



*Carcinogenesis*, 2013 Jul;34(7):1431-41. doi: 10.1093/carcin/bgt067. Epub 2013 Feb 22.

### **Estrogen receptor $\beta$ expression induces changes in the microRNA pool in human colon cancer cells.**

Edvardsson K, Nguyen-Vu T, Kalasekar SM, Pontén F, Gustafsson JÅ, Williams C.

Department of Biology and Biochemistry, Center for Nuclear Receptors and Cell Signaling, University of Houston, Houston, TX 77204, USA.

#### **Abstract**

**There is epidemiological, animal and in vitro evidence that estrogen receptor  $\beta$  (ER $\beta$ ) can mediate protective effects against colon cancer, but the mechanism is not completely understood.** Previous research has indicated critical pathways whereby **ER $\beta$  acts in an antitumorigenic fashion.** In this study, we investigate ER $\beta$ 's impact on the microRNA (miRNA) pool in colon cancer cells using large-scale genomic approaches, bioinformatics and focused functional studies. We detect and confirm 27 miRNAs to be significantly changed following ER $\beta$  expression in SW480 colon cancer cells. Among these, the oncogenic miR-17-92 cluster and miR-200a/b are strongly downregulated. Using target prediction and anticorrelation to gene expression data followed by focused mechanistic studies, we demonstrate that repression of miR-17 is a secondary event following ER $\beta$ 's downregulatory effect on MYC. We show that re-introduction of miR-17 can reverse the antiproliferative effects of ER $\beta$ . The repression of miR-17 also influences cell death upon DNA damage and mediates regulation of NCOA3 (SRC-3) and CLU in colon cancer cells. We further determine that the downregulation of miR-200a/b mediates increased ZEB1 while decreasing E-cadherin levels in ER $\beta$ -expressing colon cancer cells. Changes in these genes correspond to significant alterations in morphology and migration. Our work contributes novel data of ER $\beta$  and miRNA in the colon. **Elucidating the mechanism of ER $\beta$  and biomarkers of its activity has significant potential to impact colon cancer prevention and treatment.**