Dartmouth Scientists Pinpoint "Blueprint" for Rare & Aggressive Cancer

By Nora Al Baghdadi

A comprehensive cancer study at Dartmouth College recently paid off in a big way, when scientists finally unraveled the fatal mysteries behind a rare form of cancer. Dr. Gregory Tsongalis led a team of eighteen researchers in investigating a variety of epithelial neoplasms, also known as tumors of the appendix. Their eventual discovery could make it possible to prevent, treat and even cure types of appendix cancer that were once a death sentence.

The Geisel School of Medicine revealed the promising news on May 12, 2014, when they announced that the scientists identified the genetic blueprint for cancers of the appendix. Appendix tumors can cause serious and debilitating side effects, and unless doctors can predict they ways in which cancerous cells can mutate, they can't implement an effective course of action against them.

Dartmouth harnessed the power of next-generation DNA sequencing to profile the molecular and genetic structures of individual tumors. The scientists collected tissue samples and used the Ion AmpliSeq™ Cancer Panel, a one-of-a-kind research tool that the College already uses for colon, skin and lung cancer, to screen and sequence each of these samples.

This study actually marked the very first time that anyone has employed multi-gene panels in their efforts to develop specific, targeted treatment therapy. The scientists' unconventional methodology would soon transform the medical definitions and understandings of tumors of the appendix. They almost immediately began to recognize and analyze identical mutations in various sample types, which suggested to them that the most serious and aggressive forms of cancer might share the same gene mutations and therefore respond the same way to targeted treatments.

For example, the researchers genetically mapped the same mutations in three different types of*adenocarcinoma*, which is a type of cancer that affects mucus-secreting glands. Adenocarcinoma tumors occur throughout the body, and they cause extreme discomfort by using the body's natural moisture production in order to increase their excretion throughout the body. This very rare cancer grows slowly but surely inside the appendix, and often isn't diagnosed until it's far too late for treatment.

The Dartmouth innovators also discovered the molecular makeup of *pseudomyxoma peritonea* (PMP), which doesn't just attack the body's healthy cells; it rapidly multiplies cancerous cells along the abdomen wall and crushes the body's critical digestive organs. After studying almost forty different tissue samples from these aggressive tumors, scientists verified that low-grade appendiceal mucinous neoplasm (LAMN), an early stage of the disease, can genetically mutate into either one of its more serious and untreatable types.

According to the study that Dartmouth published in the peer-reviewed journal *Clinical Chemistry*, very little was known about how these tumors mutated or responded to treatment. Until now, patients with appendix cancer had no specialized chemotherapy regiments available to them, but that will change soon, thanks to the discovery of these key somatic mutations.

Tsongalis, who spearheaded the study and continues to explore its treatment implications, directs the Molecular Pathology department at Dartmouth-Hitchcock Norris Cotton Cancer Center. The center is one of only 41 in the country that the National Cancer Institute (NCI) recognizes as a comprehensive care center. It incorporates a dozen partner hospitals, advanced research facilities, and options for both inpatient and outpatient treatments.

Doctors and researchers can now get to work developing their own treatment plans for these specific mutations. In their abstract, the scientists emphasized the importance of examining each tumor on an individual level, which was crucial to their study's success. While appendix cancer only affects between 600 and 1,000 people in the United States every year, there's no way to prevent it and treatments usually include invasive procedures with high risks of infection. Dartmouth College's latest discovery will help patients avoid some of these risks, and it will pave the way for future researchers to better understand more common forms of cancer as well.