# Protein E-selectin ligand-1 regulates production of TGF-beta

Baylor College of Medicine
HOUSTON -- (June 9, 2010) -- Several years ago, Dr. Arthur Beaudet [1], Baylor College of Medicine's [2] chair of molecular and human genetics, was surprised to find that mice that lacked a protein called E-selectin ligand-1 were shorter than normal. He and his colleagues were hoping that the protein was involved in cell adherence, but instead their mice had a form of dwarfism.
They turned the mice and their data over to Dr. Brendan Lee [3], a professor of molecular and human genetics at BCM, and an expert in the development of bone and cartilage and the diseases that occur when that process goes wrong. This week, in the Journal of Clinical Investigation [4], he and his colleagues report [5] that the protein E-selectin ligand-1 controls how much transforming growth factor beta (TGF-beta) – a signaling molecule – is produced. In the case of these mice, the lack of E-selectin ligand-1 resulted in overproduction of TGF-beta, which affected cartilage production.

"TGF-beta is a central signaling molecule that is used by almost every cell in the body," said Lee, who is also a Howard Hughes Medical Institute [6] investigator. What it does in each cell depends on its context. Many scientists have concentrated on how to control TGF-beta – its action outside the cell and how to activate or sequester it or how it works after it binds to a cell receptor.

"This work is exciting because it is the first time anyone has described the regulation of TGF-beta on the front end," said Lee.

## Stoplight for TGF-beta production

E-selectin ligand-1 sits in the "trafficking" area of the cell called Golgi apparatus. The work by Lee and his colleagues describes how this protein binds TGF-beta as it goes through the cell, controlling how it matures.

"If E-selectin ligand-1 is lost, then you get more TGF-beta," said Lee. "It (E-selectin ligand-1) is a stoplight for TGF-beta production. Uncontrolled action by TGF-beta affects how the cartilage is formed and explain why the mice are shorter."

Even more important, this same mechanism is found throughout evolution, even in the frog, said Lee.

## Effect on other diseases

In the future, Lee said, he hopes to determine the effect of this protein on other diseases in which TGF-beta is important, including osteoporosis. TGF-beta is also

important in controlling the immune system and even the spread of cancer, he said.

"Given this new mechanism to control this process, could this be a therapeutic target for new drug development?" he said.

It is also an example of how science can branch in unexpected directions, Lee said. Beaudet did not expect the result he saw in his mice, but he knew that it would be important. Lee and his colleagues followed up on it, and, with Beaudet's help, they uncovered something new.

Others who took part in this work include Tao Yang, Roberto Mendoza-Londono, Huifang Lu, Jianning Tao, Kaiyi Li, Bettina Keller, Ming Ming Jiang, Rina Shah, Yuqing Chen, Terry K. Bertin, Feyza Engin, John Hicks and Milan Jamrich, all of BCM and Branka Dabovic and Daniel B. Rifkin of New York University Medical Center [7].

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For more information on basic science research from Baylor College of Medicine, please go to www.bcm.edu/fromthelab [10].

SOURCE [11]

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