DNA repair award highlights critical disease research

In the multidisciplinary world of the sciences, the most famed award for researchers is the Nobel prize. A less-recognized award, but high-profile nonetheless is the Albert Lasker Basic Medical Research Award. This award is for those who have helped in “understanding, diagnosis, treatment, cure, or prevention of human disease.” The current honorees to share the award, Evelyn Witkin and Stephen Elledge, both performed vital research in understanding DNA repair in bacteria and the relationship between DNA repair and aging, human birth defects, and cancer.

The dean of Harvard Medical School Jeffrey Flier said of the work that these “insights into the basic mechanisms of the DNA damage response have profoundly enriched our understanding not only of the fundamental genetics of all cellular life, but also of how we conceptualize many diseases and conditions, especially cancer.”

So what’s going on within the DNA repair?

dna repair Image not found or type unknown When DNA has been damaged, repair mechanisms can begin which help to ameliorate the damage. However, in some cases of increased severity, a cell’s damaged DNA is prevented from creating repeated erroneous copies by a pathway that leads either to its death (apoptosis) or senescence which renders it unable to reproduce further copies, and this is where the work of one of the honorees, Harvard geneticist Stephen Elledge, comes in.

Our cells are constantly undergoing changes and challenges from the environment, either from ultraviolet light, certain chemicals in food (including fully natural chemical components), smoke, and even free radical damage resulting from metabolism. DNA polymerases can remove and replace nucleotides that are in the wrong location during copying so that errors don’t persist. But this isn’t foolproof. Not only that, but it has been estimated that an individual cell can incur over one million DNA changes per day. It becomes a probability game — it is estimated that there is about one uncorrected DNA error on a particular chromosomal locus per 10,000 to 1,000,000 gametes. In isolation this is very low, however with the number of genes present, it makes the occurrence of genetic errors a certainty. Organisms have developed inspection mechanisms in addition to repair mechanisms. There are review checkpoints of DNA directly prior to replication to prevent accumulated errors which can end up as mutations within the DNA.

Unfortunately, the senescent state sends out chemical signals which triggers inflammation via the immune system and is also implicated in some effects of aging. This connection to aging has also formed some of the underpinnings of conceptual links between particular cellular aging mechanisms to certain diseases, including cancers. There are also some pediatric diseases which are caused by DNA repair systems that are faulty, and this foundational research has provided a better theoretical basis for understanding its causes.

One part humbleness, two parts providence

One thing that's been part of the canon within the various fields of science ever since rigorous experimentation was undertaken by people, is that very often, major paradigm shifts in thinking come from divergent thought processes, unexpected findings, and exploring hypotheses which seem perhaps unlikely at first. It's no different with the work of the other researcher to share in this prize, Evelyn Witkin. Her research on the DNA repair within bacteria left a trail of knowledge which Elledge picked up largely by accident decades later. He was working with yeast cells, and then when studying DNA repair in bacteria (Witkin's research), he found an interesting protein that seemed to be secreted by cells when their DNA copies became error-prone. Elledge had no intention of pursuing this finding, thinking it was nothing more than a novelty at first. But this discovery led to identifying the pathway that a problematic cell undergoes, including the protein used to communicate to the immune system its declining status.

Ben Locwin, Ph.D., M.B.A., M.S. is a contributor to the Genetic Literacy Project and is an author of a wide variety of scientific articles for books and magazines. He is also a consultant for a many industries including biological sciences, pharmaceutical, psychological, and academic. Follow him at @BenLocwin.