

Kerri Thurmon, Biochemistry

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Faculty Mentor: Dr. Lixing Reneker, Ophthalmology
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The effects of oncogenic Ras on the ocular lenses of transgenic mice

Ras is a small GTP-binding protein in the signal transduction pathways activated by growth factors. In most cell types, activation of Ras is essential for normal cell proliferation. A mutation in the Ras gene can lead to a constitutive active (or oncogenic) state of Ras regardless of the upstream stimuli present. Expression of oncogenic Ras in the tissue can result in tumor formation and cancer development. Moreover, thirty percent of human cancer is associated with a mutation in the Ras gene. When we over-express the oncogenic Ras mutant in the ocular lens of transgenic mice, we observe the formation of blood vessels in the lens, a process known as angiogenesis. Angiogenesis is a critical step during cancer development and metastasis. Therefore we can use the transgenic lens as an *in vivo* model to study the molecular mechanisms of Ras-induced angiogenesis. The purpose of this study is to examine the abnormal development of the vascular system in the lens of the oncogenic Ras transgenic mice. Histology was performed to determine the age at which angiogenesis occurs in the lens of three different Ras transgenic lines. We found that blood vessels begin to develop in the transgenic lens between embryonic days 13 and 15 after lens epithelial cell over-proliferation occurs. Furthermore, the transgenic mice from the line with the highest expression level of oncogenic Ras develop the blood vessel in the lens at the earliest stage, suggesting that angiogenesis has a direct correlation with oncogenic Ras activity. Future studies will be focused on using the RT-PCR technique to examine the expression of genes which are known to induce angiogenesis in the normal and Ras transgenic lenses.