SOUTHWESTERN NEWS

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Researchers discover transport molecule that allows boron into cells

DALLAS – Nov. 4, 2004 – Researchers at UT Southwestern Medical Center at Dallas have identified a protein that transports the essential nutrient boron into cells, where it is important for cell growth and bone development.

The findings are in the Nov. 5 edition of the journal *Molecular Cell* and are online.

The protein, NaBC1, is found in most tissues and is part of a large family of ion transporting proteins that allow charged molecules to travel across cell membranes. Ion transporters are embedded in the cell membrane, opening and closing like gates to let charged ions and molecules enter and leave the cell. The movement of these molecules affects numerous essential cellular functions.

Like other nutrients, cells must transport boron across the membrane to control its concentration within the cell. The discovery of NaBC1 may help scientists understand how cells control internal boron concentration and the role of boron in a wide range of cellular processes, such as cell growth and bone mineralization.

"NaBC1 is very specific for the transport of borate, which is found in nearly everything we eat," said Dr. Shmuel Muallem, professor of physiology and the study's senior author.

Borate, the form of boron that the body uses, is essential for plant growth, pollination and crop size but until recently, no one knew how it entered plant cells. A borate transporter discovered in the plant *Arabidopsis* by another research group was shown to be very similar to human NaBC1. Dr. Muallem, who had been studying NaBC1 in another context, hypothesized that NaBC1 was the human borate transporter.

"Since animals, including humans, get enough boron from our diets, it's hard to study the effect of boron deficiency in animal models and humans, but under conditions of malnutrition, there may be a strong effect of boron deficiency on embryonic development and, in adults, on bone maintenance and metabolic function," said Dr. Muallem.

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For animals kept on low boron diets, the effect of boron deficiency is clear. Numerous birth defects occur, including impaired growth and missing or extra limbs. Many animals cannot survive in the complete absence of boron. On the other hand, like many vitamins and minerals, too much is as bad as not enough. High levels of boron are toxic.

Dr. Muallem's group showed that human cells with NaBC1 grown in culture specifically took up boron from solution when compared to arsenic, which is chemically similar to boron. Arsenic was unable to enter cells. Similar activity was found in many cell types isolated from mouse and rat tissues.

Dr. Muallem's group noted that cells divided optimally in a specific concentration of boron, but cell division was inhibited when boron was too high or low.

Biochemical tests confirmed that well-known signaling molecules that affect growth and development were activated when boron entered cells, and that reducing the activity of NaBC1 was sufficient to block cell division.

"Because this transporter is unique in humans, it is likely to be essential for human life," Dr. Muallem said. "Finding this transporter allows us to study how boron works in the body."

Aside from its role in promoting cell division, radioactive boron is sometimes used to treat certain brain tumors. Boron-based treatments have long been hampered by the blood-brain barrier, the network of blood vessels and tissues that feed and protect the brain, because only a small amount of the compound can cross the blood-brain barrier to reach the tumor.

Dr. Muallem said that perhaps redesign of the boron-based chemicals to be transported by NaBC1 can facilitate their delivery to the tumors, and may help in improving boron radiotherapy.

Other physiology researchers who contributed to the study were Drs. Meeyoung Park, Qin Li and Nikolay Shcheynikov, all postdoctoral researchers, and Dr. Weizhong Zeng, assistant professor.

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