Scientists identify critical protein complex in formation of cell cilia

August 19 2008

An international team led by NYU Cancer Institute have identified a protein complex that regulates the formation of cilia, which are found on virtually all mature human cells and are essential to normal cell function.

The new report, published this week by *Developmental Cell* and selected as the featured publication of the open-access online edition, describes how three proteins work together to regulate the formation of primary cilia. The study led by Brian Dynlacht, Ph.D., professor of pathology and director of NYU Cancer Institute Genomics Facility, investigates these antenna-like structures, once thought to be vestigial remnants of cell evolution, which have recently emerged as a focal point of research in developmental cell biology.

"We are trying to understand the regulation of processes that are fundamental to normal cell development and health in humans," said William Y. Tsang, Ph.D., of the NYU School of Medicine and Cancer Institute, and first author of the paper. "Defective cilia are implicated in a wide range of serious illnesses such as polycystic kidney disease, retinal degeneration, and neurological disorders. Inappropriate activation of signaling molecules that normally reside at the primary cilium, may lead to certain cancers."

At the center of the process lies the protein CEP290, which normally promotes primary cilia formation in mature cells. Dr. Tsang and his colleagues discovered that a second protein, CP110, normally suppresses the function of CEP290 until cells are fully mature. At that point, CP110

is destroyed, freeing CEP290 to interact with a third protein, Rab8a, to promote cilia formation on the surface of the mature cell.

The team's findings may help to identify potential targets for future drug design.

"Ciliogenesis is a fundamental process. These structures are found in almost every type of human cell you can imagine," Dr. Tsang said. "If we can ever design drugs that will restore the formation and function of cilia even in the presence of CEP290 mutations, then that would be one way to cure the defects that lead to ciliary diseases."

Research so far has been using in vitro human cell lines. However, team members from the University of Michigan and National Eye Institute have developed a mouse model with a CEP290 mutation implicated in retinal degeneration, and the NYU group is planning a study of human CEP290 mutations to see if they can correlate genotypes to their expression in specific ciliary diseases.

Source: NYU Langone Medical Center / New York University School of Medicine