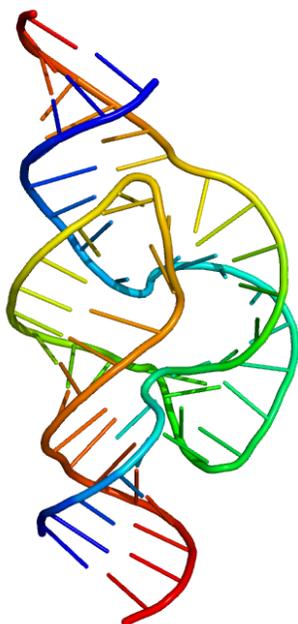


## Ribozymes Targeted to Human CCR5 mRNA for Treatment of HIV



### DESCRIPTION

CCR5 is a chemokine receptor protein found on the surface of white blood cells and is used by many forms of HIV as an entry point to infect these cells. Individuals with a homozygous deletion mutation in the CCR5 gene have a natural resistance to infection HIV-1 group M, a strain accounts for more than 90% of HIV/AIDS cases. Additionally, infected heterozygotes demonstrate long term survival, making CCR5 an attractive therapeutic target for HIV treatment and prevention; however, gene therapy and post-translational approaches are, thus far, associated with unwanted toxicities.

City of Hope has developed a novel technology for downregulating CCR5 using a CCR5-specific ribozyme. A single stranded arm of the ribozyme is complementary to the CCR5 mRNA sequence; upon binding to the target sequence, the catalytic region of the ribozyme cleaves the mRNA and interrupts production of CCR5 protein. Because the ribozyme is sequence specific for CCR5, non-target effects are eliminated, and risk of eliciting an immunogenic reaction is extremely low because the therapeutic agent is RNA rather than protein. The ribozyme can be delivered via direct injection, however more efficient dosing and longer term protection could be achieved by employing gene therapy; embedding the ribozyme in adenovirus-derived carrier RNA confers stability and cytoplasmic co-localization with the CCR5 mRNA target. Transfection of white blood cells or hematopoietic stem cells, either in vivo or through autologous transplantation, with coding sequences for the CCR5-specific ribozyme would generate a line of immune cells with HIV resistance, to prevent HIV infection in at-risk populations or maintain immune capacity in patient that are already infected.

### KEY ASPECTS

- Method for treating and preventing HIV infection targets CCR5, the entry point for HIV into T-cells
- CCR5 mRNA-specific ribozyme prohibits CCR5 protein production
- Gene therapy confers long term HIV resistance as a result of ribozyme production

### INTELLECTUAL PROPERTY

| Title                                 | US Patent Number | Issued   |
|---------------------------------------|------------------|----------|
| Ribozymes Targeted to Human CCR5 mRNA | 6,100,087        | 8/8/2000 |

### CONTACT

Matthew Grunseth, M.B.S.  
Senior Manager, Office of Technology Licensing  
Telephone: (626) 471-7221 | Email: [mgrunseth@coh.org](mailto:mgrunseth@coh.org)

This material is a summary of public domain and non-confidential City of Hope information. Additional material may be disclosed under a confidentiality agreement.