Disrupting HIV Reservoirs with Anti-HIV CRISPRs

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Currently, anti-retroviral drug combinations are highly effective against HIV-1 and can suppress virus levels very well. However, if a patient stops their therapy, HIV rapidly rebounds. This rebound of virus is now known to be caused by cells that are infected with HIV but do not produce virus, allowing them to escape drug therapy. When therapy is stopped, these cells can produce virus once again and restart the infection. These cells are called HIV reservoir cells. Thus, reducing or eliminating these reservoirs remains a highly relevant goal to eradicate HIV, especially since recent reports suggest that early intervention with antiretroviral drugs can limit the formation of such reservoirs and contribute to successful viral eradication or even drug-free virus control.

Because of the importance of reducing reservoir HIV, one of the goals for our lab is to develop novel strategies to target and remove reservoir HIV in drug-suppressed patients. However, in order to begin to test new strategies that could target reservoir cells, a better animal model is required. Thus, this project aims to develop and characterize a humanized mouse model that can be used to study HIV latency. We also aim to use a new class of targeted nucleases, molecules that can specifically disrupt DNA sequences, called the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) Cas9 system that will be able to inactivate HIV DNA in HIV reservoir cells. Finally, we will test the anti-HIV capability of these CRISPRs in the humanized mouse model, to determine whether reservoir HIV levels can be reduced.