# Expression of pluripotency-associated gene marks many types of adult stem cells

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Investigators at the Massachusetts General Hospital (MGH) Center for Regenerative Medicine and the Harvard Stem Cell Institute (HSCI) have found that Sox2 – one of the transcription factors used in the conversion of adult stem cells into induced pluripotent stem cells (iPSCs) – is expressed in many adult tissues where it had not been previously observed. They also confirmed that Sox2-expressing cells found in the stomach, testes, cervix and other structures are true adult stem cells that can give rise to all mature cell types in those tissues. The study appears in the October issue of *Cell Stem Cell*.

"We have known that Sox2 is essential for maintaining pluripotency in embryonic stem cells and neural stem cells and, with three other embryonic genes, is sufficient to convert adult cells into iPSCs," says Konrad Hochedlinger, PhD, of the MGH Center for Regenerative Medicine and HSCI, who led the study. "Our study shows that Sox2 is a much more widespread marker of adult stem cells and suggests these cells may share common genetic programs to maintain stem cell fate, findings that could be exploited to amplify or modify these cells for applications in regenerative medicine."

Hochedlinger's team set out to investigate whether genes known to be important to pluripotent stem cells – cells that can give rise to several different types of tissue – also play a role in adult stem cells, which maintain populations of particular types of tissue. Sox2 is one of four embryonic genes that are required to be expressed for the generation of iPSCs – which have many of the characteristics of embryonic stem cells

– but the other three genes are not expressed in adult stem cells. Sox2 is known to be expressed at the very earliest stages of embryonic development and to play a role in development of several types of fetal tissue. But prior to this study, its expression had been observed in only a few types of adult tissues.

In a series of experiments with mice, the researchers first showed that Sox2 continues to be expressed in specific populations of adult cells of the stomach, esophagus, testes, cervix, anus and the lens of the eye. These Sox2-expressing cells were proven to be able both to replenish their population and to give rise to the fully differentiated cells found within the particular tissue, confirming their status as adult stem cells.

Additional findings revealed that fetal tissues expressing Sox2, which are at a stage before the appearance of true stem cells, will develop into tissues that include Sox2-expressing adult stem cells and that Sox2 appears to be the only transcription factor expressed in stem cells at all stages of development – embryonic, fetal and adult. However, Sox2 expression has never been found in muscle or connective tissue, blood cells, or in organs such as the heart or kidney, indicating that other factors must play a similar role in those tissues.

"Adult stem cells are difficult to isolate and manipulate, so the fact that Sox2 appears to be a marker for many adult stem cells may allow researchers to isolate them more easily and study them in more detail," Hochedlinger explains. "Manipulation of Sox2 expression could help us push embryonic stem cells into particular types of adult stem cells and, when combined with certain growth factors, induce differentiation into desired types of tissue. All of these possibilities need to be investigated." Hochedlinger is an associate professor of Medicine at Harvard Medical School and a Howard Hughes Medical Institute Early Career Scientist.

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