CLAIMS

1. A composition comprising (i) stressed HT-29, HCT-116 and LoVo cells, and (ii) immunogenic stress proteins produced by these cells in response to a stress applied *in vitro*.

2. The composition according to claim **1**, wherein stressed HT-29, HCT-116 and LoVo cells have developed resistance mechanism in response to one or several stress[es] applied *in vitro*, selected from the group comprising radiations, thermal stress, chemical stress, metabolic stress and any combinations thereof, leading to the production of the stress proteins.

3. The composition according to claim **1** or **2**, wherein stressed HT-29, HCT-116 and LoVo cells are non-proliferative.

4. The composition according to any one of claims **1** to **3**, wherein immunogenic stress proteins are haptenated;

preferably with a hapten selected from the group comprising 2,4-dinitrophenyl (DNP); 2,4-dinitrofluorobenzene; sulfanilic acid; *N*-iodoacetyl-*N*'-(5-sulfonic-naphthyl)ethylene diamine; anilin; *p*-amino benzoic acid; biotin; fluorescein and derivatives thereof (including FITC, TAMRA, and Texas Red); digoxigenin; 5-nitro-3-pyrazolecarbamide; 4,5-dimethoxy-2-nitrocinnamide; 2-(3,4-dimethoxyphenyl)-quinoline-4-carbamide; 2,1,3-benzoxadiazole-5-carbamide; 3-hydroxy-2-quinoxalinecarbamide, 4-(dimethylamino)azobenzene-4'-sulfonamide (DABSYL); rotenone isooxazolinI(*E*)-2-(2-(2-oxo-2,3-dihydro-1*H*-benzo[*b*][1,4]diazepin-4-yl)phenozy) acetamide; 7-(diethylamino)-2-oxo-2*H*-chromene-3-carboxylic acid; 2-acetamido-4-methyl-5-thiazolesulfonamide; and *p*-methoxyphenylpyrazopodophyllamide;

more preferably with 2,4-dinitrophenyl (DNP).

5. The composition according to any one of claims **1** to **4**, being a pharmaceutical composition or a vaccine composition, and further comprising at least one pharmaceutically acceptable excipient.

6. The composition according to any one of claims **1** to **5**, comprising from about 10^5 to about 10^8 stressed HT-29, HCT-116 and LoVo cells.

7. Use of the composition according to any one of claims **1** to **6**, for the manufacture of a medicament for the treatment of cancer in a subject in need thereof.

8. An intermediate composition comprising (i) one of stressed HT-29 cells, stressed HCT-116 cells and stressed LoVo cells, and (ii) stress proteins,

wherein the one of stressed HT-29 cells, stressed HCT-116 cells or stressed LoVo cells have developed resistance mechanism in response to (i) a metabolic stress, (ii) radiations and (iii) a thermal stress applied *in vitro*, leading to the production of the stress proteins.

9. An intermediate composition comprising (i) one of stressed HT-29 cells, stressed HCT-116 cells or stressed LoVo cells, and (ii) stress proteins,

wherein the one of stressed HT-29 cells, stressed HCT-116 cells or stressed LoVo cells have developed resistance mechanism in response to (i) a metabolic stress, and (ii) a chemical stress applied *in vitro*, leading to the production of the stress proteins.

10. A method of manufacturing the intermediate compositions according to claim **8** or **9**, comprising the following steps:

a) cultivating HT-29, HCT-116 or LoVo cells in a suitable culture medium;

b) subjecting the HT-29, HCT-116 or LoVo cells cultured in step a) to one or several stress[es] *in vitro*, wherein these HT-29, HCT-116 or LoVo cells develop resistance mechanisms in response to the one or several stress[es] and thereby produce stress proteins,

c) recovering the stressed HT-29, HCT-116 or LoVo cells together with the stress proteins they have produced in step b), and

d) treating the stressed HT-29, HCT-116 or LoVo cells and the stress proteins they have produced, all together recovered in step c), with a molecule or by a process capable of rendering the stress proteins immunogenic.

11. The method according to claim **10**, wherein step c) is carried out at least several hours after completion of step b), preferably at least 12 hours or more after completion of step b).

12. The method according to claim **10** or **11**, wherein step d) comprises linking the stress proteins to or complexing the stress proteins with a means capable to confer immunogenicity.

