

Supplementary Table SI. Effect of biological mechanisms on the development of endometrial cancer (EC)

BIOLOGICAL MECHANISM [ref.]	EXPLAINING THE IMPACT ON THE DEVELOPMENT OF EC
Hyperglycemia [1–3]	<ul style="list-style-type: none"> ➤ Stimulates the growth of EC cells by providing them with a source of carbon; ➤ Induces DNA damage and oxidative stress, thereby triggering the early stages of tumorigenesis; ➤ Glucose concentration is closely related to the growth of EC cells: low glucose suppressed cell growth and proliferation, induced prominent cell apoptosis, and led to cell cycle G1 arrest, while high glucose enhanced the adhesion and invasive abilities of EC cells.
Hyperinsulinemia [1, 4–7]	<ul style="list-style-type: none"> ➤ Insulin can promote tumor genesis through a direct effect by acting upon the insulin/insulin like growth factor family of receptors or indirectly by affecting the levels of other modulators, such as insulin-like growth factors, sex hormones and adipokines; ➤ Elevates systemic levels of insulin-like growth factors, and elevated levels of both anti- and pro-inflammatory adipokines have been linked to carcinogenesis; ➤ Insulin could up-regulate the expression of vascular endothelial growth factor and, consequently, angiogenesis, a phenomenon observed in tumor growth; ➤ Insulin and insulin-like growth factors (IGFs) influence many important signaling pathways in EC cells, including the phosphatidylinositol 3-kinase (PI3K) and mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) pathways, all of which may play a key role in the occurrence and development of EC.
Chronic inflammation [5, 8]	<ul style="list-style-type: none"> ➤ Can trigger cancer development and progression; ➤ Inflammatory factors (such as tumor necrosis factor α (TNF-α), interleukin-6 (IL-6), and cyclooxygenase-2 (COX-2)) participate in carcinogenesis, which mediates cellular signal transduction, reduces tumor inhibitory function, increases cell cycling and induces oncogene expression; ➤ Activation of the NF-κB signaling pathway plays a key role in certain types of cancers in women, such as EC, breast cancer and ovarian cancer.

References

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