September 19, 2012

Broken genes: the role of DNA repair in preventing cancer

Introduction:

DNA serves as the blueprint for all living organisms on earth, but unlike most blueprints, DNA is constantly being damaged and repaired. Factors such as UV light from the sun and chemicals in cigarette smoke damage our DNA daily. Luckily, our cells contain intricate molecular machines that repair DNA damage. These DNA repair machines occasionally make mistakes, leading to permanent changes in the DNA, or mutations—the ultimate cause of cancer. This seminar will use examples of hereditary forms of cancer to show that while DNA is a source of cellular information, it is also a large chemical structure that is continually being modified and repaired. When that process is defective, mutations and cancer arise. We will end by introducing how scientists can use new discoveries about DNA damage and repair to develop more effective cancer treatments.

Speakers:

Jacob Sargent is a 2nd year PhD student in Harvard-MIT Health Sciences and Technology program. As a member of the Loparo lab, he is working to create a kinetic assay for DNA base excision repair. Jacob grew up in Bainbridge Island and studied at Rice University before working as a high school science teacher, coach, and dorm parent for four years. Outside of the lab, he enjoys running, cycling, rock-climbing, dancing, and baking...a long list to which he loves to add things.

Ben Morris is a 4th year PhD student in the Biological and Biomedical Sciences graduate program. He uses frog egg extracts to study how cells keep their genomes error-free in Johannes Walter’s lab. Ben graduated in 2009 from Harvard College with a BA in Molecular and Cellular Biology and a minor in English. As an undergraduate, he played a number of patter baritone parts in Gilbert and Sullivan operettas. He is compelled by the potential for theater to educate and affect and is exploring ways to bring scientific material to theater audiences.

Thomas Graham is a 3rd year PhD student in the Systems Biology Ph.D. program. In Joe Loparo and Johannes Walter’s labs, Thomas is working to develop new single-molecule fluorescence methods to watch double-strand break repair happening on individual molecules of DNA. A native of Chicago, Thomas double-majored in chemistry and biological sciences at the University of Chicago, and he completed an MPhil degree in chemistry at the University of Cambridge. Outside of lab, he enjoys jogging, hiking, reading, and playing the piano and pipe organ.
Glossary of Important Terms:

**Genome** - set of instructions detailing how to make all the proteins within a cell.

**DNA (deoxyribonucleic acid)** - the language of the genome. It is a molecule located within the nucleus of a cell that stores genetic information and codes instructions for how to build proteins.

**Gene** - a segment of DNA that has all of the information to make one protein.

**Protein** - a molecule, encoded by the DNA, that carries out a particular function within a cell.

**Mutation** - a change in the DNA code that can be inherited and is caused by external insults, such as UV light, or spontaneously accumulated due to errors in DNA replication.

**Mutagen** - any factor that can cause mutations, i.e. UV rays are a mutagen.

**Cancer** - a broad group of diseases characterized by uncontrolled cellular proliferation as a result of mutations in the genome.

**Cell cycle** - the life of a cell, during which it carries out its function, copies its genome, and divides to produce two duplicate cells. These events are tightly controlled by proteins acting as growth brakes or accelerators.

**Rb (retinoblastoma)** - a gene encoding a protein that suppresses cell division. Mutations in this gene produce a non-functional protein, resulting in a cancer that is also called “retinoblastoma.”

**Chronic Myelogenous Leukemia (CML)** - a cancer of the bone marrow in which white blood cells grow uncontrollably. CML is caused by a mutation that fuses two genes, Bcr and Bcr and Abl.

**Fanconi Anemia** - a genetic disease that predisposes a person to cancer by mutating DNA repair proteins.

**DNA interstrand crosslink** - an inappropriate connection between two strands of the DNA helix that prevents it from being unwound for replication.

**Chemotherapy** - cancer treatment that includes toxins that preferentially kill rapidly dividing cells to selectively target cancer cells. Older definitions included any chemical therapy used to treat cancer.

**PARP (poly ADP-ribose polymerase)** - a protein “flagging” DNA single-strand breaks for repair.

**Targeted therapy** - therapy that activates or stops the activity a specific molecule to block the growth of cancer cells.

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