1158-92-131 **Jesse Kreger*** (kregerj@uci.edu), **Natalia L Komarova** and **Dominik Wodarz**. *Effect of synaptic cell-to-cell transmission and recombination on the evolution of double mutants in HIV.*

Recombination in HIV infection impacts virus evolution in complex ways. The effect of free virus versus synaptic transmission on the evolution of double mutants, however, has not been investigated. Consistent with data, we assume spatial constraints for synaptic but not for free virus transmission. Two important effects are observed: (i) For disadvantageous mutants, synaptic transmission protects against detrimental effects of recombination on double mutant persistence. Under free virus transmission, recombination increases double mutant levels for negative epistasis, but reduces them for positive epistasis. (ii) The mode of virus spread also directly influences the evolutionary fate of double mutants. For disadvantageous mutants, double mutant production is the predominant driving force, and hence synaptic transmission leads to highest double mutant levels due to increased transmission efficiency. For advantageous mutants, double mutant spread is the most important force, and hence free virus transmission leads to fastest invasion. For neutral mutants, both production and spread of double mutants are important, and hence an optimal mixture of both transmission methods maximizes double mutant fractions. Implications for drug resistance are also discussed. (Received February 27, 2020)