Expanding the Mitochondrial Links to the DNA Damage Response

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M.A. De la Rosa[I], K. González-Arzola[I], A. Guerra-Castellano[I], S.M. García-Mauriño[I], C. Elena-Real[I], F. Rivero-Rodríguez[I], A. Velázquez-Cruz[I], S. Curran[I], A. Díaz-Quintana[I], I. Díaz-Moreno[I]

[I]IIQ - cicCartuja, Universidad de Sevilla & CSIC, Sevilla, Spain

Genome integrity is constantly battered by genotoxic agents. These can induce DNA damage that leads to cell death if not properly repaired. Most studies on the DNA repair process have focused on yeast and mammals, in which histone chaperones have been revealed as key regulators for DNA to be accessible to repair machinery. However, knowledge of their exact role in DNA damage response is far from complete, in particular in plants. Our recent studies reveal that the closely related histone chaperones human SET/TAF-Iβ and plant NRP1 are similarly involved in nucleosome assembly following DNA break in humans and plants, respectively [1,2], and that both histone chaperones interact with cytochrome c in the cell nucleus upon DNA damage. We have used Nuclear Magnetic Resonance (NMR), Isothermal Titration Calorimetry (ITC), Surface Plasmon Resonance (SPR) and Molecular Docking (MD) to provide a structural insight into the complex formed by cytochrome c with each histone chaperone. Cytochrome c competitively hinders the binding of SET/TAF-Iβ and NRP1 to core histones, thus locking their histone binding domains and inhibiting their nucleosome assembly activities [1,2]. These findings also indicate that the underlying molecular mechanism of nucleosome disassembly/reassembly needed for DNA repair is highly conserved throughout evolution.

References:
[1] González-Arzola K. et al. (2015) Proc. Natl. Acad. Sci. USA 112, 9908-9913
[2] González-Arzola K. et al. (2017) Nucleic Acids Res. 45, 2150–2165