AI-13. CIRCULATING ENDOTHELIAL PROGENITOR CELLS IN GLIOBLASTOMA PATIENTS EXPRESS INCREASED LEVELS OF c-Kit AND SCF
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Current treatment options for glioblastoma patients have modest effects on survival. Since GBMs are one of the most vascularized tumors, treatment targeting GBM vessels has recently been introduced; clinical improvement, however, is limited. Endothelial progenitor cells are bone-marrow derived cells that home to ischemic tissue, guided by chemoattractants, where they differentiate under the influence of the microenvironment, and stimulate angiogenesis by secreting proangiogenic factors. As such, EPCs play an important role in neovascularization, including in GBMs. While changes in gene expression in EPCs once they arrive at their target location are well-established, little is known about the expression of proangiogenic factors in EPCs that are circulating in the blood. Since important factors from the GBM microenvironment also enter the bloodstream, we hypothesized that changes in gene expression could already be present in circulating EPCs from GBM patients. In order to test this hypothesis, we isolated EPCs (CD34+CD133+CD45dim) by FACS from blood of healthy controls (HC) and GBM patients. We determined the expression of a panel of 54 genes involved in angiogenesis by RT-PCR. The amount of circulating EPCs were similar between HC and GBM patients. Several genes, however, were differentially expressed; EPCs from GBM patients expressed both c-kit and SCF at a higher level than HC EPCs. In GBM, SCF is an important proangiogenic factor, which binds to its receptor c-kit. Both SCF and c-kit are expressed by subsets of endothelial cells in GBMs. We are currently investigating whether EPC c-kit and SCF expression correlates with tumor endothelial cell expression, and plan to do functional studies to determine the significance of our findings in GBM neovascularization. Our findings suggests that GBMs are capable of influencing gene expression in EPCs while they are still in the circulation. Influencing circulating EPCs in GBM patients could represent a novel type of antiangiogenic therapy.