Endometrium is a unique tissue characterized by the changes in a cyclic fashion taken place under the control of estrogen and progesterone hormones. It has been shown that expression levels of various types of proteins like heat shock proteins, growth factors, cytokines and several signaling molecules those get involved in endometrial changes have clear differences at various phases of menstrual cycle. Notch signaling is an evolutionarily conserved mechanism used to regulate cell fate decision. Four Notch receptors (Notch 1-4) and two ligands jagged 1-2 have been identified in mammals. In several studies it has been demonstrated that Notch signaling is responsible for significant processes, like differentiation, proliferation and apoptosis those are finely regulated in human endometrium in order to allow a successful menstrual cycle. Notch signaling pathway has active role during the blood vessel formation in angiogenesis process for endothelial cells. One of the main morphogenetic events occurring during the menstrual cycle is formation of spiral arteries(1). In this respect, there is little known about the expression levels and localization of notch-3 and notch-4 proteins in human endometrial tissue. So the aim of this study is to investigate the expression levels of Notch-3 and Notch-4 proteins in the normal endometrial samples surgically removed from 24 women. Tissues were divided according to the menstrual cycle phases, and immunohistochemistry was applied to the sections, and the immunostaining was evaluated semiquantitatively.

In the cytoplasm of glandular epithelium cells, both Notch-3 and Notch-4 immunoreactivities were observed. The expression levels of the proteins were correlated, and they showed mild immunoreactivities in early-mid proliferative phase of the menstrual cycle in glandular epithelium. On the other hand, in late proliferative as well as early secretory phase, the expression levels of the proteins were the highest with respect to the other phases. During the late secretory phase, the expressions were mild, which is the similar situation for early-mid proliferative phase in glandular epithelium. In this study, cyclic regulation of Notch-3 and Notch-4 proteins in the endometrium is demonstrated for the first time. According to our results, cyclic expression of Notch-3 and Notch-4 proteins seems to be involved in regulation of structural changes of endometrium and any malfunctioning related to those proteins may cause several endometrial pathologies.

Fig. 1: Representative photomicrographs of Notch-3 expression in the endometrium at different phases. Mild immunoreactions belong to early-mid proliferative (a) and late secretory phases (d). Strong immunoreactivities are seen at late proliferative (b) and early-mid secretory phase (c).

Fig. 2: Representative photomicrographs of Notch-4 expression in the endometrium at different phases. Mild immunoreactions belong to early-mid proliferative (a) and late secretory phases (d). Strong immunoreactions are seen at late proliferative (b) and early-mid secretory phases (c). All magnifications are X 20.