

**FUNCTIONAL INVESTIGATION OF TUMOR AND ANGIOGENESIS SUPPRESSIVE CANDIDATE TUMOR SUPPRESSOR, CYSTEINE-RICH INTESTINE PROTEIN 2 IN NASOPHARYNGEAL CARCINOMA**

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**Abstract**

A novel candidate tumor suppressor gene (TSG), *Cysteine-rich intestine protein 2 (CRIP2)*, was identified in NPC. This gene has previously been reported to be expressed in the heart endothelium; its possible relationship with tumor development is unknown. Therefore, its contribution and functional role in NPC was investigated. **Methods/Principal findings:** *CRIP2* is down-regulated in 5/7 NPC cell lines and 42/60 (70%) patient biopsies. *CRIP2* re-expression suppresses colony formation *in vitro* and tumor growth *in vivo*. Functional studies such as invasion, HUVEC tube formation, and *in vivo* matrigel plug angiogenesis assays were used to investigate *CRIP2* gene function. Expression of *CRIP2* inhibits angiogenesis both *in vitro* and *in vivo*. Using an angiogenesis protein array, several angiogenesis-related proteins were found to be down-regulated by *CRIP2* re-expression. Analysis of conditioned media and gene expression in *CRIP2*-expressing clones validated protein array analysis results. **Conclusions and Significance:** An interesting candidate TSG, *CRIP2*, was identified. Functional studies confirm that *CRIP2* can suppress tumor growth *in vivo* and inhibit angiogenesis. Angiogenesis is important for cancer development; inhibition of angiogenesis by *CRIP2*, which down-regulates the angiogenesis and VEGF signaling pathway proteins further confirms its importance in tumor development in NPC. *CRIP2* is a potential candidate for future NPC therapeutic treatment.

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