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Requirement of Endothelial Ovol1-Slug for Tumor Angiogenesis in Colorectal Cancer

Introduction: Like all living cells, cancer cells of a growing tumor mass require nutrients to grow and divide. To support this requirement, many cancers induce a process called angiogenesis, which activates nearby blood vessels to invade growing tumors and connect it to the blood circulation. This supplies nutrients and removes waste so that the tumor can continue to grow and also provides a route by which cancer cells can detach from the primary tumor and metastasize to other tissues. One class of anti-cancer drugs aims to target this process by blocking angiogenesis, thereby limiting tumor growth. However, current anti-angiogenic drugs only narrowly target certain pro-angiogenic signals, and cancers can eventually become resistant to these drugs. To address this problem, we aim to test if the Ovol1-Slug signaling pathway is a central driver of tumor angiogenesis, which might suggest it is a better target for anti-cancer therapy than current anti-angiogenic drugs.

Hypothesis/Methods: We hypothesize that transcription factors Ovol1 and Slug are required for tumor angiogenesis and cancer growth, which manifests as smaller size and less microvascular density when these transcription factors are missing. To test this hypothesis, we have bred mice that specifically lack expression of Ovol1 and Slug in endothelial cells. Colorectal cancer tumor xenografts were then implanted into these mice, as well as in a control group of mice in which Ovol1 and Slug expression are still intact. We monitored tumor growth over 6 weeks, and then harvested tumor tissue to quantify tumor microvascular density by immunohistochemistical labeling of CD31-positive endothelial cells. We used confocal imaging to visualize labeled microvessels and calculated microvascular density using Fiji/ImageJ software.

Preliminary Results: Our results reveal that colorectal cancer tumors injected into Ovol1- or Slug-deficient mice are reduced in size compared to wild-type control animals. Correspondingly, we also find that microvascular density appears to be reduced compared to tumors grown in wild-type mice. Taken together, these data suggest that endothelial Ovol1 and Slug may be individually required for tumor angiogenesis and colorectal cancer growth.

Conclusion/Future Steps: Our data may support our central hypothesis that Ovol1-Slug signaling centrally regulates tumor angiogenesis. Improved understanding of this regulatory mechanism will be important for the future of cancer treatment, because it could accelerate development of a new class of anti-angiogenic drugs to target this pathway and more efficiently prevent tumor growth and metastasis.