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IMMUNOHISTOCHEMISTRY OF NORMAL AND HYPERPLASTIC DUCTAL BREAST EPITHELIUM

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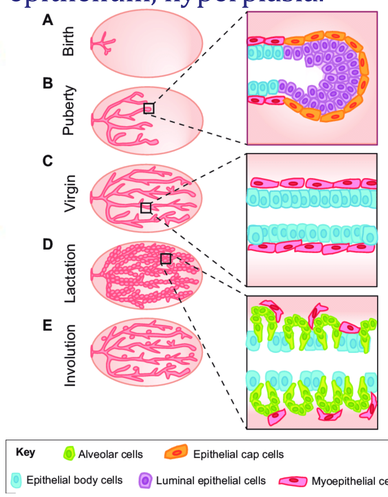
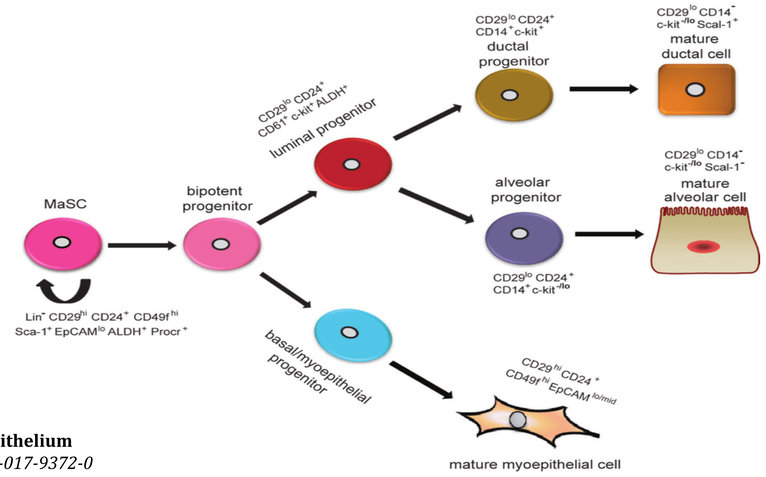
Introduction: Immunohistochemistry helps to realize a differential diagnosis of intraductal proliferative lesions of the breast. Biomarkers provide data about the grade of differentiation and size of the lesion, which are necessary to predict the risk of malignancy. **Purpose:** Immunohistochemical research of normal and hyperplastic ductal breast epithelium and the evaluation of histological subtypes according to the expression of the markers. **Keywords:** immunohistochemistry, ductal breast epithelium, hyperplasia.

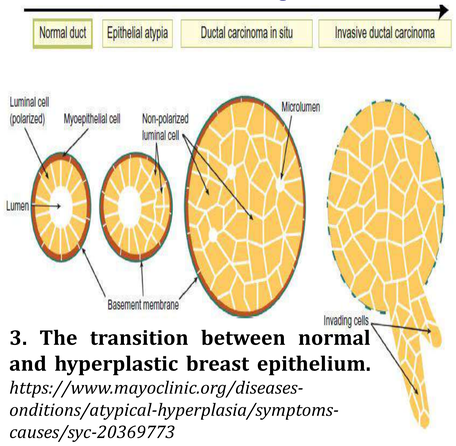


1. The morphological evolution of the breast epithelium
Rhttps://link.springer.com/article/10.1007/s10911-017-9372-0



2. The cellular hierarchy of the breast epithelium
https://www.intechopen.com/books/breast-cancer-from-biology-to-medicine/the-role-of-stem-cells-in-breast-cancer

Material and methods: In the study were included following immunohistochemical markers: CK5/6, CK7/8, 34_{β}E12, p63, E-cadherin, SMA, Ki67, ER, PR, Her2/neu. A rigorous analysis of markers expression has been realized according to DIN (ductal intraepithelial neoplasia) classification, as well has been performed the molecular profile of tumors and differential diagnosis with ductal carcinoma *in situ*.

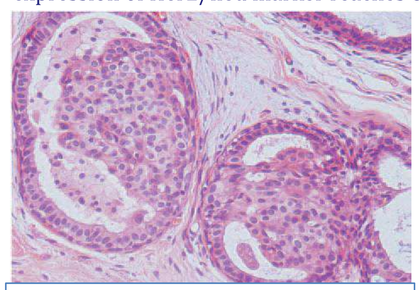


3. The transition between normal and hyperplastic breast epithelium.
https://www.mayoclinic.org/diseases-onditions/atypical-hyperplasia/symptoms-causes/syc-20369773

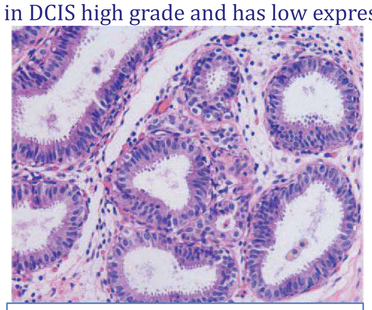
Traditional terminology	DIN terminology
UDH (usual ductal hyperplasia)	UDH (usual ductal hyperplasia)
FEA (Flat epithelial atypia)	DIN 1A (ductal intraepithelial neoplasia, grade 1A)
ADH (Atypical ductal hyperplasia)	DIN 1B (ductal intraepithelial neoplasia, grade 1B)
DCIS grade 1 (ductal carcinoma in situ, low grade)	DIN 1C (ductal intraepithelial neoplasia, grade 1C)
DCIS grade 2 (ductal carcinoma in situ, intermediate grade)	DIN 2 (ductal intraepithelial neoplasia, grade 2)
DCIS grade 3 (ductal carcinoma in situ, high grade)	DIN 3 (ductal intraepithelial neoplasia, grade 3)

