1067-92-694 **Libin Rong*** (rong2@oakland.edu), Dept of Math and Stat, Rochester, MI 48309, **Harel Dahari**, Chicago, IL 60612, **Ruy Ribeiro**, Los Alamos, NM 87545, and **Alan Perelson**, Los Alamos, NM 87545. *Hepatitis C virus drug resistance and modeling.*

About 170 million people worldwide are infected with hepatitis C virus (HCV). The current standard therapy leads to sustained viral elimination in only approximately 50% of the treated patients. Telaprevir, an HCV protease inhibitor, has substantial antiviral activity in patients with chronic HCV infection. However, in clinical trials, drug-resistant variants emerge at frequencies of 5 to 20% of the total virus population as early as the second day after the beginning of treatment. Here, using probabilistic and viral dynamic models, we show that such rapid emergence of drug resistance is expected. We calculate that all possible single- and double-mutant viruses preexist before treatment and that one additional mutation is expected to arise during therapy. Examining data from a clinical trial of telaprevir therapy for HCV infection in detail, we show that our model fits the observed dynamics of both drug-sensitive and drug-resistant viruses and argue that therapy with only direct antivirals will require drug combinations that have a genetic barrier of three to four mutations. (Received September 13, 2010)