Expression of c-MYC in Human Endothelial Cells Results in Abnormal Vascular Morphogenesis and Metabolic Reprogramming

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Angiogenesis is responsible for the development of new blood vessels from previously existing vasculature. Anomalies of the growth and differentiation of these vessels result in vascular malformations, or in extreme cases tumors of the vasculature. Angiosarcoma, a rare, aggressive, soft-tissue sarcoma, is a vascular tumor developed by a small subset of post-radiation breast cancer patients. Mutations in the RAS and PIK3CA oncogenes are associated with vascular malformations and are known to cooperate with the oncogene MYC, which has been reported to be amplified in post-radiation angiosarcoma. Given links between RAS/PIK3CA signaling and MYC expression, the effects of MYC on vasculature formation were examined, and an inducible lentivirus was created to express c-MYC in primary endothelial cells. I found that endothelial cells infected with a c-MYC lentivirus exhibit abnormal morphogenesis and altered metabolism, undergoing metabolic reprogramming to an aerobic glycolytic state. These abnormalities induced by MYC expression are consistent with a pro-growth phenotype and a role for c-MYC in driving the formation of vascular tumors such as angiosarcoma. This understanding makes MYC a potential target for vascular tumor therapy.

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