Novel Macrocyclic Molecules for Treating and Preventing HIV Infection (CG1) (Yissum)

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New compounds mimicking CD4 protein, inhibiting gp120/CD4 interaction and the consequent infection of cells by HIV

Categories	HIV/AIDS, Therapeutic Drug, Preventive Treatment
Patent Status	US patent application filed
Target Market	In 2007, HIV drugs achieved global sales of more than 9 billion dollars. Leading drugs capture more than 1 billion dollars in annual sales.

The Field

- HIV infects immune cells by the direct interaction of the virion envelope glycoproteins (gp120) with the CD4 molecule expressed on the target cells. After infection, immune cells are gradually destroyed, which leads to the inevitable lost of cell-mediated immunity and to an increased susceptibility to opportunistic infections.
- Backbone cyclization (BC) is a tool developed to impose conformational constraints on peptides by interconnecting its backbone atoms. This approach allows connecting discontinuous active residues in various conformations. Some of these conformations are similar to the arrangement of residues that constitutes the active sites of natural proteins.
- Cycloscan is a selection method in which libraries of BC are screened to discover the most active BC peptides.

Innovation Highligts

- A series of new compounds mimicking CD4 protein, discovered by the BC-Cycloscan platform, that inhibit gp120/CD4 interaction and the consequent infection of cells by HIV.
- The new compounds show high intestinal permeability and are metabolically stable, which makes them potential orally-deliverable drugs.

Development Milestones

- A series of macrocyclic molecules mimicking the CD4 structure were synthesized. Some of these molecules successfully inhibited viral penetration into cultured T-cells by inhibiting gp120/CD4 interaction. Additionally, the molecules showed high intestinal permeability in in-vitro and ex-vivo models, and were stable to intestinal enzymes.

The Opportunity

- An estimated 33.2 million people live with AIDS worldwide. Currently available anti-retroviral therapies often fail to alleviate patient’s symptoms, are very slow clearing the infection, and frequently induce the development HIV-1 strains resistant to the treatment. Nowadays, as much

as fifty percent of medicated patients have no benefit from their treatment.

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