Somatic Mutation of Vascular Endothelial Growth Factor Receptors in Juvenile Hemangioma


Gene mutations contribute to disease in one of two ways: inherited (germline) mutations passed down from parents to children, and somatic mutations (those that arise in non-sex-cells, and thus are not inherited) acquired after conception. The acquisition of somatic mutations contributes to many diseases without obvious genetic components.

This paper describes the identification of somatic gene mutations contributing to non-inherited cases of juvenile hemangioma, a common vascular tumor of childhood (often called a “strawberry mark”). In collaboration with a pediatric hospital, we were able to study 15 hemangioma tumors that had been surgically removed from children.

An assay using X-chromosome inactivation patterns established that the hemangioma tissues were likely “clonal”—that is, they resulted from proliferation of a single cell (unlike most tissues, which are derived from multiple progenitor cell types). This discovery suggested that events in a single cell could lead to tumor progression, implying the presence of underlying gene mutations.

To understand the genes that may underlie hemangioma formation, we studied the hemangioma tissue, analyzing various genes involved in blood vessel growth to identify causative gene mutations. We found that several hemangioma specimens harbored mutations in genes that encode receptors for vascular endothelial growth factor (VEGF), a potent growth factor promoting blood vessel growth.

A wide variety of tumor types rely on increased VEGF expression to support their growth, and the association of VEGF receptor mutations with highly vascular tumors such as hemangiomas helped to identify this signaling pathway as a critical element controlling tumor biology.

More recently, anti-VEGF therapies have advanced to the forefront of cancer treatment strategies. Anti-VEGF agents (e.g., bevacizumab, ranibizumab, axitinib) are effective treatments for numerous cancers and other disorders. This paper provides an opportunity to understand some of the evidence identifying the VEGF pathway as a promising target for cancer therapies.