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Broad-spectrum immunohistochemical epithelial markers: a review☆

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Summary A relatively large number of broad-spectrum immunohistochemical epithelial markers that can be used as part of the screening panels employed in the recognition of the main cell lineages during the initial evaluation of a poorly differentiated tumor are currently available. Variations exist in the sensitivity and specificity of the individual markers that have traditionally been used for the demonstration of epithelial differentiation and in the pitfalls associated with these markers. This article reviews not only the reactivity of the various pan-keratin antibodies that are often used to assist in the demonstration of epithelial differentiation, but also that of those that have recently become available. A review of the non-keratin, broad-spectrum epithelial markers that have been recognized as being useful is also presented.

1. Introduction

The recognition of epithelial differentiation in well- or moderately differentiated carcinomas does not pose significant diagnostic difficulty on routine histologic preparations since evidence of such differentiation (eg, keratinzation or glandular formation) is usually apparent. In those instances in which the neoplasm shows little or no evidence of epithelial differentiation, immunohistochemical studies using a variety of broad-spectrum epithelial markers are often necessary to either confirm or rule out the epithelial nature of the tumor. *Broad-spectrum epithelial markers* is the term used to refer to those markers that are frequently expressed in a wide range of epithelial tumors. In the initial evaluation of a poorly differentiated tumor in surgical pathology, these markers are employed as part of the screening panel used in the recognition of the major lineages (ie, epithelial, mesenchymal, lymphoid, and melanocytic). The purpose of this article is to present a review of some broad-spectrum epithelial markers that are currently available for the demonstration of epithelial differentiation in poorly differentiated tumors.

2. Keratins

Keratins are the main cytoskeletal component of epithelial cells and the most diverse group of intermediate filaments. Fifty-four functional keratin genes have been identified in humans [1]. These genes have been subdivided into 28 type I genes and 26 type II genes that form 2 clusters of 27 genes each on chromosome 17q12-q21 and 12q11-q13, respectively. Keratins have been subdivided into 2 major sequence types corresponding to class I and class II of the current classification of intermediate filaments [2]. Type I is comprised of 17 epithelial and 11 hair keratins, and type II

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Table 1 Broad-spectrum, anti-keratin monoclonal antibodies that can be used in formalin-fixed, paraffin-embedded tissues

Clone	Reactivity	Commercial source
AE1/AE3	K1-K6, K8, K10, K14, K15, K16, K19	Abcam, AbD Serotec, Abnova, Biorbyt, Biocare Medical, Cell Marque, Chemicon (Millipore), Covance, Dako, Fitzgerald Industries, GeneTex, Invitrogen, LSBio, Novocastra, Novus Biologicals, Progen, Santa Cruz Biotechnology, Thermo Scientific, Vector
AE1/AE3/5D3	K1-K6, K8, K10, K14, K15, K16, K18, K19	Abcam, Biocare Medical
AE1/AE3/PCK26	K1-K6, K8, K10, K14, K15, K16, K19	Ventana
KL1	K1, K2, K5-K8, K11, K14, K16-K18	Abcam, AbD Serotec, Abnova, Accurate, Acris, Beckman Coulter, Biorbyt, GeneTex, LSBio, Novus Biologicals
OSCAR	K7, K8, K18, K19	Acris Antibodies, Cell Marque, Covance
CK22	K1-K8, K10, K11, K13-K19	Accurate, Medite
CK23 (also known as KRT23)	K1-K6, K8, K10, K11, K14-K16, K18, K19	Abcam, Accurate, Atlas, Novus Biologicals
MAK-6 (KA4 & UCD/PR-10.11)[a]	K8, K14, K15, K16, K18, K19	Invitrogen
Lu-5	K1, K5, K6, K8, K14, K18, K19	Abcam, AbD Serotec, Accurate, BioGenex, GeneTex, LS Bio, Novus Biologicals, Progen, Thermo Scientific
MNF116	K5, K6, K8, K17	Abcam, Accurate, Dako, GeneTex, Novus Biologicals, Santa Cruz Biotechnology
LP34	K5, K6, K18	Abcam, AbD Serotec, GeneTex, LSBio, Novocastra, Santa Cruz Biotechnology, Vector
B311.1	K4-K6, K8, K10, K13, K18	Abcam, Accurate, GeneTex, Santa Cruz Biotechnology
Pan-CK	K4-K8, K10, K13-K16, K18	Thermo Scientific
5D3	K8, K18	Abcam, BioGenex, Biorbyt, GeneTex, LSBio, Novocastra, Novus Biologicals, Progen, Santa Cruz Biotechnology, Thermo Scientific, Vector, Ventana
5D3/LP34	K5, K6, K8, K18	Abcam, Abnova, Accurate, GeneTex, Novocastra, Novus Biologicals
34βE12	K1, K5, K10, K14	Abcam, Abnova, Biocare Medical, Biorbyt, Cell Marque, Chemicon, Dako, Enzo Life Sciences, LSBio, Novocastra, Novus Biologicals, Thermo Scientific, Vector
34βE12/C51/AE1	K1, K5, K8, K10, K14-K16, K19	BioGenex
DE-SQ	K13, K14, K15, K16	Abcam, GeneTex, Novus Biologicals
C-11	K4-K6, K8, K10, K13, K18	Abcam, Abnova, Accurate, BioGenex, GeneTex, Novocastra, Thermo Scientific, Vector
C-50	K5, K18	Abcam, Abnova, Accurate, GeneTex
C50	K5, K8	Accurate, Santa Cruz Biotechnology
RCK102	K5, K8	Abcam, Abnova, Santa Cruz Biotechnology
CK223	K4, K5, K6, K8, K10, K13, K18	Abcam
KA4	K14, K15, K16, K19	BD Biosciences

[a] Clone KA4 recognizes K14, 15, 16, and 19; clone UCD/PR-10.11 recognizes K8 and 18.

is composed of 20 epithelial and 6 hair keratins [1]. Keratins are resistant to degradation, show great fidelity of expression, and are very antigenic. All keratins have a common structure, which consists of a central alpha-helical rod domain of 310 amino acid residues that is flanked on either side by head and tail domains. The head domain is the amino terminus, while the tail domain is the carboxyl terminus.