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Ultrastructural changes of the extracellular matrix in human uterine leiomyoma and squamocellular cervical carcinoma

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Leiomyomata are the most common benign uterine tumors and are a major cause of gynecological morbidity and infertility. Squamocellular cervical carcinoma, in turn, is a common gynecologic malignancy. However, their etiopathogenesis remains poorly understood. The aim of this study was to characterize from an ultrastructural point of view the changes occurring in the extracellular matrix (ECM) of human uterine cervices with leiomyoma or squamocellular carcinoma. Eight women, aged 45-58, underwent laparoscopic myomectomy (n=5) or vaginal hysterectomy (endometrial carcinoma, n=3). Samples were processed for transmission electron microscopy, and digital images were obtained from either semithin and thin resin-embedded sections. The lamina propria of the uterine cervix with leiomyoma was generally filled by a dense and disarranged ECM, wherein twisted collagen fibers with a regular banding and diameter, predominated. Collagen tended to be closely-packed and compartmentalized into large lacunar-like spaces by very thin (ca. 0,25 μm) and long (> 10 μm) cytoplasmic processes originating from myofibroblastic, smooth muscle or interstitial Cajal-like cells. Fibril-forming channels or fibripositors (Birk et al., 1989; Starborg et al., 2008), were sometimes identified and consisted of isolated collagen fibrils surrounded by plasma membrane. Very electron dense core-like aggregates (1-2 μm length x 1-1,5 μm width) scattered within the lacunar-like spaces. Cores consisted of structures whose diameter was similar to that of collagen (ca. 71 nm) but showing a gradient of decreasing electron density from the core itself towards peripheral mature collagen fibers; in between these fibers, intermediate electron dense ones laid (fibrillin microfibrils?). Leiomyoma showed more and denser ECM with respect to carcinoma, the latter evidencing numerous and heterogeneous, actively proliferating cancer cells, leaving few and small intercellular spaces wherein macrophages, mast cells and plasma cells, were sometimes observed. The abnormal orientation of collagen fibers in leiomyoma contributes to the fibrotic and stable ECM and may also facilitate local tumor invasion. Therapy in these cases should target ECM dissolution, rather than solely inhibiting cell proliferation.

References

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Starborg et al. (2008) Electron microscopy in cell-matrix research. Methods 45: 53-64.

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