

**Report 77:** Emerging research areas and technologies at the interface of DNA repair and environmental health

**Convener:** Scott Williams

**Brief History:**

Our genomes are continually damaged as cells duplicate their chromosomes, and as a consequence of oxidation, environmental exposure to chemicals and DNA-damaging radiation. Oxidative DNA damage from reactive oxygen species, during inflammation, or upon exposure to environmental agents poses threats to all cell types. Ionizing radiation and non-ionizing radiation from external sources such as diagnostic X-rays further mount a constant assault on our genomes. As a first line of defense, the cellular DNA repair machinery recognizes perturbations and responds to DNA damage with initiation of multifaceted responses. We aimed to identify research priorities and emerging areas to maintain the NIEHS at the forefront of the integrated study of DNA repair and genome maintenance, and its impacts on environmental health.

**Discussion Highlights:**

- The cellular DNA repair machinery is a critical modulator of environment induced disease. Perturbations in DNA repair can contribute to susceptibility to exposures. Also, environmental factors have the capacity to modulate DNA repair, and are poorly understood.
- DNA damage responses to environmental exposures are multi-level. These involve not only the recognition and enzymatic repair of damaged DNA, but complex and poorly understood cellular signaling, epigenetic modifications to chromatin, and dynamic assembly and disassembly of multi-protein repair and signaling complexes. The impacts of epigenetic marks on DNA repair, and the establishment of marks in chromatin are ill-defined.
- Non-coding RNAs in regulation DNA damage response was mentioned as a possible unknown.
- Many DNA repair genes are impacted by mutations that increase cancer risk and are linked to neurodegenerative disorders, but the roles for DNA repair capacity variation in complex diseases (eg Autism, PD) is unknown.
- There are possible undefined links between nutrition and aging and their impacts on cellular energetics (e.g. ATP and nucleotide pools) on the efficiency of DNA repair.

**Recommendations:**

- It will be key to promote multilevel studies, from basic molecular mechanisms to understand DNA repair enzymology, to utilizing systems biology and proteomic studies to better define global cellular DNA damage responses.

- The DNA repair response in the context of chromatin and the impacts of epigenetic (eg Histone modifications) is in its infancy. A detailed understanding DNA repair in global chromosome architecture is needed.
- Support of enabling technologies (next gen sequencing, quantum dot technologies mentioned) will be required to support integrated approaches.

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