Forsyth scientists trigger cancer-like response from embryonic stem cells

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Scientists from The Forsyth Institute, working with collaborators at Tufts and Tuebingen Universities, have discovered a new control over embryonic stem cells' behavior. The researchers disrupted a natural bioelectrical mechanism within frog embryonic stem cells and trigged a cancer-like response, including increased cell growth, change in cell shape, and invasion of the major body organs. This research shows that electrical signals are a powerful control mechanism that can be used to modulate cell behavior.

The team of Forsyth Institute scientists, led by Michael Levin, Ph.D., Director of the Forsyth Center for Regenerative and Developmental Biology, have identified a new function for a potassium (KCNQ1) channel, mutations of which are known to be involved in human genetic diseases such as Romano-Ward and Jervell-Lange-Nielsen syndromes.

The team interrupted the flow of potassium through KCNQ1 in parts of the Xenopus frog embryo. This resulted in a striking alteration of the behavior of one type of embryonic stem cell: the pigment cell lineage of the neural crest. When mutated, these pigment cells over-proliferate, spread out, and become highly invasive of blood vessels, liver, heart, and neural tube, leading to a deeply hyper-pigmented tadpole.

The body's natural biophysical signals, driven by ion transporter proteins and resulting in endogenous voltage gradients and electric fields, have been implicated in embryonic development and regeneration. The data in this study, which will be published in the *Proceedings of the National*

Academy of Sciences on October 13, 2008, have not only elucidated a novel role for the KCNQ1 channel in regulating key cell behaviors, but for the first time have also revealed the molecular identity of a biophysical switch by means of which neoplastic-like properties can be conferred upon a specific embryonic stem cell sub-population. These data reveal that key properties of embryonic stem cells can be controlled through bioelectrical signals, identify transmembrane voltage potential as a novel regulator of neural crest function in embryonic development, and demonstrate that potassium flows can be an important aspect of cellular environment, which is known to regulate both cancer and stem cells.

"In regenerative medicine, a key goal is to control the number, position, and type of cells," said the paper's first author, Junji Morokuma, Ph.D. "This research is especially exciting because it shows the importance of electrical signals for changing cell behavior, identifies a new role in developmental and cell biology for the KCNQ1 ion channel, and strengthens the link between stem cells and tumor cells. Added Doug Blackiston, Ph.D., paper co-author, "In the future, this work may lead to a greater understanding of the causes of cancer and ways to potentially halt its metastasis, as well as suggesting new techniques by which stem cells may be controlled in biomedical applications."

Source: Forsyth Institute