The Petals of Cancer

By Diego Anguiano

Cancer. What is cancer? Cancer is a genetic mistake in our DNA that causes mutations to occur in the proteins that build our body. Some of these mutations in proteins will lead to cancers, such as the brain cancer glioblastoma. Being able to cure diseases such as glioblastoma is important because they are almost always fatal. For example, glioblastoma has a 5-year survival rate of 4.7% and a median survival rate of 14 months (Adamson et al., 2009). Knowing how to fix DNA and the proteins that are produced from it, are key to understanding cancer.

Fixing problems in DNA is important because it is the blueprint of life, in that it contains everything you need to make an organism: be it a plant, a lizard, a fungus, or a human being. The DNA of each organism is uniquely capable of building that organism. And this construction machinery is organized in several forms of 3-dimensional structures called chromatin.

Chromatin is formed by nucleosomes. These nucleosomes each contain eight histone proteins that help wrap DNA into a compact form. Altering the way histones bind to DNA can affect whether or not genes are expressed. Thus, when histones are affected it is called "epigenetic modification," which are defined as changes that affect the expression of a gene without changing the actual DNA sequence. Epigenetic modifications are akin to adding or taking something away, for example removing petals from a flower or adding color to a black and white picture on a computer software. Some of these changes may be permanent (removing petals from a flower) while others may only be temporary (you can undo something on a computer software).

Sometimes errors can occur during epigenetic modification, perhaps a little too many petals are pulled. In the case of histones, mistakes can be a more dangerous event. For example, an error

in one of the eight histone proteins may result in changes in gene expression associated with cancer, including glioblastoma (Adamson et al., 2009; Yuen & Knoepfler, 2013).

A key goal of my research is to help understand how epigenetic errors occur in glioblastoma. And in glioblastoma, eleven percent contain a histone mutation, while pediatric cases contain a mutation 70-80% on one of the eight histone proteins: histone H3.3.

My research goal is to pinpoint the biological role played by histone H3.3 to present new avenues of cancer treatment and to aid our fundamental knowledge of glioblastoma. I have designed a virus that can tell a brain cell to produce histone H3.3. Why would I want a brain cell to produce more histone H3.3? Because cancer cells in the brain do the same thing, they make more H3.3 protein than necessary. My hope is that by causing brain cells to produce more of a protein—in the controlled environment of a laboratory—I'll be able to characterize the role of histone H3.3. For example, to better understand how increasing H3.3 affects chromatin structure and gene expression. And to define what genes are expressed inappropriately in glioblastoma patients. I hope that one day, this gained knowledge, along with the knowledge of thousands of scientists, will produce treatments that will save millions of lives.

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