MedicalXpress

How cells remodel after UV radiation

December 19 2013

Researchers at the University of California, San Diego School of Medicine, with colleagues in The Netherlands and United Kingdom, have produced the first map detailing the network of genetic interactions underlying the cellular response to ultraviolet (UV) radiation.

The researchers say their study establishes a new method and resource for exploring in greater detail how cells are damaged by UV radiation and how they repair themselves. UV damage is one route to malignancy, especially in skin cancer, and understanding the underlying repair pathways will better help scientists to understand what goes wrong in such cancers.

The findings will be published in the December 26, 2013 issue of *Cell Reports*.

Principal investigator Trey Ideker, PhD, division chief of genetics in the UC San Diego School of Medicine and a professor in the UC San Diego Departments of Medicine and Bioengineering, and colleagues mapped 89 UV-induced functional interactions among 62 protein complexes. The interactions were culled from a larger measurement of more than 45,000 double mutants, the deletion of two separate genes, before and after different doses of UV radiation.

Specifically, they identified interactive links to the cell's chromatin structure remodeling (RSC) complex, a grouping of protein subunits that remodel chromatin – the combination of DNA and proteins that make up a cell's nucleus – during cell mitosis or division. "We show that RSC

is recruited to places on genes or DNA sequences where UV damage has occurred and that it helps facilitate efficient repair by promoting nucleosome remodeling," said Ideker.

The process of repairing DNA damage caused by UV radiation and other sources, such as chemicals and other mutagens, is both simple and complicated. DNA-distorting lesions are detected by a cellular mechanism called the nucleotide excision repair (NER) pathway. The lesion is excised; the gap filled with new genetic material copied from an intact DNA strand by special enzymes; and the remaining nick sealed by another specialized enzyme.

However, NER does not work in isolation; rather it coordinates with other biological mechanisms, including RSC.

"DNA isn't free-floating in the cell, but is packaged into a tight structure called chromatin, which is DNA wound around proteins," said Rohith Srivas, PhD, a former research scientist in Ideker's lab and the study's first author. "In order for repair factors to fix DNA damage, they need access to naked DNA. This is where chromatin remodelers come in: In theory, they can be recruited to the DNA, open it up and allow repair factors to do their job."

Rohith said that other scientists have previously identified complexes that perform this role following UV damage. "Our results are novel because they show RSC is connected to both UV damage pathways: transcription coupled repair – which acts on parts of DNA being expressed – and global genome repair, which acts everywhere. All previous remodelers were linked only to global genome repair."

The scientists noted that the degree of genetic rewiring correlates with the dose of UV. Reparative interactions were observed at distinct low or high doses of UV, but not both. While genetic interactions at higher

doses is not surprising, the authors said, the findings suggest low-dose UV radiation prompts specific interactions as well.

Provided by University of California - San Diego