The Chordoma Genome Project

uncovering the root cause of chordoma

The Chordoma Foundation is spearheading the Chordoma Genome Project to systematically discover the underlying genetic changes that drive chordoma, and that could provide clues to guide the development of new treatment.

Changes in DNA can guide treatment

Cancer is caused by changes, known as mutations, in a cell's DNA that cause the cell to multiply out of control. By identifying these mutations, scientists gain valuable insight into the mechanisms by which a cancer survives and proliferates. Identifying the mutations that cause chordoma would quickly focus research efforts on the highest value targets, and would provide a starting point for developing new targeted treatments, or even repurposing already-approved drugs.

Understanding DNA

A cell's DNA consists of four different chemicals, each representing a different letter, strung together in a chain that is three billion letters long. This four-letter alphabet forms an instruction book called the *genome* that governs how the cells behave. Every cell in the body contains a copy of the same genome but different types of cells read different sections. Alterations in the genome can cause the cell to misbehave, and become cancerous. These alterations can involve misspelling a single letter, deleting a word, duplicating pages, or even removing whole chapters. Identifying all of these changes in a cancer genome gives a complete picture of the underlying cause of that particular cancer.

Scientists believe that reading (known as *sequencing*) the full genome is the quickest path towards developing new targeted treatments for cancers like chordoma. Until recently it was not possible to sequence whole genomes and scientists could only read a few thousand letters a time. In fact, it took $3 billion from 1990-2003 to sequence the first full genome. Since then sequencing technology has evolved at a staggering rate to the point where a full genome can be sequenced for under $100,000. At this price, efforts have begun to sequence full genomes for breast, lung, pancreatic, and other cancers. As costs decrease over the next 5-10 years, eventually this analysis will be done on every type of cancer.

Unfortunately, full genome sequencing currently remains cost-prohibitive for the Chordoma Foundation. But there is a very good short-term alternative. Surprisingly, the regions of DNA that give instructions to the cell (called *exons*) account for only about %1.5 of the 3-billion-letter human genome. Therefore sequencing all the exons (called the *exome*), provides a good survey of the most likely cancer-causing abnormalities.

Cutting-edge collaborative science

The Chordoma Genome Project will involve several different complementary types of genomic analysis, representing the most in-depth study of this or any other rare cancer ever conducted. To identify cancer-causing mutations, scientists must compare tumor DNA to normal DNA from the same individuals. This type of experiment requires very high quality DNA, which is not possible to obtain from most existing tumor samples. Thankfully, Dr. Adrienne Flanagan at the University College London (UCL) has collected tumor samples and normal DNA that are suitable for whole genome-sequencing.

The Chordoma Genome Project will involve collaboration between Dr. Flanagan and genomics experts at the National Human Genome Research Institute (NHGRI) in the US, and the Sanger Institute in Cambridge, England – two of the most renowned genomics centers in the world. NHGRI led the sequencing of the first human genome, and the Sanger Institute currently has the largest and most advanced set of sequencing machines in the world.

Importantly, data that is generated will be placed in the public domain so that all scientists interested in chordoma can bring their expertise to bear on this disease. Given the novelty of whole exome sequencing, the results will likely produce discoveries that could attract more widespread interest in chordoma, and larger amounts of research funding. Furthermore, this project could identify new cancer-causing genes which would have widespread impact for other types of cancer.

Implementation

The Chordoma Genome Project will be carried out in phases over several years, and will eventually include full genome sequencing. The first phase will involve whole exome sequencing of 10 chordomas, as well as more targeted sequencing of specific genes of interest in 25 chordomas. The Chordoma Foundation is currently seeking to raise $250,000 to fund the first phase of the Chordoma Genome Project. The project will start as soon as we provide funding and data will be generated within a few months. You are invited to take part in finding a cure for chordoma by investing in this groundbreaking research.