# Researchers develop human stem cell line containing sickle cell anemia mutation

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Researchers at Johns Hopkins have established a human cell-based system for studying sickle cell anemia by reprogramming somatic cells to an embryonic stem cell like state. Researchers at Johns Hopkins have established a human cell-based system for studying sickle cell anemia by reprogramming somatic cells to an embryonic stem cell like state. Publishing online in *Stem Cells* on May 29, the team describes a faster and more efficient method of reprogramming cells that might speed the development of stem cell therapies.

“We hope our new cell lines can open the doors for researchers who study diseases like sickle cell anemia that are limited by the lack of good experimental models,” says Linzhao Cheng, Ph.D., an associate professor of gynecology and obstetrics, medicine and oncology and a member of the Johns Hopkins Institute for Cell Engineering.

The research team first sought to improve previously established methods for reprogramming of adult cells into so-called induced pluripotent stem (iPS) cells, which look and behave similarly to embryonic stem cells and can differentiate into many different cell types. After testing several different genes, they were able to improve reprogramming efficiency by adding a viral protein known as SV40 large T antigen.

Using both fetal and adult human skin cells, the researchers introduced the four genes previously reported sufficient for cell reprogramming and compared the efficiency of reprogramming in the presence or absence of

large T antigen. Without large T, cells form embryonic stem cell-like clusters in three to four weeks. With large T, the cells started looking like embryonic stem cells in just 12 to 14 days.

“Not only did T speed up reprogramming, we also found that it increases the total number of reprogrammed cells, which is great because often in reprogramming, not all cells go all the way,” says Cheng, who explains that rigorous follow-up tests are required to determine if the reprogrammed cells really behave like pluripotent embryonic stem cells. “Many of them look right but they’re probably just half cooked-like a boiled egg, you just can’t tell the difference by looking at the outside,” he says.

Having established a faster, more efficient method, the team then reprogrammed human cells that contain the mutation associated with sickle cell anemia. Embryonic stem cell-like clusters were visible 14 days after they initiated reprogramming and from these clusters the researchers established three different cell lines that both look and behave like human embryonic stem cells.

“One challenge to studying blood diseases like sickle cell anemia is that blood stem cells can’t be kept alive for very long in the lab, so researchers need to keep returning to patients for more cells to study,” says Cheng. “Having these new cell lines available might enable some bigger projects, like screening for potential drugs.”

Source: Johns Hopkins Medical Institutions

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