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Role of SREBP and related molecules in the development of endometrial cancer

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Oncogenic growth signal regulates glucose, glutamine and lipid metabolism to provide the bioenergy and biosynthetic requirements of rapidly dividing tumor cells. A class of membrane-bound transcription factors known as sterol regulatory element-binding proteins (SREBPs) activate the genes encoding the enzymes required to produce cholesterol and unsaturated fatty acids. In this study, we discussed the anticancer role of SREBP and its target genes, lipid and cholesterol metabolism enzymes in the development of endometrial cancer. This study comprised 45 patients with endometrial adenocarcinoma, who were further categorized into Grade 1 (n = 15), Grade 2 (n = 15), and Grade 3 (n = 15). The control group consisted of 29 endometrial tissues without an endometrial cancer diagnosis. SREBP, ATP-citrate lyase (ACLY), acetyl-CoA carboxylase (ACC), fatty acid synthase (FASN), acetyl CoA acetyltransferase (ACAT) and 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) gene expressions were examined using the real-time polymerase chain reaction (RT-PCR) method. The gene expressions of the patient group were higher than the control group (P <0.05), and there were differences between the grades of the patient group (P <0.05). In general comparison, it was observed that SREBP expression increased in the patient group compared to the control group. While the SREBF1 increased in grade 2 (p=0.0001), the SREBF2 increased in grade 1(p=0.0001). The findings imply that whereas lipogenesis might exhibit various tissue-specific behaviours linked to a few pathways, it might also have a direct connection to endometrial cancer.

Keywords: Cholesterol, Endometrial adenocarcinoma, Gene expressions, Lipogenesis, Sterol regulatory element-binding proteins (SREBP)