Always on Guard: Spontaneous Bursts of p53 in Cycling Cells

Alexander Loewer, Eric Batchelor, Giorgio Gaglia and Galit Lahav

Department of Systems Biology, Harvard Medical School, Boston, MA 02115, USA

THE tumor suppressor protein p53 is activated by stress and leads to cellular outcomes such as apoptosis and cell cycle arrest. Its activation must be highly sensitive to ensure that cells react appropriately to damage. However, proliferating cells often encounter transient damage during normal growth, where cell cycle arrest or apoptosis may be unfavorable. How does the p53 pathway achieve the right balance between high sensitivity and tolerance to intrinsic damage? Using quantitative time-lapse microscopy of individual human cells we found that proliferating cells show spontaneous pulses of p53, which are triggered by an excitable mechanism during cell cycle phases associated with intrinsic DNA damage. However, in the absence of sustained damage, post-translational modifications keep p53 inactive, preventing it from inducing p21 expression and cell cycle arrest. Our approach of quantifying basal dynamics in individual cells can now be used to study how other pathways in human cells achieve sensitivity in noisy environments.