"World Congress on Breast Cancer" on August 03-05, 2015 Birmingham, UK

Diagnostic utility of immunohistochemical staining for basal keratins, K5 and K14, and p63 in the differential diagnosis of malignant glandular lesions

Igor Buchwalow, Thomas Loening, Markus Tiemann, Ivan Pavlov & Werner Boecker

Institute for Hematopathology and Albertinen Pathology, Hamburg, Germany,
& Belgorod State University, Belgorod, Russia

In previous studies, we demonstrated that K5/K14-positive basal cells of the stratified glandular epithelia of breast and salivary tissue co-expressing p63 give rise to both glandular and/or myoepithelial cell lineages. Here we analyzed the co-expression of p63 with keratins K5 and K14 in tumor cells and in their physiological p63/K5/14+ counterparts in the breast and salivary gland. The epithelium of the breast and salivary gland and some tumors arising from these glands revealed p63/K5/14-positive progenitor cells which differentiate to glandular cell lineages via intermediary cells, with a sequential expression of basal and lineage specific proteins.

The cells of this immunophenotype (p63/K5/14) may be regarded as putative adult progenitor cells. This study provides evidence that cells undergoing malignant transformation tend to be fairly early progenitors of the glandular lineage. We generated corresponding stem-cell models describing the role of the immunophenotypically identical progenitor p63/K5/14+ cells in both the glandular benign proliferative and neoplastic lesions. This concept may serve as a valuable tool in understanding benign and malignant glandular lesions of the human breast and salivary glands.

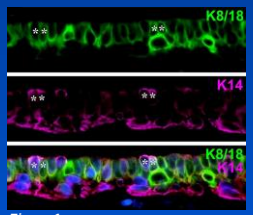


Figure 1

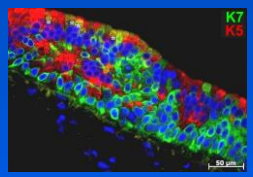


Figure 2

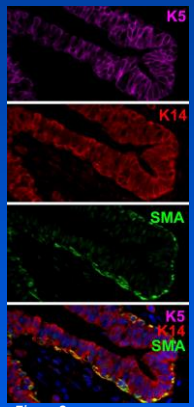


Figure 3

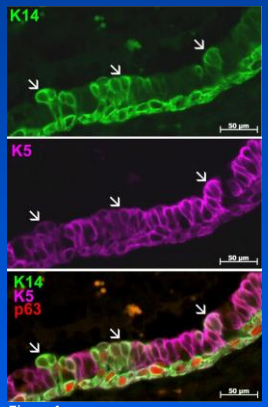


Figure 4

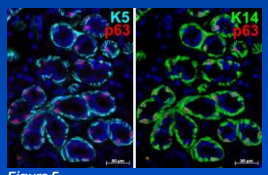


Figure 5

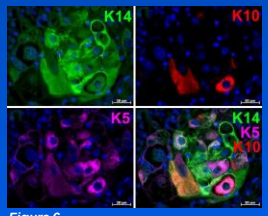


Figure 6

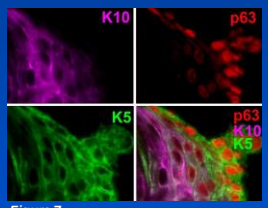


Figure 7

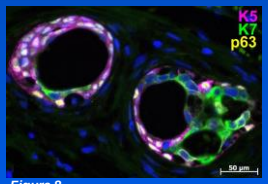


Figure 8

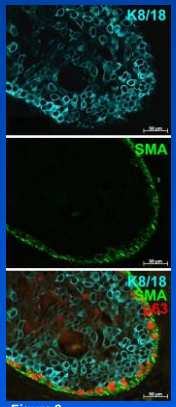


Figure 9

Figure 1. Duct wall of the mammary gland. Co-localization of K14 and K8/18 is revealed through the coincidence (marked with asterisks) of the two labels resulting in a hybrid color, indicating the route of glandular differentiation as in figure 2.

Figure 2. Excretory duct wall of the salivary gland. Co-localization of K5 and K7 is revealed through the coincidence (marked with asterisks) of the two labels resulting in a hybrid colorlike in Figure 1.

Figure 3. Duct wall of the mammary gland. Most cells, including luminal cells, co-express both "basal" keratins, K5 and K14, but only cells in the basal layer express additionally SMA, indicating the final step of myoepithelial differentiation as in Figure 4.

Figure 4. Duct wall of the mammary gland. Both "basal" keratins, K5 and K14, are co-expressed in many cells, including luminal cells (marked with arrows), but only K5/14-positive basal myoepithelial cells express p63, reflecting the route of myoepithelial differentiation.

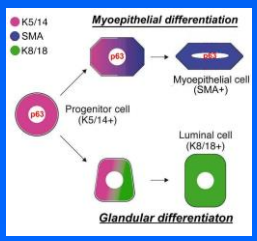
Figure 5. Acini of the salivary gland. Like in the mammary gland (Figure 4), only K5/14-positive basal myoepithelial cells express p63 at the final step of myoepithelial differentiation.

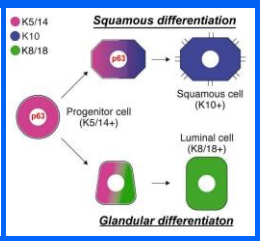
Figure 6. Adenomyoepithelial tumor of the breast with focal squamous metaplasia. Co-localization of K5 (pink), K14 (green) and K10 (red) is revealed through the coincidence of the three labels resulting in a hybrid orange color thus reflecting the route of squamouse differentiation from K5/14-positive cells. Note the transition of K5- and/or K14-positive cells to K10-positive squamous cells.

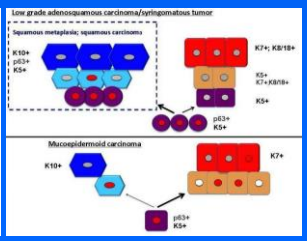
Figure 7. Syringoma of the nipple. Squamous metaplasia with p63+K5+ cells at the periphery which differentiate towards K10+ positive squamous cells. Note that during this differentiation p63 is down regulated.

Figure 8. Syringoma. This picture shows differentiation towards K7+ glandular cells. The glandular cells do not express p63.

Figure 9. Usual ductal hyperplasia of the human breast. Notice p63+SMA+ myoepithelial cells at the periphery. Proliferating cells express glandular keratin K8/18. Occasional cells in the proliferating mass express p63 which are K5-positive (not shown here).







Models of progenitor relationships. **In normal duct epithelium p63+/K5+ progenitors give rise to glandular cells (K8/18+) via intermediary cells. Likewise, in normal nipple squamous epithelium, immunphenotypically identical p63+/K5+ progenitors give rise to p63+/K5+/K10+ cells, which then mature to K10+ squamous cells. The similarity in immunphenotypical appearance of progenitors in these epithelia and the fact that they differentiate either in breast epithelial or in squamous cells suggest robust lineage commitments in each site. All three tumors (squamous carcinoma, low-grade adenosquamous carcinoma/syringomatous tumor, mucoepidermoid carcinoma) and squamous metaplasia contain p63+/K5+ progenitors, which differentiate to squamous (K10+) and glandular (K7+/K8/18+) cells through intermediary stages. The squamous lineage differentiation of all tumor types mirrors the normal squamous epithelium of the ectoderm of which the organs arise. The different cell lineages may arise via reprogramming the target physiological progenitors during malignant transformation.**