Immunohistochemical Analysis of Keratin Distribution in Eccrine Poroma

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Although eccrine poroma has been thought of as a neoplasm of the intradermal eccrine duct, this interpretation bas not been entirely confirmed. In this study, twenty-five cases of eccrine poroma were retrieved and analyzed by immunobistochemical techniques, using various kinds of monoclonal antikeratin antibodies. Comparative immunohistochemical observations of eccrine poroma and normal eccrine glands revealed that the poroma cells expressed immunophenotypes similar to those of the basal cells of dermal eccrine ducts. Sweat-ductlike structures showed similar staining patterns to those observed in the inner cells of dermal eccrine ducts. Some cystic spaces were similar to those observed in the secretory cells of eccrine glands. Eccrine poroma is, therefore, speculated to originate via the proliferation and expansion of the basal cells of eccrine ducts, although it is very difficult to prove the histogenesis. Some tumor cells may differentiate toward inner cells of the eccrine ducts, forming ductal lumina, whereas other tumor cells differentiate toward eccrine secretory regions, forming some cystic spaces. (Am J Pathol 1993, 142:231-239)

Eccrine poroma was first described as a definite histopathological entity by Pinkus and coworkers¹ in 1956. Pinkus believed that the lesion was a benign neoplasm of the acrosyringeal portion of the epidermis. This strictly limited interpretation, however, has not been entirely confirmed. There have been contrasting observations in enzyme histochemical studies on eccrine poroma. Sanderson and Ryan² reported that certain histochemical reactions resembled those displayed by the dermal part of the normal eccrine sweat duct rather than by the intraepidermal part. The histochemical studies of Hashimoto and Lever³ revealed a striking similarity between the tumor cells and the cells of the adult acrosyringium. On the other hand, the first electron microscopic examination of a case of eccrine poroma revealed that the tumor cells, except for the luminal cells, appeared to be identical to the cells that constitute the outer layer of the intraepidermal eccrine duct.³ In some areas, however, other electron microscopic examinations showed separations between tumor cells, as seen in intradermal duct formation.⁴ Thus, some of the tumor cells in eccrine poroma and most, if not all, of the tumor cells in dermal duct tumor, are thought to be differentiated toward dermal duct cells.5

Recent observations that keratin composition varies greatly among different epithelia raise the possibility that detailed analyses of keratins may allow the identification of various tumors.^{6–10} In this study, therefore, we used various kinds of monoclonal antikeratin antibodies to determine the tissue distribution of various keratins in the expectation that these data could be helpful in investigating the nature and differentiation of eccrine poroma.

Materials and Methods

Twenty-five cases of eccrine poroma were retrieved from the files of the Department of Dermatology, Teikyo University School of Medicine, and the Department of Dermatology, Kanto Communication Hospital. For immunohistochemical studies, the tissue blocks were deparaffinized, rehydrated, rinsed in phosphate-buffered saline, and then stained by the avidin-biotin-complex method.¹¹ Sections were then counterstained with methyl green, and finally mounted. Trypsinization of sections was performed before staining with some anticytokeratin antibodies. The primary antibodies used in this study are shown in Table 1.

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Antibody	Specificity	Antibody source	Ref.
346B4	СК 1	Enzo	9
AF3	CKs 1 to 8	Boehringer	14
346E12	CKs 1, 5, 10, and 11	Enzo	9
BCK102	CKs 5 and 8	Sanbio	15
35BH11	CK 8	Enzo	9
4.1.18	CK 8	Boehringer	
CAM5.2	CKs 8 and 18	Becton-Dickinson	16
NCL5D3	CKs 8, 18, and 19	Sanbio	
PKK1	CKs 8, 18, and 19	Labsystems	17
AE1	CKs 10, 14 to 16, and 19	Boehringer	14
KL 1	CK 11	Immunotech	18
Ks 13 1	CK 13	Boehringer	19
170 2 14	CK 19	Boehringer	
Involucrin	Involucrin (polyclonal)	Biomedical Tech	
CEA	CEA (polyclonal)	Dakopatts	

Table 1. List of Antibodies Used in This Study

Results

Light Microscopic Findings

Most eccrine poromas consisted of broad, anastomosing bands (Figure 1A). Cells comprising the tumor (so-called poroma cells) were uniformly small, cuboidal epithelial cells with lightly basophilic round nuclei and moderate amounts of pale to lightly eosinophilic cytoplasm. They were connected by intercellular bridges. In most, but not in all, eccrine poroma, narrow ductal lumina and, occasionally, cystic spaces were found within the tumor bands. They were lined by an eosinophilic cuticle similar to that which lines the lumina of eccrine sweat ducts (Figure 1B) or by a single row of luminal cells (Figure 1C). Some of the large cystic spaces were directly lined by smooth-surfaced cells (Figure 1C).

