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Novel chromatin regulatory activity of ESCO2 in cancer and neural development

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Abstracts

EG-12. NOVEL CHROMATIN REGULATORY ACTIVITY OF ESCO2 IN CANCER AND NEURAL DEVELOPMENT

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ESCO2 has a well characterized role in the stabilization of the cohesin ring through its acetyltransferase activity. Quantitative PCR studies comparing RNA from tissue collected from ependymoma biopsies and tissue from non-tumor brain, show an increased level of ESCO2 transcription in ependymoma. High levels of ESCO2 protein expression in ependymoma tissue samples were confirmed via immunostaining and confocal microscopy. ESCO2 expression ordinarily peaks during mitosis in order to stabilize the cohesin ring, and is reported to increase the rate of replication. However, some ESCO2 expressing cells are not mitotic in these tumors. Because of the detrimental effects of deletion of ESCO2 on neural development and its high expression in ependymoma, a type of tumor that exhibits many characteristics of primitive neural cells, the current study sought to investigate the broader role of ESCO2 in primitive neural cells. Studies carried out in Zebrafish were performed to explore the possibility of an additional role for ESCO2 as a regulator of neural development. QPCR on Zebrafish embryos at developmental timepoints indicated that ESCO2 expression was highest 48 hours post-fertilization, and then declined thereafter. Confocal microscopy on transgenic NeuroD-EGFP embryos at 24-96 hpf confirmed that the proportion of ESCO2 positive brain cells decreases by 96 hpf, that non-mitotic ESCO2 expressing cells decline, and that 48 hpf appear to display a unique pattern of ESCO2 staining associated with the 4th ventricle. Using FACS and subsequent chromatin immunoprecipitation studies, Esco2- bound chromatin was isolated from NT2 neural progenitor cells and NeuroD-EGFP+ transgenic zebrafish, and utilized to identify novel sites of Esco2 regulation. The data obtained suggests an additional layer of neural regulatory activity that may be unrelated to the reported SMC3 acetyltransferase activity of ESCO2, and that could play a role in neural pathologies such as cancer. Esco2 may be a novel therapeutic target for ependymoma.