The Role of Stress Inducible Protein 1 in Brain Tumor Angiogenesis

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The cochaperone STI1 forms a protein complex with Hsp70 and 90 that supports protein folding. STI1 is secreted associated to endosomal vesicles, once in extracellular space, it interacts with prion protein (PrP^C) on plasma membrane and triggers several trophic effects, such as proliferation, protection against cell death, differentiation and migration. Hypoxia-driven STI1 secretion allows the interaction with PrP^C triggering angiogenesis stimulation in experimental ischemia, contributing to post-ischemia brain recovery. Together, these findings suggest the involvement of STI1-PrP^C complex to the mechanisms related to angiogenesis. The ability of tumor cells in stimulate blood vessel formation is an essential hallmark for tumor growth and, consequently, a matter of intense research for new therapeutic targets. The aim of this study is to evaluate the angiogenic potential of STI1-PrP^C complex using *in vivo* and *in vitro* approaches. The mouse brain tumor cell line GL261-luciferase was chosen to study *in vivo* angiogenesis in transgenic mice expressing different levels of STI1 and PrP^C. Preliminary results indicate that STI1 haploinsufficient ($STI1^{+/-}$) and overexpressing STI1 mice inoculated with GL261 cells have increased survival rate when compared to wild-type ones. *In vivo* imaging indicated increased bioluminescence signal in $STI1^{+/-}$ and overexpressing mice. $STI1^{+/-}$ mice present larger tumors with increased blood vessel formation, as assessed by CD31 immunstaining. Moreover, *in vitro* analyses in HUVEC (human umbilical vein endothelial cells) tube formation assay suggest that recombinant STI1 has angiogenic activity. Additional *in vivo* and *in vitro* experiments will be carried out to understand the functions of STI1 and its receptor PrP^C in angiogenesis associated processes.