1099-92-164 **Rossitza N. Irobalieva** (irobalie@bcm.edu), **Jonathan M. Fogg** (fogg@bcm.edu), **Daniel J. Catanese, Jr.**, **Anna K. Barker** (anna.barker@bcm.edu), **Michael F. Schmid** (mschmid@bcm.edu), **Wah Chiu** (wah@bcm.edu) and **Lynn Zechiedrich*** (elz@bcm.edu), One Baylor Plaza, Mail-stop: BCM-280, Baylor College of Medicine, Houston, TX 77030. *How linking number affects the structure and reactivity of DNA.* Preliminary report.

The negatively charged sugar-phosphate backbone contains no genetic information yet forms the accessible exterior of the DNA double helix. Hydrophobic bases, the readout of the genetic code, are buried within the interior of the helix. We hypothesized that the seemingly contradictory requirements of DNA stability and readout are accomplished via a tightly-regulated switch whereby torsional strain causes localized structural alterations, including base-flipping, denaturation, and other non-B-DNA structures. Molecular dynamic simulations had indicated that our hypothesis was correct (Randall, G.L., Zechiedrich, L., and Pettitt, B.M. (2009) Nucleic Acids Res 37, 5568), but it had never been tested directly. Using tiny, closed circles of DNA, we demonstrate that the structural alterations brought about by torsional stress, base-flipping and denaturation in the underwound, negatively supercoiled direction, and likely inside-out Pauling-like DNA in the overwound, positively supercoiled direction, facilitate access to the genetic code to initiate DNA readout. Funded by NIH T90DK070121 (R.N.I.), NIH P41RR02250 (W.C.), and NIH R01AI054830 and the Human Frontier Science Program (L.Z.). (Received February 06, 2014)