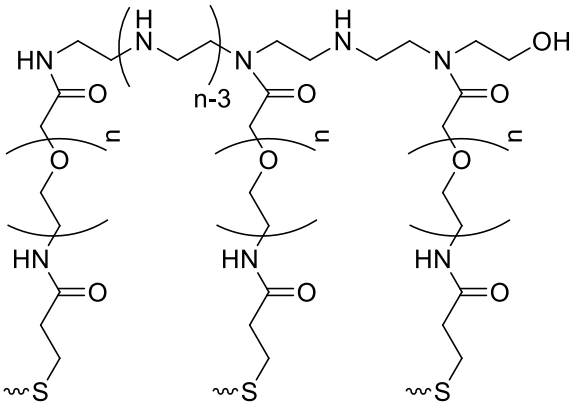
12. The polyplex of any one of claims 1 to 11, wherein the polymeric conjugate is a diconjugate of the formula (i)-(viii), linked to said targeting moiety/moieties:

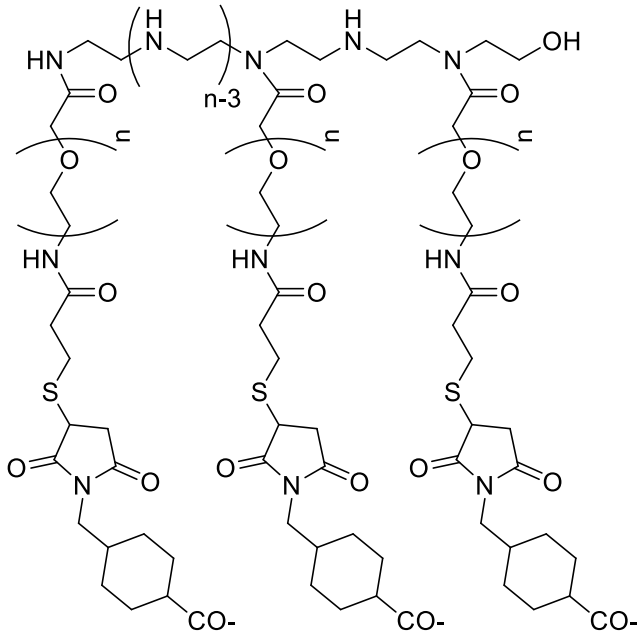
(i) ;

(ii) ;

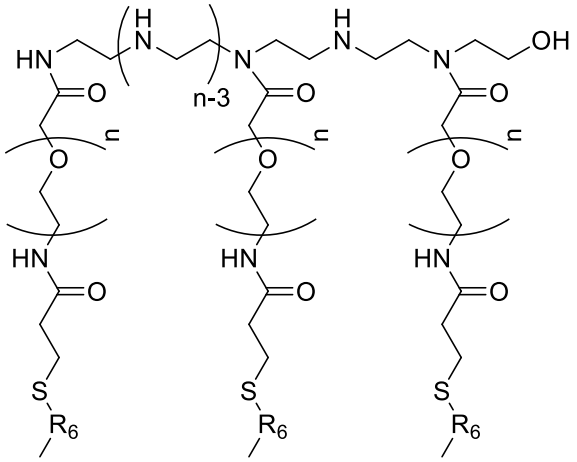
(iii) -(NH-(CH_2)$_7$-CO)-Phe-Phe-(NH-CH_2-CH(NH_2)-CO)-Asp-Cys-PEG_{2k}-LPEI;

(iv) -(NH-(CH_2)$_7$-CO)-Phe-Gly-Trp-Trp-Gly-Cys-PEG_{2k}-LPEI;

(v) ;

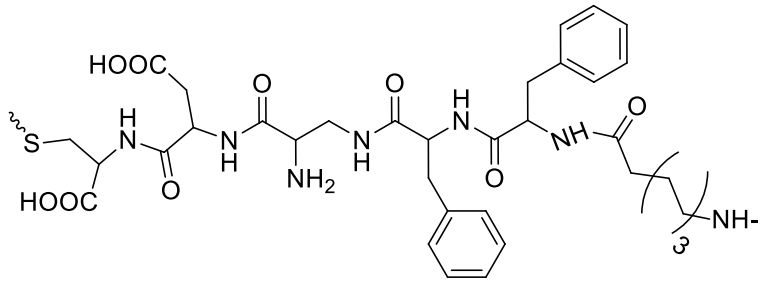
(vi) 