The eccrine poroma appears to arise from the epidermis, and it extends into a highly vascular dermis. There are, however, two variants of this tumor. One is hidroacanthoma simplex,¹² which is entirely enclosed within the epidermis, where it appears as discrete aggregates, and the other is dermal duct tumor,¹³ which is largely or entirely located in the dermis, where it consists of variously shaped tumor islands containing ductal lumina. In our studies, there were two cases with hidroacanthoma simplex and one case with dermal duct tumor.



Immunohistochemical Observations

Eccrine Poroma

There were no significant differences in immunophenotypes among hidroacanthoma simplex, dermal duct tumor, and eccrine poroma. Cytokeratins (CKs) were present in all cases. However, each CK revealed different staining patterns. Tumor cells, including poroma and luminal cells, revealed positive staining with antibody AE3,¹⁴ which is specific for CKs 1 to 8 and antibody RCK102,¹⁵ which is specific for CKs 5 and 8 (Figure 2A). The RCK102 usually reacted intensely with the inner surfaces or luminal cells of the ducts and cysts, whereas there was occasional intense staining with AE3.

With antibody 34β E12,⁹ which is specific for CKs 1, 5, 10, and 11, most poroma cells revealed weak immunostaining. In addition, the luminal cells lining the ducts or cysts revealed positive staining, and the inner surfaces of these ducts and cysts revealed strong positive staining (Figure 3A).

Immunostaining with antibody 170.2.14, which is specific for CK19 and antibody AE1,¹⁴ which is specific for CKs 10, 14/15, 16, and 19, was observed in the luminal cells of sweat-ductlike lumina and cystic spaces. Tumor cells around these ducts and cysts also showed positive staining. However, although

weak staining with AE1 was noted in most poroma cells (Figure 4A), most of these cells failed to react to 170.2.14 (Figure 5A).

Immunostaining with antibody CAM5.2,¹⁶ which is specific for CKs 8 and 18, was noted on the inner surfaces of cystic spaces. Some luminal cells of the cystic spaces also showed positive staining with CAM5.2 (Figure 6A). However, small ducts, morphologically similar to eccrine ducts, revealed negative staining.

Immunoreactivity with the antibodies directed against CKs of simple epithelium $(35\beta$ H11⁹ against CK8; 4.1.18 against CK8; PKK1¹⁷ against CKs 8, 18, and 19; NCL5D3 against CKs 8, 18, and 19) was similar to that with CAM5.2. Antibody KL1,¹⁸ which is specific for K11, also revealed similar staining to that with CAM5.2. With KL1, PKK1, and 4.1.18, however, weak staining was occasionally noted in the small ducts that were morphologically similar to eccrine ducts.

The monoclonal antibody $34\beta B4$,⁹ which is specific for CK1, and the antibody Ks13.1,¹⁹ which is specific for CK13, failed to react with any tumor cells. Antibody to involucrin also failed to react with any tumor cells, although occasional weak staining was noted in some luminal surfaces. Carcinoembryonic antigen (CEA) was detected on the inner surfaces of some cystic spaces and ductal lumina. An



Figure 2. Immunobistochemical staining with antibody RCK102 (against CKs 5 and 8). Eccrine poroma (A): Tumor cells reveal positive staining. The arrow indicates the sharp transition between the tumor and the positively stained basal keratinocytes in the adjacent epidermis (original magnification \times 13.2). Normal eccrine gland (B): Positive staining is noted in the outer cells of the dermal eccrine ducts. However, the acrosyringium (arrowheads) is not stained (original magnification \times 66).



