IMMUNE THERAPIES IN DEVELOPMENT

NOTE: several fact sheets describe drugs that are being tested against HIV:

- Fact sheet 410: nucleoside analog reverse transcriptase inhibitors (nukes)
- Fact sheet 430: non-nucleoside analog reverse transcriptase inhibitors (NNRTIs or non-nukes)
- Fact sheet 440: protease inhibitors
- Fact sheet 460: attachment and fusion inhibitors

Fact sheet 470: new classes of antiviral drugs. ***These drugs have not been approved by the Food and Drug Administration (FDA) for use against HIV.***

IMMUNE STIMULATORS

We can think of most antiviral drugs as "offense", attacking the virus to slow down its multiplication. Another approach to treating HIV infection is "defense", strengthening the immune response of people who are infected. This Fact Sheet describes new immune stimulators being developed.

CYTOKINES

Some of these treatments use the body's own chemical messengers (cytokines) to increase the immune system's response to HIV. Different cytokines carry different messages to cells of the immune system. Some cytokines tell a cell to start multiplying; others can tell a cell to self-destruct.

- **Interferon** exists in the body in several forms. Hemispherx Biopharma is testing **Ampligen,** a form of interferon, in Phase II and Phase III trials. It is supposed to activate some of the cell's own defenses against viruses.
- The best-known cytokine is **interleukin-2 (IL-2, Aldesleukin, Proleukin)** by Novartis. See Fact Sheet 472 for more information on Interleukin-2. It is currently in Phase III trials. Bayer Corporation is studying **Bay 50-4798**, a modified recombinant form of IL-2, in Phase II trials.
- **Interleukin-7** is being developed by Cytheris Corp as a general immune system booster. CYT107 is in Phase I/II trials and showed positive interim results. It increased both CD4 and CD8 cell counts. It is given in 3 weekly injection.
- **Multikine** by Cel-Sci Corporation, is a mixture of several different cytokines. It is in Phase I human trials.
- **Tumor necrosis factor alpha (TNF-α)** is an immune system protein that is over-produced in immune disorders. Advanced Biotherapy is studying a TNF-α blocker in a Phase I trial.

VACCINE-LIKE TREATMENT

Another approach to stimulating the immune system is similar to vaccination, except that it is used in people who are already infected with HIV. **HRG214** by Virionyx is a genetically engineered group of antibodies to HIV. It is called a "passive immuno-therapeutic pharmaceutical." HRG214 is in Phase I/II trials.

A recent study of ALVAC vaccine plus Remune found a delay in viral load rebound when treatment was interrupted.

A recent study showed that a combination of vaccines against HIV and interleukin-2 (IL-2) increased immune responses to HIV and allowed some people to stop antiviral therapy for up to a year.

AGS-004 by Argos takes a sample of a patient's virus and extracts RNA. The RNA is loaded into dendritic cells that are administered to the patient, stimulating an immune response to the virus. It is in Phase 2a trials. **DermaVir** is applied as a skin patch. It is in Phase I/II trials. Another new therapeutic vaccine is **VIR201**. It is in Phase I/IIa trials.

OTHER IMMUNE MODULATORS

- **AVR118** by Advanced Viral Research showed good results against AIDS wasting and anorexia in a Phase I/II study.
- **Cytolin** by Cytodyn is designed to improve the immune system's ability to fight HIV. It is given as an intravenous infusion. Cytolin is in Phase II trials.
- **HspE7** by StressGen Biotechnologies is being tested in Phase II and Phase III trials for tumors related to human papillomavirus (HPV, see fact sheet 510).
- **Immunitin (HE2000)** by Hollis-Eden Pharmaceuticals is a new drug that works on an infected person's immune system. It is designed to strengthen the "humoral" immune response which is responsible for producing antibodies. HE2000 is being tested in Phase II trials.
- **IR103** is a combination of Remune by the Immune Response Corporation, which stimulates an immune response to HIV, and Amplivax by Hybridon which uses gene technology to enhance immune responses. IR103 is in a Phase I trial.
- **MDX010** is an artificial antibody product. Medarex is testing it against HIV in Phase II trials.
- **Murabutide** is under study by Dr. Georges Bahr in France. It uses fragments of bacteria to stimulate the overall immune response. Murabutide is given by injection. Phase I results, published in 2003, were promising in terms of increases in CD4 cells and lower viral loads.
- **Resveratrol** is a chemical found in several plants and the skin of red grapes. It protects plants against pathogens and may have other immune-boosting properties. It is being studied in a Phase I trial in people with HIV.
- **Reticulose** by Advanced Viral Research Corporation is a nucleic acid that stimulates the cell-killing arm of the immune system. It is administered as a subcutaneous (beneath the skin) injection. Early clinical trials showed that patients receiving Reticulose had increases in their CD4 and CD8 cells, weight increases, and fewer opportunistic infections than patients receiving placebo. No toxic side effects have been reported yet. Reticulose is in Phase III trials.
- **SP-6310** by Samaritan Pharmaceuticals normalizes levels of cortisol, a stress hormone. A Phase II study is being developed.
- **Tesamorelin (TH9507)** by Theratechnologies is a growth hormone inducer. It is being studied in Phase III to treat visceral fat accumulation in lipodystrophy. Marketing rights for the United States have been sold to Serono.
- **Tucaresol** by GlaxoSmithKline is an immune stimulator in Phase I trials.
- **Zenapax (daclizumab or anti-CD25)** is being studied by the National Institutes of Health as a way to reduce viral load beyond what ART can achieve.

DRUGS NO LONGER IN DEVELOPMENT

The following drugs are no longer being developed for use against HIV:

WF10 by Dimethaid Research
SP-01A by Samaritan Pharmaceuticals has been replaced by SP-6310 (see above).

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