

P006 Dephosphorylation of tyrosine-phosphorylated H2AX regulates apoptosis and cell survival decisions
Peter J. Cook^{1,2}, Bong Gun Ju^{1,3}, Francesca Telese¹, Xiangting Wang¹, Christopher K. Glass⁶, and Michael G. Rosenfeld^{1,5,#}

¹ Howard Hughes Medical Institute, School of Medicine, University of California, San Diego

² Department of Biology Graduate Program, School of Medicine, University of California, San Diego

³ Department of Life Science, Sogang University, Seoul 121-742, Korea

⁵ Department of Cellular and Molecular Medicine, School of Medicine, University of California, San Diego, 9500 Gilman Drive, La Jolla, California 92093

Life and death fate decisions allow cells to avoid massive apoptotic death in response to genotoxic stress. While much of the regulatory mechanism controlling DNA damage/repair and apoptosis is well characterized, the precise molecular strategies that adjudicate DNA repair or apoptosis remain incompletely understood. Here, we report that a nuclear protein tyrosine phosphatase is involved in promoting effective DNA damage repair over apoptosis in response to genotoxic stress in specific tissue/cell types by executing a damage-signal dependent dephosphorylation of an H2AX C-terminal tyrosine phosphate (Y142). This post-translational modification modulates the ability of γ H2AX to function as an active determinant of repair/survival versus apoptotic responses to DNA damage through differential recruitment of either DNA repair or pro-apoptotic factors, revealing a dual phosphorylation/phosphatase H2AX-dependent binary switch that modulates survival/cell death decisions during mammalian organogenesis.