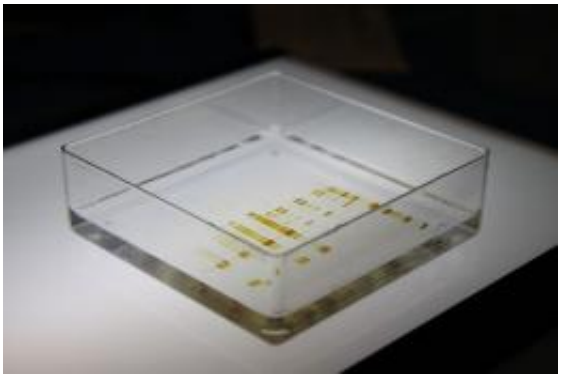
New characteristics of premature aging protein discovered

November 16 2010



Glavy Lab gel culture

(PhysOrg.com) -- Dr. Joseph Glavy at Stevens Institute of Technology studies the smallest and most basic elements of life. The Assistant Professor of Chemical Biology runs the Glavy Lab, where advanced student scientists study the nuclear pore complexes (NPCs) in cells, observing the minutest mechanisms of life as they unfold during mitosis. The Glavy Lab's formal purpose is to study the NPC at the molecular level in the pursuit of the unknown or unexpected in the well-studied but not always well-understood nuclei of living cells.

His team has uncovered a disease-related protein outside of its known range and published the results in the August 2010 issue of Cell Cycle. The article's co-authors, Dr. Simarna Kaur, Tommy White, and Amanda DiGuilio are current or recent students of Stevens Institute of

Technology.

The NPC is a supramolecular assembly that provides gateways for molecular trafficking between DNA with a cell's nucleus and the cytoplasm within the cell membrane walls in eukaryotic cells. Protein, RNA, ions, and other small molecules are transported through the NPC on their way into the nucleus. The composition of the NPC is about thirty proteins, called nucleoporins (Nups), which are arranged quasi-symmetrically and in subcomplexes that break apart during mitosis in some cells.

Dr. Glavy investigated interactions within the NPC of mammalian cells while a post-doctoral researcher at Rockefeller University in New York City. Unlike other living cells, the mammalian cell NPC breaks down around DNA during mitosis, allowing specific Nup subcomplexes to be isolated and studied in the lab, but also leaving room for something to go wrong in the reorganization of the nucleus . Focused on the very specific Nup 107-160 subcomplex, the Glavy Lab had been looking for what might go wrong during mitosis.

But rather than genetic mutations, the lab discovered something far more important within Nup 107-160: the Werner Helicase Interacting Protein 1 (WHIP). WHIP's moniker derives from its interaction with Werner protein, which maintains genome stability and conversely is responsible for the progeria disease Werner's Syndrome. This adult-onset disease causes premature aging and increased susceptibility to other old-age diseases such as cancer, heart disease, and diabetes.

The initial discovery of WHIP within the NPC, when it had been associated with the Werner protein, prompted further exploration to deduce the role of WHIP during mitosis. The scientists isolated the NPC subcomplex and used immunofluorescence and immunoblotting to detect the presence and movement of WHIP during mitosis. They discovered

WHIP interacting within the NPC autonomous of Werner protein, demonstrating a novel relation.

In addition to its connection with gene-stabilizing Werner protein, WHIP may play an independent, unique role in the cell cycle. Beyond supporting DNA replication, WHIP may also function to detect genetic damage. The authors look forward to future work that will further understanding of this protein's role in maintaining genome stability, and in completing some of that important work themselves.

It may be years before the Glavy Lab's insights into WHIP can be turned into therapies for sufferers of Werner Syndrome and other progeria diseases, but this new look into the workings of the body creates hope for future treatments and other advances in biology and medicine.

"Cell biology is a growing, multi-disciplinary field that is establishing a foundation of knowledge for the future," says Dr. Glavy. "We are beginning to establish tangible relations between biology and disease and advancing towards an understanding of gene repair and expression that might help with drug development in the future."

Provided by Stevens Institute of Technology