4. Classification DIN (ductal intraepithelial neoplasia),by WHO in 2007.
Intraepithelial neoplasia, table 4-1, p.181, by Maode Lay

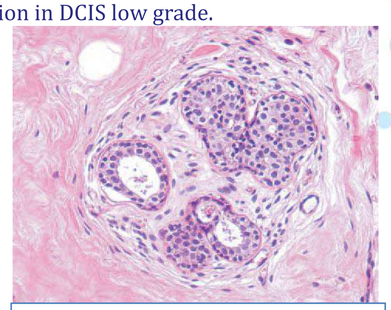
Results: The ductal and lobular units are consisted of luminal and basal epithelial cells. Luminal cells express CK7/8, CK18/19. The basal compartment contains cells which are immunostained by CK5, CK7, CK14, CK17. UDH (usual ductal hyperplasia) expresses CK5, CK5/6, 34_{β}E12. ADH (atypical ductal hyperplasia) is positive for E-cadherin. In flat epitelial atypia (FEA) the cells are immunostained by CK19, ER, PR. In 75%, DCIS (ductal carcinoma in situ) is positive for ER, PR, E-cadherin. The 34_{β}E12 receptor is expressed in 90% of UDH. The expression of CK5/6 occurs in 96% of ADH and DCIS. The expression of Her2/neu marker reaches 80% in DCIS high grade and has low expression in DCIS low grade.



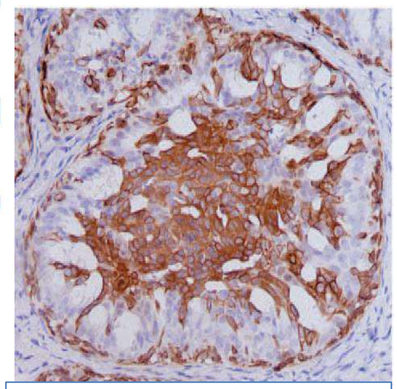
5. UDH (USUAL DUCTAL HYPERPLASIA)
Intraepithelial neoplasia, fig.4-7, p.183, by M.L.



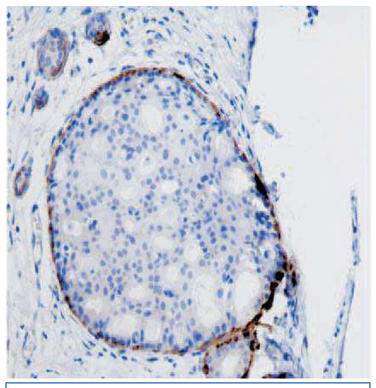
6. FEA (FLAT EPITHELIAL ATYPIA), DIN1A. *Intraepithelial neoplasia, fig.4-8, p.186, by M.L.*



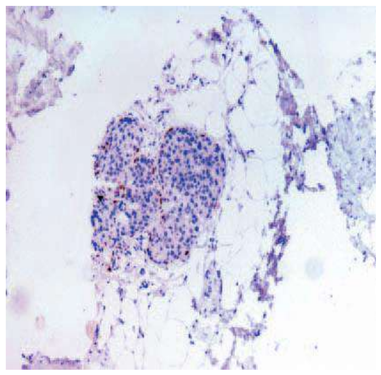
7. ADH ,DIN1B. *Intraepithelial neoplasia, fig..4-12,p.191, by M.L.*



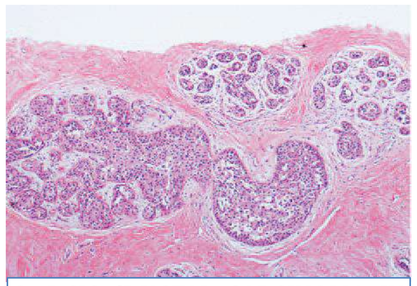
11. Immunostaining of CK5/6 in UDH. Proliferative epithelium is positive for CK5/6. *Intraepithelial neoplasia, fig.4-23,p.205, by M.L.*



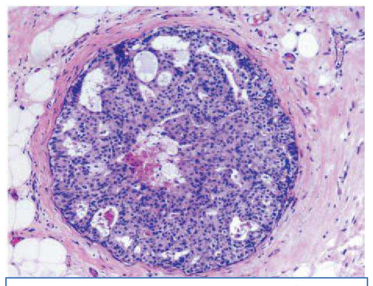
12. The Presence of Myoepithelium in DCIS. Myoepithelial cells are strongly positive for SMA. *RIntraepithelial neoplasia, fig.4-25,p.207,by M.L.*



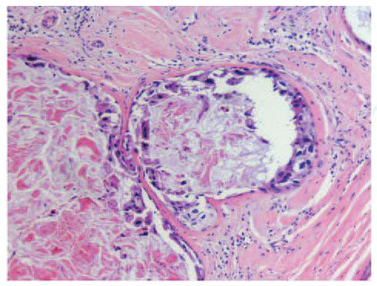
13. Immunostaining of CK5/6 in ADH. *Intraepithelial neoplasia, fig.4-24,p.206,by M.L.*



8. DCIS (DUCTAL CARCINOMA IN SITU) DIN1C, grade 1. *Intraepithelial neoplasia, fig.4-14,p.206, by. M.L.*



9. DCIS, DIN1C, grade 2. *Intraepithelial neoplasia, fig.4-17,p.196, by M.L.*



10. DCIS, DIN1C, grade 3. *Intraepithelial neoplasiia, fig.4-21,p.200, by M.L.*

Conclusions: The application of immunohistochemical markers aids the assessment of morphological diagnosis of breast epithelium hyperplasia. Cytokeratins are superior to others in the establishment of cellular source of proliferative lesion and provide an efficient differential diagnosis with malignancies.

Scientific supervisor: Fulga Veaceslav, associate professor