The human endometrium, during every reproductive cycle, undergoes extensive tissue remodelling in response to cyclical hormonal changes. Estrogens stimulate proliferation and re-establishment of the stromal and vascular components of the tissue including many proteins and several transcription factors, especially angiogenic factors, that are important for DNA replication and cell division. Angiogenesis, the formation of new blood vessels, plays an important role in the remodelling of endometrial tissue. Notch is a transmembrane receptor which belongs to a growth factor family. It is structurally and functionally conserved during evolution and it regulates cell fate specification, stem cell maintenance, and initiation of differentiation in embryonic and postnatal tissues. The mammalian family of Notch protein consists of four different isoforms (Notch 1-4) and its ligands can be classified into two classes as Jagged 1-2. Activation of Notch signaling pathway promotes the development of the vascular system in embryo, normal adult tissues, and cancerous lesions. Notch genes and their ligands are known to be expressed in endothelial cells, however little is known about their expression in the human endometrium, and their role in the cyclical endometrial changes. The purpose of this study was to investigate the cellular localization of Notch-1 and Jagged-1 in normal endometrium at different endometrial phases under the control of steroid hormones by immunohistochemistry.

Endometrial tissue samples were obtained from 24 women with regular menstrual cycles operated because of benign gynecological conditions. Menstrual cycle phases were determined and immunohistochemistry was applied to the sections and the immunostaining was evaluated semiquantitatively.

Notch-1 and Jagged-1 immunoreactivities were both detected on cell membranes. The expression of both proteins were correlated and they showed weak immunoreactivities in early-mid proliferative phase of the menstrual cycle in both glandular epithelium and stromal cells. On the other side, in late proliferative and early secretory phases, the expressions of the proteins were the highest among the other phases of the cycle. During the late secretory phase the expressions were weak as in the early-mid proliferative phase in the glandular epithelium and stromal cells. According to our knowledge, this is the first study which shows cyclic regulation of Notch signaling pathway in the endometrium. Notch signaling pathway is shown to have an important role in cyclic structural changes of endometrium and disregulation of these functions may lead to several endometrial pathologies.
Fig. 1: Representative photomicrographs of Notch-1 expression in the endometrium at different cycles. Weak immunoreactions belong to early-mid proliferative (a) and late secretory phases (d). Strong immunoreactions are observed at late proliferative (b) and early-mid secretory phases (c). All magnifications are X 20.

Fig. 2: Representative photomicrographs of Jagged-1 expression in the endometrium at different cycles. Weak immunoreactions belong to early-mid proliferative (a) and late secretory phases (d). Strong immunoreactions are observed at late proliferative (b) and early-mid secretory phases (c). All magnifications are X 2.