New role for the JNK protein

July 14 2010

Put simply, a tumor is the result of out-of-control cell growth. To assure that the cell cycle - the cell's process of duplicating itself to make more cells - goes smoothly, a large network of proteins tells other proteins what to do and when to do it. When any of these layers of protein regulation fail, cell growth can get out of hand. A new study led by Ze'ev Ronai, Ph.D., associate director of Sanford-Burnham's National Cancer Institute-designated Cancer Center, reveals a new player in cell cycle control. These findings, which appeared online in *Nature Cell Biology* on June 27, showed that JNK, a protein already well known for other duties, also regulates the cell cycle.

"This was totally unexpected of JNK," explained Gustavo Gutierrez, Ph.D., postdoctoral researcher in Dr. Ronai's laboratory and first author of the study. "We already knew that JNK helps cells respond to stress, such as damage caused by ultraviolet radiation. We thought we already knew how the major components of the cell cycle were regulated. This study really changes the thinking by connecting the two."

On the molecular level, JNK influences cellular functions by tagging other proteins with a phosphate chemical group (a process known as phosphorylation), a common mechanism cells use to turn enzymes on and off. Phosphorylation is so important that when JNK goes awry, a number of different disorders can result, such as cancer, diabetes or neurodegenerative diseases.

The part JNK plays in controlling the cell cycle is completely new. In this study, JNK activity was found to regulate the function of one of the

major drivers of the cell cycle, a protein complex known as the APC/C. According to this, and related research recently published by Dr. Gutierrez and Dr. Ronai in the Journal of Biological Chemistry, JNK acts like an assembly line inspector; its presence and activity ensures that the cell cycle moves along smoothly. Any problems push JNK to halt the process at certain 'checkpoints.' If all systems look good, the cell cycle progresses. If not, minor damage is fixed or, if beyond repair, the whole process is scrapped.

"Certain situations where JNK is hyperactive, as seen in some human tumors, might also influence the cell cycle and promote genomic instability," said Dr. Ronai. "Our laboratory is now assessing this possibility using a mouse model that was engineered based on these new discoveries."

More information: Gutierrez GJ, Tsuji T, Chen M, Jiang W, Ronai ZA. Interplay between Cdh1 and JNK activity during the cell cycle. Nature Cell Biology. 2010 Jul;12(7):686-95.

Provided by Sanford-Burnham Medical Research Institute