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## New form of stem cell communication rescues diseased neurons

*International effort demonstrates cross-talk between implanted stem cells and diseased cells in mouse model*

LA JOLLA, Calif., February 1, 2010 -- Investigators at Sanford-Burnham Medical Research Institute (Sanford-Burnham, formerly Burnham Institute for Medical Research), the Karolinska Institutet, Beth Israel Deaconess Medical Center (BIDMC), Harvard Medical School and Université Libre de Bruxelles have demonstrated in mouse models that transplanted stems cells, when in direct contact with diseased neurons, send signals through specialized channels that rescue the neurons from death. These direct cell-to-cell connections may also play a role in normal development by laying down the blueprint for more mature electrical connections between neurons and other cells. The research was published in the journal *Proceedings of the National Academy of Sciences* on February 1.

While it was already known that stem cells will seek out diseased cells in the brain, the international group of scientists showed, both in tissue culture and in mice, that the stem cells actively bring diseased neurons back from the brink via cross-talk through gap junctions, the connections between cells that allow molecular signals to pass back and forth. Significantly, the stem cells do not need to differentiate into the specific type of neuron to provide this therapeutic effect. The researchers also believe this protective mechanism may be active in other cell types and play a role in many diseases. For example, some of their preliminary work shows that these mechanisms may rescue damaged neural fibers in adult spinal cord injuries.

"We showed a while ago that stems cells may exert a therapeutic effect on damaged or diseased host systems by secreting therapeutic factors and 'bathing' the dying cells," said Evan Snyder, M.D., Ph.D., director of the Stem Cell and Regenerative Biology program at Sanford-Burnham. "However, we did not know that stem cells can also exert their action through direct cell-to-cell contact. Indeed, we believe that this may be a newly-recognized way in which stem cells communicate with the cells around them, not only under diseased conditions but during normal development."

"Grafted neural stem cells of mouse and human origin make early gap junction contact with cells in the host brain that benefit endangered host neurons, even rescuing them from impending cell death," added Richard L. Sidman, M.D., Professor of Neuropathology (Neuroscience) at BIDMC, Boston and Harvard Medical School.

Beginning with tissue culture studies, the team found that neural stem cells (NSCs, including human NSCs) integrated into the neural circuitry, coordinated signaling (as measured by calcium fluxes) and protected injured neurons. The team replicated these findings in diseased mice (including those that have a disorder similar to Huntington's disease) and spinal-injured rats. The scientists, led by Eric Herlenius, Ph.D., of the Karolinska Institutet and Dr. Snyder, hypothesized that communication through gap junctions was the mechanism for the protective effect. Subsequently, the researchers disabled gap junctions, which diminished the therapeutic effect and validated the gap junction hypothesis.

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### About Sanford-Burnham Medical Research Institute

Sanford-Burnham Medical Research Institute (formerly Burnham Institute for Medical Research) is dedicated to discovering the fundamental molecular causes of disease and devising the innovative therapies of tomorrow. Sanford-Burnham, with operations in California and Florida, is one of the fastest-growing research institutes in the country. The Institute ranks among the top independent research institutions nationally for NIH grant funding and among the top organizations worldwide for its research impact. From 1999 – 2009, Sanford-Burnham ranked #1 worldwide among all types of organizations in the fields of biology and biochemistry for the impact of its research publications, defined by citations per publication, according to the Institute for Scientific Information. According to government statistics, Sanford-Burnham ranks #2 nationally among all organizations in capital efficiency of generating patents, defined by the number of patents issued per grant dollars awarded.

Sanford-Burnham utilizes a unique, collaborative approach to medical research and has established major research programs in cancer, neurodegeneration, diabetes, and infectious, inflammatory, and childhood diseases. The Institute is especially known for its world-class capabilities in stem cell research and drug discovery technologies. Sanford-Burnham is a nonprofit public benefit corporation. For more information, please visit [www.sanford-burnham.org](http://www.sanford-burnham.org).

### About Beth Deaconess Medical Center

Beth Israel Deaconess Medical Center is a patient care, teaching and research affiliate of Harvard Medical School, and consistently ranks among the top four in National Institutes of Health funding among independent hospitals nationwide. BIDMC is clinically affiliated with the Joslin Diabetes Center and is a research partner of the Dana-Farber/Harvard Cancer Center. BIDMC is the official hospital of the Boston Red Sox. For more information, visit [www.bidmc.harvard.edu](http://www.bidmc.harvard.edu).

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