**Summary of the invention**

The Inventors were able to show that, surprisingly, original pharmaceutical compositions as described in the Examples below induced an efficient antigen-specific immune protection against SIV in macaques. Moreover, when said SIV-specific immune protection was induced, the Inventors showed that it prevented SIV replication/dissemination and the subsequent establishment of the infection *in vivo*.

Indeed, the Inventors have surprisingly shown that upon administering a pharmaceutical composition as disclosed here either mucosally or by the intradermal or intraepithelial route, virus replication was significantly inhibited, or even abrogated or prevented.

Actually, the Inventors could observe for the first time that a non-cytotoxic CD8+T cell response suppressed the early activation of SIV antigen-presenting CD4+T cells in macaques. Thus, without wishing to be bound by theory, the pharmaceutical compositions according to the present disclosure~~invention~~ induce an unexpected new type of virus-specific immunotolerance upon mucosal or intradermal or intraepithelial administration to subjects. This immunotolerance appears to be a HIV Gag and/or Pol antigen-specific suppressive CD8+T cell-induced immunotolerance (also named herein "Ts" immunotolerance for "T suppressive" immunotolerance), which is MHC (for "Major Histocompatibility Complex")-Ib/E-restricted and non-cytotoxic.

In the light of the results reported herein, it is provided by the present disclosure~~invention~~ a novel pharmaceutical composition capable of achieving a "Ts" immunotolerance as defined above for preventing and/or treating an HIV disease in humans.

In one aspect, there is provided a pharmaceutical composition, comprising a mixture of two separate components, said components being (i) a particulate antigen having one or more epitopes from HIV Gag and/or Pol proteins and (ii) a non-pathogenic bacterium selected from the group consisting of BCG and non-pathogenic lactic acid bacteria.

An object of the present disclosure~~invention~~ is thus to provide a pharmaceutical composition comprising a mixture of an antigen and a non-pathogenic living bacterium, wherein, preferably, said antigen is particulate and/or it has one or more epitopes from HIV Gag and/or Pol proteins, and wherein said bacterium is preferably *Lactobacillus plantarum*.

In another aspect, there is provided a simultaneous use of: a particulate antigen having one or more epitopes from HIV Gag and/or Pol proteins; and a non-pathogenic living bacterium selected from the group consisting of BCG and non-pathogenic lactic acid bacteria, in the manufacture of a combined pharmaceutical composition for preventing and/or treating an HIV disease in a human in need thereof.

In a further aspect, there is provided a use of a pharmaceutical composition as defined herein in the manufacture of a medicament for preventing and/or treating an HIV disease in a human in need thereof.

In yet another aspect, there is provided a use of a pharmaceutical composition as defined herein in the manufacture of a medicament for protecting a human against HIV.

In another aspect, there is provided a use of a pharmaceutical composition as defined herein in the manufacture of a medicament for protecting a human from HIV seroconversion.

It is another object of the present disclosure~~invention~~ to provide a pharmaceutical composition as described herein, for use as a vaccine.

Another object of the present disclosure~~invention~~ is to provide a method for preventing and/or treating an HIV disease in a human in need thereof, comprising at least the step of mucosally (preferably orally) or intradermally or intraepithelially administering an effective amount of a pharmaceutical composition as mentioned above to said human.

Yet another object of the present disclosure~~invention~~ is to provide a method for protecting a human against HIV, comprising at least the step of mucosally (preferably orally) or intradermally or intraepithelially administering an effective amount of a pharmaceutical composition as mentioned above to said human.

Yet another object of the present disclosure~~invention~~ is to provide a method for protecting a human from HIV seroconversion, comprising at least the step of mucosally (preferably orally) or intradermally or intraepithelially administering an effective amount of a pharmaceutical composition as mentioned above to said human.

Yet another object of the present disclosure~~invention~~ is to provide a pharmaceutical kit for preventing and/or treating an HIV disease in a human in need thereof, comprising:

- in a first container, an antigen; and
- in a second container, a non-pathogenic bacterium,

wherein said antigen and said bacterium are in pharmaceutically acceptable carriers for mucosal or intradermal or intraepithelial administration, wherein preferably said antigen is particulate and/or it has one or more epitopes from HIV Gag and/or Pol proteins, and wherein said bacterium is preferably *Lactobacillus plantarum*.

**Brief description of the drawings**

The present invention is illustrated by the following figures to which reference is made in the non-limiting examples below.

Figure 1: Intravenous (i.v.) SIVmac239 challenge of rhesus macaques pretreated with an intravaginal iSIV/BCG.

Figure 2: Intrarectal (i.r.) SIVmac239 challenge of rhesus macaques pretreated with an intravaginal iSIV/BCG.

Figure 3: Repeated SIVmac239 challenges (3 times by i.v. and 2 times by i.r.) of rhesus macaques pretreated with an intravaginal iSIV/BCG.

Figure 4: Intravenous SIVmac239 challenge of rhesus macaques pretreated with an intravaginal iSIV/BCG plus an intradermal booster.

Figure 5: Intrarectal SIVmac239 challenge of rhesus macaques pretreated with an intravaginal iSIV/BCG plus an intradermal booster.