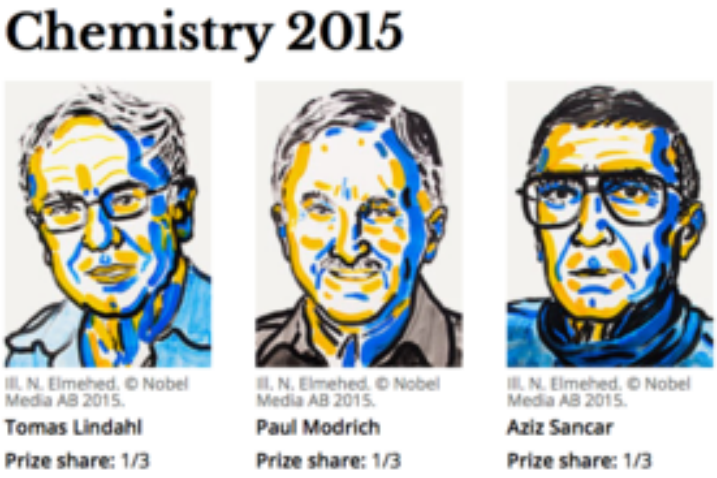
Discovery of DNA Repair Methods Wins 2015 Chemistry Nobel Prize

Three scientists who found ways that cells fix damaged DNA—staving off cancer and other diseases—have won this year's prize

By Josh Fischman October 7, 2015



There are three reasons we are not constantly riddled with cancer, and today the scientists who discovered those reasons—three ways that cells repair damaged DNA that can ruin bodies--won the 2015 Nobel Prize for Chemistry.

This morning The Royal Swedish Academy of Sciences announced the coveted prize is going to Tomas Lindahl from the Francis Crick Institute and Clare Hall Laboratory in Hertfordshire, England; Paul Modrich from the Howard Hughes Medical Institute and Duke University School of Medicine in North Carolina in the United States; and Aziz Sancar from the University of North Carolina in Chapel Hill, also in the U.S. "I know, over the years, that I'd been mentioned for the prize," Lindahl said in a telephone call to the academy. "But hundreds of people get considered every year so I feel very lucky."

He and the other two researchers, working independently over the last 40 years, described three different mechanisms that create errors in DNA—the molecule that controls cell behavior—and the different ways that chemical and biological processes fix many of these problems.

"All forms of cancer start with DNA damage," said biochemist Claes Gustafsson, one member of the Nobel chemistry committee. "If you do not have DNA repair, we would have a lot more cancer. That's how important this is." He added that

the repair techniques let us understand how cigarette smoke, sunlight, and even mundane substances like water can damage DNA and point to ways that the damage can be rectified.

It is not just about cancer, Diane Grob Schmidt, president of the American Chemical Society, told *Scientific American* in an interview. “The understanding that we have of these mechanisms help us design drugs to repair all sorts of DNA errors,” she said. There are also several genetic diseases caused by the inability of cells to fix DNA properly, for instance, and work on the repair methods aids understanding of these ailments and how to treat them.

The discoveries illustrate the crucial and central role of chemistry, Schmidt added. “These mechanisms are fundamentally about the making and breaking of chemical bonds,” she said.

Scientists used to believe that DNA molecules were extremely stable. After all, they had to reliably transmit genetic information from generation down to generation. Then in the 1970s Lindahl demonstrated that the neat double helix and its components constantly decay. Every day, hundreds of those components, the DNA building block chemicals abbreviated as A, T, C, and G, get knocked out of their places. If the process continued unabated, the development of life on Earth would have been impossible. This insight led Lindahl to discover a series of enzymes and reactions, called *base excision repair*, which constantly works to fight this decay. The C building block, for instance, is repeatedly broken down into another molecule that should not be in DNA. The enzymes Lindahl found identify that broken molecule and rebuild it into a C.

Sancar found that cells use another technique to repair damage to DNA caused by ultraviolet light, the same thing that gives you a sunburn. This DNA fix is called nucleotide excision repair. People born with defects in this repair system will develop skin cancer if they are exposed to sunlight. Excision enzymes cut out the DNA lesions. The cell also uses this repair system to correct DNA damage people get after they are born, when they encounter mutagenic substances.

Finally, Modrich found out how a cell corrects errors that occur during a vital biological process: Cell division, when DNA is replicated. This copying process is supposed to produce identical strands of DNA but often there are stretches of the new stand that do not match up. The set of cellular chemicals that Modrich found, a complex called mismatch repair, scans the strands and fixes them, reducing the error frequency during replication by about a thousand times during each replication cycle.

“Without all of these repair mechanisms.” Lindahl said, “we would not be long-lived.” For finding them, he and the two other scientists will split $1 million dollars in three equal shares.