—Photogravure—

Immunohistochemical Analyses of Cytokeratin in Breast Cancers from Old and New Eras

Hiroyuki Takei[1], Keiko Yanagihara[1], Tomoko Kurita[1], Miki Iwamoto[1], Natsuki Seki[2], Hideko Hoshina[3], Tadashi Yokoyama[2], Koji Yamashita[1], Shinya Iida[4] and Eiji Uchida[5]

[1]Department of Breast Surgery, Nippon Medical School
[2]Department of Surgery, Nippon Medical School Tama Nagayama Hospital
[3]Department of Breast Surgery, Nippon Medical School Musashi Kosugi Hospital
[4]Department of Breast Oncology, Nippon Medical School Chiba Hokusoh Hospital
[5]Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School

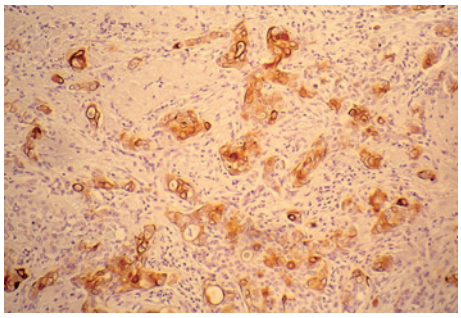

Fig. 1

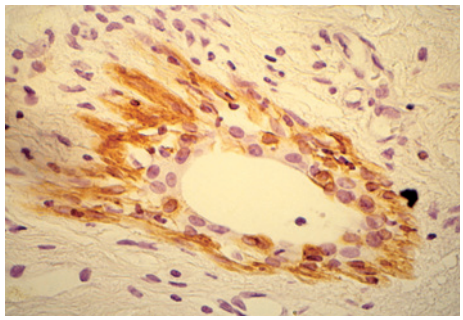

Fig. 2

Breast cancers can be classified with multigene assays into the following subtypes: luminal A, luminal B, human epidermal growth factor receptor 2 (HER2)-enriched, and basal[1]. These subtypes are constitutively defined by means of immunohistochemical staining for estrogen receptor (ER), progesterone receptor, HER2, and Ki67[2], and the basal subtype is uniquely negative for ER, progesterone receptor, and HER2[2]. Most cases of the basal subtype are positive for cytokeratins 5, 6, 14, and 17[3,4].

High molecular weight (HMW) cytokeratins (cytokeratins 1, 5, 10, and 14)[5] are reportedly present in 21% of cases of invasive carcinoma of the breast[6] **(Fig. 1)**, which are also positive for myoepithelial cells[6] **(Fig. 2)**. Expression of HMW cytokeratins is significantly correlated with high histological grades and the absence of ER[6]. Furthermore, HMW cytokeratins are positive in all cases of ductal hyperplasia but is negative in most cases of atypical ductal hyperplasia and ductal carcinoma in situ[7].

A low molecular weight (LMW) cytokeratin (cytokeratin 8)[5] is reportedly present in 65% of cases of invasive carcinoma of the breast[8] **(Fig. 3)**. Cytokeratin 8 is also significantly correlated with low histological grades and ER positivity[8]. Cytokeratin 8 is present in most breast epithelial cells in cases of ductal hyperplasia, atypical ductal hyperplasia, and ductal carcinoma in situ[9]. A high level of cytokeratin 8 immunostaining is associated with a favorable prognosis of breast cancer, and reduced or absent staining is associated with an unfavorable outcome[4,8].

Conflict of Interest: The authors have no conflicts of interest to declare.

Correspondence to Hiroyuki Takei, M.D, Department of Breast Surgery, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan

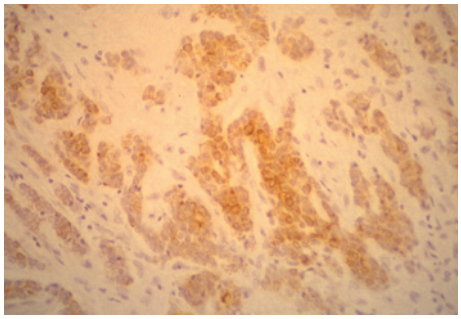

Fig. 3

Fig. 1 Immunohistochemical staining for high molecular weight (HMW) cytokeratin in an invasive ductal carcinoma of the breast

Staining for HMW cytokeratins was observed in the cytoplasm and membranes of cancer cells that had invaded the stroma (original magnification, ×200). A monoclonal antibody 34betaE12 (Enzo Life Sciences, Inc., Farmingdale, NY, USA) against HMW cytokeratins (cytokeratins 1, 5, 10, and 14) was applied to formalin-fixed, paraffin-embedded tissue.

Immunohistochemical methods have been described in detail in previous studies[6,8].

Fig. 2 Immunohistochemical staining for high molecular weight (HMW) cytokeratins in a nonmalignant mammary duct

Staining for HMW cytokeratins was observed in nonmalignant myoepithelial and epithelial cells (original magnification, ×400). The monoclonal antibody 34betaE12 against HMW cytokeratins was applied to formalin-fixed, paraffin-embedded tissue.

Immunohistochemical methods have been described in detail in previous studies[6,8].

Fig. 3 Immunohistochemical staining for cytokeratin 8 in an invasive ductal carcinoma of the breast

Staining for cytokeratin 8 was observed in cytoplasms of cancer cells that had invaded the stroma (original magnification, ×200). The monoclonal antibody 35betaH11 (Enzo Life Sciences, Inc.) against cytokeratin 8 was applied to formalin-fixed, paraffin-embedded tissue.

Immunohistochemical methods have been described in detail in previous studies[6,8].

References

1. Cancer Genome, Atlas Network: Comprehensive molecular portraits of human breast tumours. Nature 2012; 490: 61–70.
2. Goldhirsch A, Winer EP, Coates AS, et al.: Panel members. Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. Ann Oncol 2013; 24: 2206–2223.
3. Dabbs DJ, Chivukula M, Carter G, Bhargava R: Basal phenotype of ductal carcinoma in situ: recognition and immunohistologic profile. Mod Pathol 2006; 19: 1506–1511.
4. Moll R, Divo M, Langbein L: The human keratins: biology and pathology. Histochem Cell Biol 2008; 129: 705–733.
5. Moll R, Franke WW, Schiller DL, Geiger B, Krepler R: The catalog of human cytokeratins: patterns of expression in normal epithelia, tumors and cultured cells. Cell 1982; 31: 11–24.
6. Takei H, Iino Y, Horiguchi J, et al.: Low and high molecular weight cytokeratins in invasive breast carcinoma. Oncol Rep 1997; 4: 33–38.
7. Moinfar F, Man YG, Lininger RA, Bodian C, Tavassoli FA: Use of keratin 35betaE12 as an adjunct in the diagnosis of mammary intraepithelial neoplasia-ductal type-benign and malignant intraductal proliferations. Am J Surg Pathol 1999; 23: 1048–1058.
8. Takei H, Iino Y, Horiguchi J, et al.: Immunohistochemical analysis of cytokeratin #8 as a prognostic factor in invasive breast carcinoma. Anticancer Res 1995; 15: 1101–1105.
9. Shao MM, Chan SK, Yu AM, et al.: Keratin expression in breast cancers. Virchows Arch 2012; 461: 313–322.

E-mail: takei-hiroyuki@nms.ac.jp Journal Website (http://www.nms.ac.jp/jnms/)