;

(vii) 

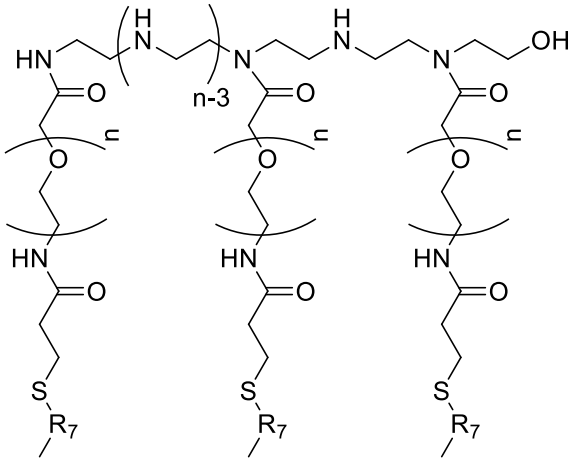
,

wherein R_6 is

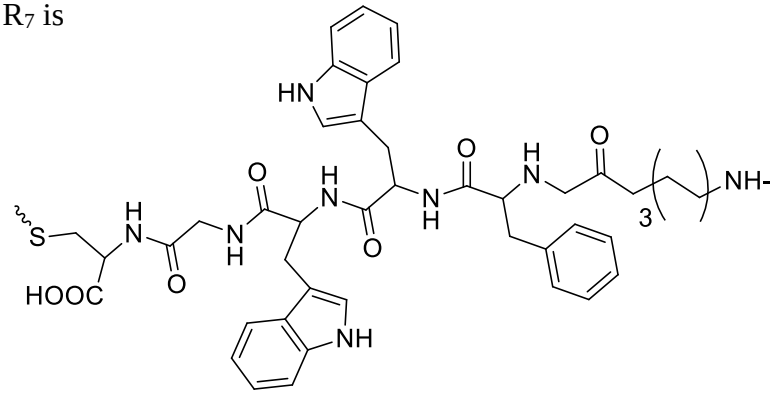


; or

(viii)



wherein R_7 is



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13. The polyplex of claim 12, wherein

(a) said targeting moiety is $HOOC(CH_2)_2$-CH(COOH)-NH-CO-NH-CH(COOH)-$(CH_2)_2$-CO- (DUPA residue), and said polymeric conjugate is of the formula (iii) of claim 12;

(b) said targeting moiety is $HOOC(CH_2)_2$-CH(COOH)-NH-CO-NH-CH(COOH)-$(CH_2)_2$-CO- (DUPA residue), and said polymeric conjugate is of the formula (vii) of claim 12;

(c) said targeting moiety is $HOOC(CH_2)_2$-CH(COOH)-NH-CO-NH-CH(COOH)-$(CH_2)_2$-CO- (DUPA residue), and said polymeric conjugate is of the formula (iv) of claim 12; or

(d) said targeting moiety is $HOOC(CH_2)_2$-CH(COOH)-NH-CO-NH-CH(COOH)-$(CH_2)_2$-CO- (DUPA residue), and said polymeric conjugate is of the formula (viii) of claim 12.

14. The polyplex of any one of the preceding claims, wherein each strand of said dsRNA has 20-300 ribonucleotides.

15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polyplex of any one of claims 1 to 14.

16. Use of the polyplex of any one of claims 1 to 14, or the pharmaceutical composition of claim 15, for the manufacture of a medicament for the treatment of prostate cancer.

17. The use of claim 16, wherein the polyplex is to be administered or used in combination with immune cells.

18. The use of claim 17, wherein said immune cells are tumor-infiltrating T-cells (T-TILs), tumor specific engineered T-cells, or peripheral blood mononuclear cells (PBMCs).