HPSC based therapy for HIV disease using RNAi to CCR5.

Grant Award Details

HPSC based therapy for HIV disease using RNAi to CCR5.

Grant Type: Disease Team Research I

Grant Number: DR1-01431

Project Objective: Stem cell gene therapy for HIV using RNAi to CCR5

Investigator:

Name: Irvin Chen

Institution: University of California, Los Angeles

Type: PI

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Name: Geoff Symonds

Institution: Calimmune, Inc.

Type: Co-PI

Disease Focus: HIV/AIDS, Immune Disease, Infectious Disease

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $9,905,604

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: HPSC based therapy for HIV disease using RNAi to CCR5.

Public Abstract: RNA interference is a naturally occurring means to block the function of genes in our body. We propose that RNA interference can be used to block HIV-1 infection and its reproduction within the body. When RNA interference is introduced into a stem cell, its blocking activity will be present throughout the lifetime of the stem cell, theoretically the lifespan of a human being. Thus, in theory an effective stem cell RNA interference therapy will require only a single treatment as opposed to the current lifetime administration of anti-HIV-1 drugs often accompanied by serious side effects. In nature, some individuals carry a genetic mutation that renders them resistant to HIV-1 infection. This mutation prevents HIV-1 from attaching to the white blood cells. Our RNA interference approach will be to mimic this natural situation by blocking the activity of this "co-receptor" within infected individuals by creating a new blood system that carries the RNA interference therapy. This therapy will be developed as a combination with other gene therapeutic reagents to protect the new blood system from HIV infection.

Statement of Benefit to California: The need for novel approaches to the treatment of HIV infection has never been greater, because new infections continue to occur at undiminished rates, in California and across the nation, despite decades of prevention efforts. Moreover, the number of people living with HIV is rising steadily, thanks to improved management of HIV infection. As a result, California, which ranks second in the nation in diagnosed cases of HIV infection, behind only New York, has identified 67,500 men, women, and children who carry the virus. (Estimates of the number of Californians who are infected but have yet to be diagnosed range as high as 33,513.) Not all of the state's HIV-positive residents are currently on therapy, but eventually virtually all of them will be—and many of them will receive their drugs through government-supported programs. In addition, the longer these infected individuals live, the more likely they are to avail themselves of a range of support services that the state pays for. The drugs themselves, which are routinely administered in combination, are initially effective in suppressing viral replication in infected individuals, but their potency diminishes over time, even as the toxic effects of therapy accumulate.

California, which is supporting the nation's second-highest case-load of HIV-positive individuals, can expect to see that number grow at a rate of 5,000-7,000 a year for the foreseeable future. The cost of providing life-sustaining medications and social services to this burgeoning population will also continue to rise, not arithmetically but exponentially—because as increasing numbers of infected individuals fail standard drug regimens, it will be necessary to shift them to newer, more expensive treatments, and as the side effects of therapy become more manifest, it will be necessary to prescribe drugs to combat those toxicities, adding to the overall drug burden for patients and the overall cost of drug therapy for the state.

In such circumstances, the prospect of stem-cell based therapy that will require "only a single treatment" is especially compelling. In theory, RNA interference might effectively cure individuals infected with HIV, by blocking the ports through which the virus enters CD4 cells and destroys the body's immune system. And even if RNA interference proves only partially effective in blocking viral entry, it could significantly suppress viremia while sparing patients the toxicities associated with drug therapy. This would be a boon to infected individuals, but it would also be a benefit to uninfected Californians, because reductions in viremia in infected individuals translate into a reduction in the community burden of HIV infection—and that, in turn, reduces the overall rate of new infections statewide.