

Re-expression of an embryonic signaling pathway in melanoma utilizes different receptors

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Metastatic melanoma is a highly aggressive skin cancer whose incidence is on the rise at an alarming rate. Research has revealed that metastatic tumor cells share similar signaling pathways with embryonic stem cells to sustain plasticity and growth. However, major regulators of these pathways are often missing in tumor cells, thus allowing uncontrolled tumor growth and spreading to occur.

During early vertebrate development, Nodal, an embryonic growth factor that governs the growth, pattern and position of tissues, is critical for normal maturation. Nodal plays a significant role in maintaining the pluripotency of [embryonic stem cells](#), meaning the ability of [stem cells](#) to differentiate into any of the three germ layers that comprise the body. The recent discovery of Nodal's re-expression in several aggressive and [metastatic cancers](#) has highlighted its critical role in self-renewal and maintenance of the stem cell-like characteristics of [tumor cells](#) such as melanoma. However, the signaling pathway receptors utilized by melanoma cells to propagate Nodal's effect remain(s) mostly anecdotal and unexplored.

The laboratory of Mary J.C. Hendrix, PhD made the novel discovery that embryonic stem cells and metastatic melanoma cells share a similar repertoire of receptors known as Type I serine/threonine kinase(s), but diverge in their Type II receptor expression. Further testing indicated that metastatic [melanoma cells](#) and embryonic stem cells use different

receptors for Nodal signal transduction. These findings reveal the divergence in Nodal signaling between embryonic stem cells and [metastatic melanoma](#) that can impact new therapeutic strategies targeting the re-emergence of embryonic pathways in cancer.

This work is published in the *International Journal of Cancer*. Mary J.C. Hendrix, PhD points out: "Nodal-expressing tumor cells don't respond favorably to conventional therapies, supporting the premise that a combinatorial approach to targeting Nodal subpopulations within tumors, along with a front-line therapy, would constitute a more rational approach for treating aggressive cancer". Zhila Khalkhali-Ellis, PhD, senior research scientist in the Hendrix laboratory and the lead author says: "Our discoveries are important for advanced stage aggressive melanoma. Given that limited therapeutic options are currently available for this cancer, we have the opportunity to investigate whether the receptors can be modulated so that the signaling molecule can be neutralized to decrease aggressive behavior." The research was supported by the National Institutes of Health.

More information: Khalkhali-Ellis Z, Kirschmann DA, Seftor EA, Gilgur A, Bodenstine TM, Hinck AP, Hendrix MJC. Divergence(s) in Nodal Signaling Between Aggressive Melanoma and Embryonic Stem Cells. *International Journal of Cancer*. Available online September 9, 2014.

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