

# Researchers identify Achilles heel of common childhood tumor

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Researchers have discovered a mechanism for the rapid growth seen in infantile hemangioma, the most common childhood tumor.

The tumors, which are made up of proliferating blood vessels, affect up to 10 percent of children of European descent, with girls more frequently afflicted than boys. The growths appear within days of birth—most often as a single, blood-red lump on the head or face—then grow rapidly in the ensuing months. The development of infantile hemangioma slows later in childhood, and most tumors disappear entirely by the end of puberty. However, while the tumors are benign, they can cause disfigurement or clinical complications. This new research offers hope for the most severe of these cases, pointing at a potential, non-invasive treatment for the condition.

These findings, the result of a collaboration between scientists from Harvard Medical School and the Harvard School of Dental Medicine, Children's Hospital Boston, and the de Duve Institute at the Catholique University of Louvain in Brussels, will be published October 19 in *Nature Medicine*.

In this study, researchers looked at tissue isolated from nine distinct hemangioma tumors. They found that the endothelial cells that lined the affected blood vessels were all derived from the same abnormal cell. Like other tumors, hemangiomas are caused by the abnormal proliferation of tissue. Since no other type of cell within the tissue displayed the same self-replicating tendency, the scientists concluded

that the endothelial cells were the source of the tumors' growth.

Looking further, the team discovered that the endothelial cells behaved as if they were activated by a hormone called vascular endothelial growth factor (VEGF). VEGF usually binds to a specific receptor, one that sits on the outskirts of the cell and prevents VEGF from telling the cell to proliferate. However, the researchers found that at least two gene mutations were capable of setting off a chain of events that ultimately stymied those receptors. That allowed VEGF to trigger unchecked growth in the endothelial cells.

These findings open up new treatment options, according to study leader Bjorn R. Olsen, the Hersey Professor of Cell Biology at Harvard Medical School and Professor of Developmental Biology and Dean for Research at Harvard School of Dental Medicine. "What the data suggests is that any therapy that is directed against vascular endothelial growth factor – anti-VEGF therapy – is the rational therapy to use in these tumors," says Olsen.

This will be good news to the many children and families affected by the disorder. Though most cases have little impact on children's lives and many cases even go unnoticed, Olsen estimates that 10 percent of infantile hemangioma sufferers experience significant side-effects. These can include psychological stress brought on by the social challenges of disfigurement, as well as physical complications caused by large, badly-placed tumors that obstruct vision, respiration, or other bodily functions.

Anti-VEGF therapies have already been approved for other conditions, including macular degeneration and certain types of cancer. The next step for Olsen's team is to get approval to test these therapies in clinical trials.

Meanwhile, Olsen and his colleagues continue to mine these tumors for more answers. "After finding out why these tumors grow, we are now starting to direct our research at understanding why they regress," he said. "Knowing that and being able to induce that regression in the rapidly growing tumors, or induce regression of the blood vessels in malignant tumors, would be very effective."

Source: Harvard Medical School

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