What is the DNA Damage Response?

Our DNA is under constant threat of damage from a variety of physical and chemical sources. From the natural byproducts created when we digest food to ultraviolet light from the sun, a multitude of factors can react with our DNA and cause chemical changes. Some risk factors for DNA damage – such as smoking cigarettes – can be eliminated, but others cannot.

If left unchecked, chemical changes to DNA can have severe health consequences, leading to cancer and other diseases related to cell growth. But cells are equipped with multiple mechanisms to counteract DNA damage. If detected, damaged DNA can be repaired by molecular machinery found in cells. These molecular tools can remove or restore the damaged portion of DNA.

Getting the right tools to fix DNA in the right place and at the right time is a delicate process that has to be carefully calibrated and choreographed within every cell. The DNA Damage Response (DDR) refers to the pathway that senses DNA damage and sets in motion the needed steps to repair and protect DNA.

Today, much is known about how the DDR controls DNA repair, and these insights have led to a better understanding of the health consequences when steps in this process go awry. But several decades ago, much of how this process works remained a mystery. In the 1940s, Dr. Evelyn Witkin discovered bacteria that were resistant to the damaging effects of UV light. Her discovery revealed a critical, cell division "checkpoint" that prevents bacterial cells from giving rise to daughter cells until their DNA has been repaired. In the 1980s, Dr. Stephen J. Elledge pursued a DNA damage-responsive pathway in more complex organisms, uncovering a signal transduction pathway that sensed alterations in DNA and broadcast that information throughout the organism to optimize survival. His discoveries led to an understanding of how human cells maintain stability of their genomes to prevent diseases such as cancer and neurodegeneration.

Dr. Witkin and Dr. Elledge's contributions to the field over careers that have spanned many decades have laid the foundation for the current understanding of the DDR. Today, research teams all over the world, including Dr. Elledge's lab at Brigham and Women's Hospital and Harvard Medical School, are continuing to uncover new components related to the DNA damage and DNA replication regulatory pathways, and are exploring how these pathways could inform cancer therapies in the future.