Figure 3. Immunobistochemical staining with antibody $34\beta E12$ (against CKs 1, 5, 10, and 11). Eccrine poroma (A): Poroma cells reveal weak staining (original magnification \times 13.2). Normal eccrine gland (B): Eccrine ducts are positively stained, especially strong staining is noted in the luminal cells of the eccrine ducts. In the eccrine secretory elements, only myoepithelial cells (arrowheads) show positive staining (original magnification \times 66).

eosinophilic cuticle lining the ductal lumina was also stained intensely.

Normal Eccrine Gland

Table 2 summarizes the immunophenotypes oftumor cells in eccrine poroma, based on the previously described results. With antibody AE3 against CKs 1 to 8, eccrine secretory elements and eccrine ducts revealed positive reactions, although the acrosyringium and low-



Figure 4. Immunobistochemical staining with antibody AE1 (against CKs 10, 14 to 16, and 19). Eccrine poroma (A): Positive staining is observed in the luminal cells of sweat-ductlike lumina and cystic spaces. Weak staining is also noted in most poroma cells (original magnification \times 13.2). Normal eccrine gland (B): Strong staining is noted in the inner cells of the acrosyringium and dermal eccrine ducts. Outer cells of the eccrine ducts and basal keratinocytes in the epidermis also show positive staining (original magnification \times 66).



Figure 5. Immunohistochemical staining with antibody 170.2.14 (against CK 19). Eccrine poroma (A): Positive staining is observed in the luminal cells of sweat-ductlike lumina and cystic spaces. However, most poroma cells fail to react to 170.2.14 (original magnification \times 13.2). Normal eccrine gland (B): Positive staining (arrowheads) is noted in the inner cells of the acrosyringium and dermal eccrine ducts. However, the outer cells of the eccrine ducts usually reveal negative staining (original magnification \times 66).

ereccrine ducts showed weak staining. The acrosyringium did not stain with antibody RCK102 against CKs 5 and 8; however, positive staining was noted in the outer cells of the dermal eccrine ducts (Figure 2B). In the eccrine secretory elements, myoepithelial cells and eccrine secretory cells showed positive staining, although occasional weak staining was noted in the eccrine secretory cells.

With antibody $34\beta E12$ against CKs 1, 5, 10, and 11, the acrosyringium and dermal eccrine ducts were positively stained; especially strong staining

was noted in the luminal cells of the acrosyringium and dermal eccrine ducts. In the eccrine secretory elements, only myoepithelial cells showed positive staining (Figure 3B).

With antibody 170.2.14 against CK 19, positive staining was noted in the inner cells of the acrosyringium and dermal eccrine ducts. However, the outer cells of the eccrine ducts usually revealed negative staining, although occasional weak staining was noted (Figure 5B). In the eccrine secretory elements, myoepithelial cells and eccrine secretory



Figure 6. Immunobistochemical staining with antibody CAM5.2 (against CKs 8 and 18). Eccrine poroma (A): Positive staining is noted on the luminal cells of some cystic spaces. However, small ducts (arrowbeads), morphologically similar to eccrine ducts, reveal negative staining (original magnification \times 13.2). Normal eccrine gland (B): Eccrine secretory elements show positive staining. However, the eccrine ducts (arrowbeads) and acrosyringium reveal negative staining (original magnification \times 66).

Antibody	CKs	Poroma cell	Luminal cell of ductal lumina	Inner surface of ductal lumina	Luminal cell of cystic spaces	Inner surface of cystic spaces
34βB4	1		-	-	-	-
AE3 34βE12	1, 5, 10, and 11	+ ±	++	++	++	+ +
RCK102 35βH11	5 and 8 8	+ -	+ - (±)	+ - (±)	+ + (±)	+ +
4.1.18 CAM5.2	8 8 and 18	-	± –	± _	$+(\pm) + (\pm)$	+ +
NCL5D3	8, 18, and 19	-	-	-	$+(\pm)$	+
AE1	10, 14 to 16, and 19	± (-)	+	+	+ (±)	+
KL I Ks 13.1	13	_	± -	± -	+ (±) -	+ _
170.2.14 Involucrin	19	_	+ _	+ _	+	+ -
CEA		-	± (-)	+	-	+

 Table 2. Immunohistochemical Staining in Eccrine Poroma

-, ±, and +: staining intensity-negative, weak, positive, respectively. (): occasional staining.

cells showed positive staining, although incidental weak staining was noted in the latter.

