

Public release date: 1-Jun-2009

Contact: Elizabeth Andrews
elizabeth.andrews@childrens.harvard.edu
617-919-3110
[Children's Hospital Boston](#)

Stem cell protein offers a new cancer target

LIN28, which maintains cell 'stemness,' is abundant in advanced cancers and transforms cells to cancerous state

A protein abundant in embryonic stem cells is now shown to be important in cancer, and offers a possible new target for drug development, report researchers from the Stem Cell Program at Children's Hospital Boston.

Last year, George Daley, MD, PhD, and graduate student Srinivas Viswanathan, in collaboration with Richard Gregory, PhD, also of the Stem Cell Program at Children's, showed that the protein LIN28 regulates an important group of tumor-suppressing microRNAs known as let-7. Increasing LIN28 production in a cell prevented let-7 from maturing, making the cell more immature and stem-like. Since these qualities also make a cell more cancerous, and because low levels of mature let-7 have been associated with breast and lung cancer, the discovery suggested that LIN28 might be oncogenic.

Now, publishing Advance Online in *Nature Genetics* on May 31, Daley, Viswanathan and colleagues show directly that LIN28 can transform cells to a cancerous state, and that it is abundant in a variety of advanced human cancers, particularly liver cancer, ovarian cancer, chronic myeloid leukemia, germ cell tumors and Wilm's tumor (a childhood kidney cancer). They believe that overall, LIN28 and a related protein, LIN28B, may be involved in some 15 percent of human cancers. By blocking or suppressing LIN28, it might be possible to revive the let-7 family's natural tumor-suppressing action.

"Linking this protein to advanced cancer is a very exciting new result," says Daley, Director of Stem Cell Transplantation at Children's, and also affiliated with Children's Division of Hematology/Oncology, the Dana-Farber Cancer Institute and the Harvard Stem Cell Institute. "It gives us a new target to attack, especially in the most resistant and hard-to-treat cases."

LIN28, which is abundant in embryonic stem cells and prevents them from differentiating into specific cell types, was originally discovered to influence embryonic development in worms some 25 years ago. Development, stem cell generation and carcinogenesis are known to be closely related, but until last year's study connected LIN28 to let-7, it hadn't been clear how.

"LIN28 is a fascinating protein that acts both in stem cells and cancers, and is teaching us that cancer is often a disease of stem cells," says Daley.

Viswanathan, Daley and colleagues are busily searching for ways to inhibit LIN28, which could provide promising new drugs for advanced cancer.

The study was funded by the National Institutes of Health, the NIH Director's Pioneer Award, Burroughs Wellcome Fund, the Leukemia and Lymphoma Society and the Howard Hughes Medical Institute.

Children's Hospital Boston is home to the world's largest research enterprise based at a pediatric medical center, where its discoveries have benefited both children and adults since 1869. More than 500 scientists, including eight members of the National Academy of Sciences, 12 members of the Institute of Medicine and 12 members of the Howard Hughes Medical Institute comprise Children's research community. Founded as a 20-bed hospital for children, Children's Hospital Boston today is a 397-bed comprehensive center for pediatric and adolescent health care grounded in the values of excellence in patient care and sensitivity to the complex needs and diversity of children and families. Children's also is the primary pediatric teaching affiliate of Harvard Medical School. For more information about the hospital and its research visit: www.childrenshospital.org/newsroom.