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Shock tactics: Bioelectrical therapy for cancer and birth defects?

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Stem cell therapies hold increasing promise as a cure for multiple diseases. But the massive potential of a healthy stem cell has a flip side, as faulty regulation of stem cells leads to a huge range of human diseases. Even before birth, mistakes made by the stem cells of the foetus are a major cause of congenital defects, and cancer is also caused by the body losing control of stem cell function. Guiding stem cells along the correct pathways and, where necessary, reversing their mistakes is the goal of everyone in this field.

Now, Michael Levin and colleagues from Tufts University, Medford, MA, have identified a novel and readily modifiable signal by which an organism can control the behaviour of stem cell offspring. Their work is published in Disease Models *& Mechanisms* on October 19th, 2010.

Levin's laboratory works on an intriguing phenomenon: bioelectrical signalling. There is always a difference in voltage, called the transmembrane potential, between the inside and outside of all cells, and controlling exactly what this difference is turns out to be vitally important. Specialised protein checkpoints sited in a cell's outer membrane regulate ion flow in and out of the cell, producing voltage gradients. These, combined with more conventional protein-based signalling systems, can specify cell destiny.

Levin's team already knew from collaborative work with David Kaplan's lab, also at Tufts, that the properties of human stem cells growing in artificial culture could be drastically altered by changing their

transmembrane potential. Now they have taken this work one important step further, by asking whether tampering with the transmembrane potential of one kind of cell can have a domino effect in a whole organism, altering the destiny of other cell types. To do this, they focused on the development of neural crest stem cells, which are responsible for directing development of the face and heart, but which also generate melanocytes, the pigment cells of the skin.

Using frog tadpoles and melanocytes as a model system, they showed that tweaking the transmembrane potential of a tiny population of 'instructor' cells sends a signal to developing melanocytes that causes them to overgrow and start to resemble metastatic cancer cells. Most excitingly, they found that the signal can travel over long distances in the tadpole, and that the messenger carrying it is serotonin – an important neurotransmitter involved in mood regulation and many other aspects of nervous system function.

This novel bioelectrical method of changing stem cell behaviour has huge implications. It is very likely that there are similar 'instructor' cells that direct other important cell populations, and changing their voltage gradients would be relatively easy (Levin's lab simply used an anti-parasitic drug already available on prescription). The resulting bioelectrical therapy could potentially be harnessed to improve regenerative repair after injury, repair birth defects and detect and prevent cancer.

More information: Douglas Blackiston, Dany S. Adams, Joan M. Lemire, Maria Lobikin and Michael Levin (2010). Transmembrane potential of GlyCl-expressing instructor cells induces a neoplastic-like conversion of melanocytes via a serotonergic pathway. *Dis. Model. Mech.* [in press] dmm.biologists.org/