13. The method according to claim **12**, wherein the means capable to confer immunogenicity is an hapten;

preferably the hapten is selected from the group comprising 2,4-dinitrophenyl (DNP); 2,4-dinitrofluorobenzene; sulfanilic acid; *N*-iodoacetyl-*N*'-(5-sulfonic-naphthyl)ethylene diamine; anilin; *p*-amino benzoic acid; biotin; fluorescein and derivatives thereof (including FITC, TAMRA, and Texas Red); digoxigenin; 5-nitro-3-pyrazolecarbamide; 4,5-dimethoxy-2-nitrocinnamide; 2-(3,4-dimethoxyphenyl)-quinoline-4-carbamide; 2,1,3-benzoxadiazole-5-carbamide; 3-hydroxy-2-quinoxalinecarbamide, 4-(dimethylamino)azobenzene-4'-sulfonamide (DABSYL); rotenone isooxazoline; (*E*)-2-(2-(2-oxo-2,3-dihydro-1*H*-benzo[*b*][1,4]diazepin-4-yl)phenozy)acetamide; 7-(diethylamino)-2-oxo-2*H*-chromene-3-carboxylic acid; 2-acetamido-4-methyl-5-thiazolesulfonamide; and *p*-methoxyphenylpyrazopodophyllamide;

more preferably the hapten is 2,4-dinitrophenyl (DNP).

14. The method according to any one of claims **10** to **13**, for manufacturing the intermediate compositions according to claim **8**, wherein step b) comprises subjecting the HT-29, HCT-116 or LoVo cells cultured in step a) to the following stresses *in vitro*, applied concomitantly or successively:

(i) an *in vitro* culture in a depleted medium, under hypoxia, and/or at low pH;
preferably an *in vitro* culture in low serum culture conditions in a 2 % FBS culture medium,

(ii) an *in vitro* radiation with a total dose ranging from about 0.25 to about 25 Gy, preferably from about 1 to about 15 Gy, preferably for a period ranging from about 1 to about 20 minutes;
preferably an *in vitro* radiation with a total dose of 10 Gy for a period of about 1 to about 5 minutes, and

(iii) an *in vitro* thermic choc at a temperature ranging from about 38°C to about 45°C, applied to the cells for a period ranging from about 15 minutes to about 4 hours;
preferably an *in vitro* thermic choc at a temperature of about 42°C for a period of about 60 minutes.

15. The method according to any one of claims **10** to **13**, for manufacturing the intermediate compositions according to claim **9**, wherein step b) comprises subjecting the HT-29, HCT-116 or LoVo cells cultured in step a) to the following stresses *in vitro*, applied concomitantly or successively:

(i) an *in vitro* culture in a depleted medium, under hypoxia, and/or at low pH;
preferably an *in vitro* culture in low serum culture conditions in a 2 % FBS culture medium,

(ii) an *in vitro* exposition to at least one or several chemotherapeutic agents and/or alcohols, for a period ranging from about 6 hours to about 120 hours.

16. The method according to claim **15**, wherein:

- the cells are HT-29 cells and the *in vitro* exposition at (ii) is to about 13 µM oxaliplatin for a period of about 72 hours; or
- the cells are HCT-116 cells and the *in vitro* exposition at (ii) is to about 315 nM SN-38 (7-ethyl-10-hydroxy-camptothecin) for a period of about 48 hours; or
- the cells are LoVo cells and the *in vitro* exposition at (ii) is to about 5 µM fluorouracil (5-FU) for a period of about 48 hours.

17. A method of manufacturing the composition according to any one of claims **1** to **6**, comprising the following steps:

a. obtaining six intermediate compositions according to claims **8** and **9**, wherein the six intermediate compositions are:

1) an intermediate composition according to claim **8** comprising stressed HT-29 cells and stress proteins,

2) an intermediate composition according to claim **8** comprising stressed HCT-116 cells and stress proteins,

3) an intermediate composition according to claim **8** comprising stressed LoVo cells and stress proteins,

4) an intermediate composition according to claim **9** comprising stressed HT-29 cells and stress proteins,

5) an intermediate composition according to claim **9** comprising stressed HCT-116 cells and stress proteins,

6) an intermediate composition according to claim **9** comprising stressed LoVo cells and stress proteins,

b. mixing these six intermediate compositions together;
preferably wherein these six intermediate compositions are mixed together in an equal ratio of stressed HT-29, HCT-116 and LoVo cells.