

## Scientific Abstract:

The development of a safe and effective prophylactic HIV-1 vaccine is a global health priority. Wyeth Research is pursuing development of a combination HIV vaccine regimen consisting of CTL multi-epitope peptides (HIV CTL MEP) and facilitated DNA technology (HIV-1 *gag* DNA + *IL-15* DNA or *IL-12* DNA) platforms. It is anticipated that a combination prime/boost approach will build on the strengths of each technology and provide the desired breadth and robustness of cellular immune responses that are required to confer protective immunity. In Part A of this clinical protocol, priming with HIV-1 *gag* DNA (1500 mcg) will be tested with escalating doses of *IL-15* DNA (0, 100, 500 and 1500 mcg). Some subjects at the highest *IL-15* DNA dose will receive boost vaccinations with the same HIV-1 *gag* DNA + *IL-15* DNA regimen. In Part B, priming with HIV-1 *gag* DNA (1500 mcg) + *IL-15* DNA (at the maximum safe and tolerated dose from Part A) will be followed by boost vaccination(s) with HIV-1 *gag* DNA + *IL-15* DNA, or HIV CTL MEP/ RC529-SE /GM-CSF, or with HIV-1 *gag* DNA + *IL-12* DNA. The *IL-15* DNA and *IL-12* DNA plasmids in this protocol use the human genes for *IL-15* and *IL-12*.

The multicenter, randomized, placebo-controlled, double blinded study will involve 144 HIV-uninfected healthy adult participants.

In a study in rhesus macaques, the humoral and cellular immune responses elicited by a RNA optimized SIV *gag* DNA construct were substantially enhanced by coimmunization with rhesus *IL-15* expressing plasmid DNA.

The objectives of the proposed study HVTN 062 are:

### *Part A*

- To evaluate the safety and tolerability of intramuscular administration of HIV-1 *gag* DNA vaccine and HIV-1 *gag* DNA vaccine plus *IL-15* DNA

### *Part B*

- To evaluate the safety and tolerability of intramuscular administration of HIV-1 *gag* DNA vaccine plus *IL-15* DNA as a priming series followed by boost vaccinations with HIV CTL MEP vaccine, or HIV-1 *gag* DNA vaccine plus *IL-15* DNA, or HIV-1 *gag* DNA vaccine plus *IL-12* DNA

vaccine approach may be able to raise enough immunity to protect against HIV. The study will involve 144 healthy adult participants who do not have HIV. In the trial, some people will get one kind of vaccine for initial and later booster vaccinations, some will receive one kind of vaccine for initial vaccinations and a different vaccine for booster vaccinations, and some people will receive a salt water solution without any HIV vaccine. The multicenter, randomized, placebo-controlled, double blinded study will be done at three sites through Harvard University. Other sites may be added later. None of the vaccines can cause HIV infection or AIDS.

Similar vaccines have been tested in monkeys, and the effect of the vaccines on the immune system could be measured in the blood.

The main purpose of the present study is to make sure that the vaccines and the adjuvants are all safe and cause no serious or bothersome side effects.