With antibody AE1 against CKs 10, 14 to 16, and 19, strong staining was noted in the inner cells of the acrosyringium and dermal eccrine ducts. The outer cells of the eccrine ducts also showed positive staining (Figure 4B). In the eccrine secretory elements, myoepithelial cells and eccrine secretory cells showed positive staining, although occasional weak staining was noted in the latter.

With antibody KL1 against CK 11, eccrine secretory elements and the inner surfaces of the eccrine ducts, including the acrosyringium, revealed positive staining, although the staining intensity on the inner surface of the eccrine ducts was weak. Occasional staining was noted in the luminal cells of the eccrine ducts.

With antibody PKK1 against CKs 8, 18, and 19, eccrine secretory elements revealed positive reactions, although incidental weak staining was noted in the eccrine secretory cells. The inner surfaces of the eccrine ducts were weakly stained, although the acrosyringium showed negative staining.

With the antibodies directed against CKs of simple epithelium (35β H11 against CK 8; CAM5.2 against CKs 8 and 18; and NCL5D3 against CKs 8, 18, and 19), eccrine secretory elements showed positive staining (Figure 6B). Eccrine ducts and acrosyringium revealed negative staining, although occasional weak staining was noted on the inner surfaces of the eccrine ducts.

With antibody 4.1.18 against CK 8, myoepithelial cells showed positive staining, and eccrine secretory cells showed weak staining. Weak staining was also noted on the inner surfaces of the eccrine ducts.

No reactivity with antibody 34βB4 against CK 1 and antibody Ks13.1 against CK 13 was noted in the eccrine ducts or secretory elements. However, occasional weak staining with Ks13.1 was noted on the inner surfaces of the eccrine ducts.

In the eccrine secretory elements, the inner surfaces of the lumina and the canaliculi were not stained with anti-human involucrin antibody. The lining epithelium of the dermal eccrine ducts and acrosyringium was also negative for involucrin, although occasional weak staining was noted on the inner surfaces of the eccrine ducts and acrosyringium.

Carcinoembryonic antigen was detected only on the inner surfaces of the lumina and the canaliculi in the eccrine secretory components. Occasional staining was observed in the inner cells of the dermal ducts and acrosyringium.

These immunohistochemical staining results in normal eccrine glands are summarized in Table 3.

Discussion

Each type of tissue in the body may, at least theoretically, give rise to a neoplasm, and, generally, these tumors will manifest some features of differentiation toward the parent tissue. Many such lesions of the skin have been recognized as the neoplastic counterparts of glandular or ductal portions of skin appendages. The term, eccrine poroma, has been applied to a tumor that manifests features of the distal eccrine sweat duct or sweat pore. The opinion, however, that this tumor is a benign neoplasm of the acrosyringeal portion of the epidermis, has been questioned by some authors, and it is likely that deeper parts of the sweat apparatus may be involved.

Recently, some alterations in epidermal protein expression (synthesis) have been described in certain epidermal diseases, including psoriasis,²⁰ ver-

