

By blocking key signal, researchers maintain embryonic stem cells in vital, undifferentiated state

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In a paper published in this week's Online Early Edition of the *Proceedings of the National Academy of Sciences*, researchers from the University of California, San Diego School of Medicine identify a key gene receptor and signaling pathway essential to maintaining human embryonic stem cells in an undifferentiated state.

While the ability of human embryonic [stem cells](#) (hESCs) to become any type of mature cell, from neuron to heart to skin and bone, is indisputably crucial to [human development](#), no less important is the mechanism needed to maintain hESCs in their pluripotent state until such change is required.

In a paper published in this week's Online Early Edition of *PNAS*, researchers from the University of California, San Diego School of Medicine identify a key gene receptor and signaling pathway essential to doing just that – maintaining hESCs in an undifferentiated state.

The finding sheds new light upon the fundamental biology of hESCs – with their huge potential as a diverse therapeutic tool – but also suggests a new target for attacking [cancer stem cells](#), which likely rely upon the same receptor and pathway to help spur their rampant, unwanted growth.

The research, led by principal investigator Karl Willert, PhD, assistant professor in the Department of Cellular and Molecular Medicine,

focuses upon the role of the highly conserved WNT signaling pathway, a large family of genes long recognized as a critical regulator of stem cell self-renewal, and a particular encoded receptor known as frizzled family receptor 7 or FZD7.

"WNT signaling through FZD7 is necessary to maintain hESCs in an undifferentiated state," said Willert. "If we block FZD7 function, thus interfering with the WNT pathway, hESCs exit their undifferentiated and pluripotent state."

The researchers proved this by using an antibody-like protein that binds to FZD7, hindering its function. "Once FZD7 function is blocked with this FZD7-specific compound, hESCs are no longer able to receive the WNT signal essential to maintaining their undifferentiated state."

FZD7 is a so-called "onco-fetal protein," expressed only during embryonic development and by certain human tumors. Other studies have suggested that FZD7 may be a marker for cancer stem cells and play an important role in promoting tumor growth. If so, said Willert, disrupting FZD7 function in cancer cells is likely to interfere with their development and growth just as it does in hESCs.

Willert and colleagues, including co-author Dennis Carson, MD, of the Sanford Consortium for Regenerative Medicine and professor emeritus at UC San Diego, plan to further test their FZD7-blocking compound as a potential cancer treatment.

More information: The WNT receptor FZD7 is required for maintenance of the pluripotent state in human embryonic stem cells, www.pnas.org/cgi/doi/10.1073/pnas.1323697111

Provided by University of California - San Diego

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