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A major step seen for stem-cell research

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Scientists link molecule to growth of brain cells

By **Bruce Lieberman**

UNION-TRIBUNE STAFF WRITER

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San Diego scientists have identified a molecule that prompts embryonic stem cells from mice to grow into brain cells, a significant advance in stem-cell biology that might someday be applied in humans.

The scientists, at The Scripps Research Institute and the Genomics Institute of the Novartis Research Foundation in La Jolla, screened 50,000 molecules manufactured in a lab before pinpointing one that appeared to trigger the change.

"This is an important step in our efforts to understand how to modulate stem-cell proliferation and fate," said Peter Schultz, a professor of chemistry at Scripps who worked on the study published today in the *Proceedings of the National Academy of Sciences*.

Scientists hope to one day use stem cells from humans to replace diseased cells destroyed by Parkinson's and Alzheimer's, multiple sclerosis, diabetes and a long list of other diseases.

Embryonic stem cells are believed to be the progenitor cells in embryos that grow into every other cell in the body. Scientists do not yet know exactly how stem cells grow into brain, heart, lung, liver, bone and other types of cells.

Discovering exactly how that happens will be the key to growing cells in the lab and inducing the process in humans. Human embryonic stem-cell biology remains controversial because it requires destroying embryos to obtain stem cells.

Federal restrictions have so far hampered human stem-cell research, but scientists study stem cells from mice as a model for understanding human stem-cell biology.

Scientists around the world have attempted to coax stem cells in the

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lab to become specific types of cells by bathing them in growth factors, hormones and other chemicals. But even when that appears successful, they have not been able to identify exactly which chemicals are prompting the change, or what precisely is happening.

In the Scripps study, Sheng Ding, its lead author, and Schultz used powerful computers and other equipment to screen a library of 50,000 small organic compounds – a process called high throughput screening.

They found that one chemical called TWS119 binds to an enzyme in the stem cells called GSK-3beta. The enzyme has many functions, but the scientists found that its interaction with TWS119 prompted the cell to become a brain cell.

The Scripps scientists still do not know exactly how their molecule binds to the enzyme in the stem cell. Also, their molecule is synthetic and does not exist naturally. The researchers do not yet fully understand which natural process their molecule is replicating.

"This is just a first important step toward understanding the detailed mechanisms of neuronal differentiation," said Ding.

The Scripps work offers a new approach to figuring out how stem cells grow into specific types of cells, said Fred Gage, a neuroscientist and stem-cell biologist at the Salk Institute for Biological Studies in La Jolla.

"I think in part it's a demonstration of the power of these high throughput screening methods for coming up with candidate molecules," Gage said.

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