

DATE: September 10, 2009
CONTACT: Yivsam Azgad, Tel: 972-8-934-3856/2
EMAIL: Yivsam.azgad@weizmann.ac.il / news@weizmann.ac.il

Weizmann Institute Scientists Discover A New Protein Partnership That Leads to Pediatric Tumor Regression

Why are some pediatric cancers able to spontaneously regress? Prof. Michael Fainzilber and his team of the Weizmann Institute's Biological Chemistry Department seem to have unexpectedly found part of the answer. Further research toward a better understanding of the mechanism of action might hopefully lead, in the future, to the development of drugs that will be able to induce regression of certain tumors.

TrkA is a particular cell receptor well known for its "pro-life advocacies:" When nerve growth factor proteins bind to TrkA receptors, it activates the receptors into promoting the growth and survival of neurons.

So when Fainzilber, together with Ph.D. student Liraz Harel, postdoctoral student Dr. Barbara Costa, technician Zehava Levy and former Ph.D. student Dr. Marianna Tcherpakov, carried out screening tests to identify other molecules involved in this signaling cascade, it took them by surprise to learn that TrkA may not be who it seems. They found that if TrkA teams up with another molecule called CCM2 – the newly-identified player in this signaling cascade – they become "partners in crime," with TrkA turning into a cell killer!

However, though paradoxical, this atypical behavior may actually be rooting for life after all. This idea comes from findings concerning pediatric tumors of neural origin, specifically, medulloblastoma – the most common malignant brain tumor and the second most common malignancy among children less than 20 years of age; and neuroblastoma – the most common extracranial solid cancer in childhood. Neuroblastoma displays unusual behavior, being one of the few human malignancies known to demonstrate spontaneous regression in some cases, but nobody knows how or why. Studies have shown that the tumors with positive prognosis usually express TrkA, while aggressive forms of the tumor do not. However, how TrkA induces tumor regression is yet unknown and the mechanism was an enigma.

What if CCM2 was the missing piece to the tumor regression puzzle? Together with a group of scientists in Germany who were conducting a large scale gene expression study in tumors from neuroblastoma patients, they checked the expression levels of CCM2 and TrkA from the patient samples collected. The results were clear-cut: TrkA and CCM2 were always expressed together in certain tumors – those that showed the highest incidences of regression and patient survival!

They confirmed their results by blocking the expression of either TrkA or CCM2 in some cells, which resulted in cell survival. On the other hand, by introducing CCM2 to cells lacking it, cell death was induced if TrkA was also present, suggesting that this mechanism could lead to tumor regression.

This research, recently published in *Neuron*, is one of the first to elucidate this paradoxical “pro-cell death” behavior of TrkA and the first to identify CCM2 as a crucial accessory in this particular pathway, as well as describing in detail just how these two molecules interact.

Prof. Michael Fainzilber's research is supported by the M.D. Moross Institute for Cancer Research; the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation; the Helen and Martin Kimmel Institute for Stem Cell Research; the Irving B. Harris Foundation; and Mr. and Mrs. Michael Salzberg, Bethesda, MD. Prof. Fainzilber is the incumbent of the Chaya Professorial Chair for Molecular Neuroscience.

The Weizmann Institute of Science in Rehovot, Israel, is one of the world's top-ranking multidisciplinary research institutions. Noted for its wide-ranging exploration of the natural and exact sciences, the Institute is home to 2,600 scientists, students, technicians and supporting staff. Institute research efforts include the search for new ways of fighting disease and hunger, examining leading questions in mathematics and computer science, probing the physics of matter and the universe, creating novel materials and developing new strategies for protecting the environment.

Weizmann Institute news releases are posted on the World Wide Web at <http://wis-wander.weizmann.ac.il>, and are also available at <http://www.eurekalert.org>.