1107-92-430 Claus T Kadelka* (ckadelka@vt.edu), Seda Arat, Ross Donatelli, Marschall Furman, Madeleine Weinstein, Chris Heinen and Reinhard Laubenbacher. The regulatory effect of microRNAs on the DNA mismatch repair pathway.

Although failure of DNA Mismatch Repair (MMR) is associated with microsatellite instability and colorectal cancer, little is known about MMR except for its biochemical pathway. By assembling known regulatory interactions, we introduce a novel gene regulatory network of MMR, which uses a recently introduced time- and state-discrete modeling framework that accounts for the cell's inherent stochasticity. This model provides phenotypic predictions for MMR's response to hypoxia and DNA damage. By showing that overexpressing microRNAs increases robustness while knocking them out seems to have the opposite effect, we substantiate the hypothesis that microRNAs can stabilize network dynamics, thus enhancing genomic stability. In addition to providing a gene regulatory network of MMR, our model yields experimentally verifiable predictions and enables further analysis of the potential stabilizing effect of microRNAs on dynamics of biological networks. (Received January 20, 2015)