Estrogen represses anti-apoptotic genes expression via MiR-23a: contribution to sex differences in the development of hepatocellular carcinoma

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BACKGROUND: Hepatocellular carcinoma (HCC) is the most frequent primary tumor of the liver and occurs mainly in men. Estrogen (E2) has been reported to exert a protective role in this gender disparity seen in HCC. Dysregulation of microRNA(s) is well known to be implicated in cell proliferation and apoptosis in HCC. However, it remains to be determined whether E2 plays a role in regulating miRNA(s) expression, thus inhibiting HCC development. METHODS: Differential expression of miRNA(s) in apoptotic pathway was examined by microarray analysis in estrogen receptor a (ER-a) positive liver cancer cell line Snu387, treated with or without E2. Expression profiles of the microRNAs were verified using qRT-PCR. RESULTS: We identified 28 upregulated miRNAs and 35 downregulated miRNAs in the Snu387 cancer cells in an E2-dependent manner. Among these miRNAs, the expression ofmiR-23a, a candidate miRNA targeting IL-6R(interleukin 6 receptor) and XIAP (X-linked inhibitor of apoptosis), was up-regulated in E2-treated liver cancer cells. Significant downregulation of IL-6R and XIAP mRNA expressions (all with P\0.001) was detected in E2-treated liver cancer cells as compared to non-treated cells. Inhibition of miR-23a binding to its target mRNAs led to a significant increase in IL-6R and XIAP expression (all with P\0.05). CONCLUSIONS: Our results confirmed that E2 had a protective effect on development of HCC, and its mechanism may be mediated through the induction of miR-23a expression which inhibits the anti-apoptotic effects induced by cancer cells.