Familial Segregation of Hemangiomas and Vascular Malformations as an Autosomal Dominant Trait


Gene mutations contribute to disease in one of two ways: inherited (germline) mutations are passed down from parents to children, and somatic mutations are acquired at some point after conception. The inheritance of germline mutations accounts for diseases “running in families,” and can give researchers clues regarding which genes may be playing a role in specific disorders.

This paper describes six rare families in which hemangiomas (common, benign vascular tumors of childhood—often known as “strawberry marks”) appear to be inherited from one generation to the next. This pattern of inheritance suggests the presence of a dominant gene mutation being passed from parents to children and underlying hemangioma development. Prior to this paper, familial clustering of hemangiomas (suggesting a genetic component) had never been described in the literature.

This discovery led to subsequent work in which the genetic region harboring the suspected disease gene was mapped to a position on chromosome 5. We discovered that hemangioma-causing mutations reside in genes that encode receptors for vascular endothelial growth factor (VEGF), a potent growth factor that promotes 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 a number of cancers and other disorders. Breakthrough therapies like anti-VEGF agents are always preceded by research to identify promising drug targets; this paper provides an opportunity to understand some of the evidence that led to the identification of the VEGF pathway as a promising target for cancer therapies.

Link: http://archderm.ama-assn.org/cgi/reprint/134/6/718