Antibody	Intraepidermal duct		Dermal duct		Secretory portion	
(CKs)	Location	Results	Location	Results	Location	Results
34βB4 (1)	Inner surfaces Luminal cells Periluminal cells	- - +	Inner surfaces Luminal cells Basal cells	 - + → -	Inner surfaces Secretory cells Myoepithelial cells	- - -
AE3 (1 to 8)	Inner surfaces Luminal cells Periluminal cells	± ± ±	Inner surfaces Luminal cells Basal cells	$\begin{array}{c} + \\ + \rightarrow \pm \\ + \rightarrow \pm \end{array}$	Inner surfaces Secretory cells Myoepithelial cells	+ + +
34βE12 (1, 5, 10, and 11)	Inner surfaces Luminal cells Periluminal cells	+ + (±)* ±	Inner surfaces Luminal cells Basal cells	++ ++ + → ±	Inner surfaces Secretory cells Myoepithelial cells	- - +
RCK102 (5 and 8)	Inner surfaces Luminal cells Periluminal cells	- - -	Inner surfaces Luminal cells Basal cells	$\begin{array}{c} - \rightarrow + \\ - \rightarrow \pm \\ + \rightarrow \pm \end{array}$	Inner surfaces Secretory cells Myoepithelial cells	- (±)* - (±)* +
35βH11 (8)	Inner surfaces Luminal cells Periluminal cells	 	Inner surfaces Luminal cells Basal cells	± (-)* - -	Inner surfaces Secretory cells Myoepithelial cells	+ + +
4.1.18 (8)	Inner surfaces Luminal cells Periluminal cells	± (-)* - (±)* -	Inner surfaces Luminal cells Basal cells	+ (±)* - → + -	Inner surfaces Secretory cells Myoepithelial cells	± (+)* ± (+)* +
CAM5.2 (8 and 18)	Inner surfaces Luminal cells Periluminal cells		Inner surfaces Luminal cells Basal cells	- (±)* - -	Inner surfaces Secretory cells Myoepithelial cells	+ + +
NCL5D3 (8, 18, and 19)	Inner surfaces Luminal cells Periluminal cells	- - -	Inner surfaces Luminal cells Basal cells	- (±)* - -	Inner surfaces Secretory cells Myoepithelial cells	+ + +
PKK1 (8, 18, and 19)	Inner surfaces Luminal cells Periluminal cells		Inner surfaces Luminal cells Basal cells	- → ± - -	Inner surfaces Secretory cells Myoepithelial cells	$(\pm)^{*}$ + $(\pm)^{*}$ +
AE1 (10, 14 to 16, and 19)	Inner surfaces Luminal cells Periluminal cells	++ ++ -	Inner surfaces Luminal cells Basal cells	++ ++ + → -	Inner surfaces Secretory cells Myoepithelial cells	$(\pm)^{*}$ + $(\pm)^{*}$ +
KL1 (11)	Inner surfaces Luminal cells Periluminal cells	± ± +	Inner surfaces Luminal cells Basal cells	± ± (-)* -	Inner surfaces Secretory cells Myoepithelial cells	+ + ±
Ks 13.1 (13)	Inner surfaces Luminal cells Periluminal cells	- (±)* - -	Inner surfaces Luminal cells Basal cells	- (±)* - -	Inner surfaces Secretory cells Myoepithelial cells	- - -
170.2.14 (19)	Inner surfaces Luminal cells Periluminal cells	+ + -	Inner surfaces Luminal cells Basal cells	+ + - (±)*	Inner surfaces Secretory cells Myoepithelial cells	+ (±)* + (±)* +
Involucrin	Inner surfaces Luminal cells Outer cells	- (±)* - (±)* -	Inner surfaces Luminal cells Basal cells	- (±)* - (±)* -	Inner surfaces Secretory cells Myoepithelial cells	
CEA	Inner surfaces Luminal cells Outer cells	+ - (+)* -	Inner surfaces Luminal cells Basal cells	+ - (+)* -	Inner surfaces Secretory cells Myoepithelial cells	+ - -

Table 3. Immunohistochemical Staining in Normal Eccrine Glands

-, \pm , +, and ++: staining intensity—negative, slight, moderate, and strong, respectively. \rightarrow : staining intensity changes in the lower portion of eccrine ducts.

():* occasional staining.

rucae,²¹ and epidermal neoplasms.²² During the last few years several laboratories have developed monoclonal or polyclonal antibodies against epidermal proteins such as involucrin and specific subtypes of keratin polypeptides that seem to participate or have a specific function in epidermal differentiation.²³ The specificity of these antibodies for various epidermal

structures makes them potentially useful for the analysis of normal and pathologic keratinization and for determining the histogenesis of epidermal neoplasms.¹⁴

Enzyme histochemical staining has shown the prevalence of eccrine enzymes in eccrine poroma.²⁻⁴ The concept that eccrine poroma is a

epidermal neoplasma with differentiation toward eccrine sweat apparatus was also supported in our study by the findings of CEA on the inner surfaces of the ductal lumina and cystic spaces within the tumor, because CEA is not detected in other epithelial neoplasms of the skin. Although the immunohistochemical localization of CKs in the normal epidermis and the pilary apparatus was not described in this article, in another study we found that there were no similarities in CK expression in eccrine poroma, normal epidermis, and the pilary apparatus (unpublished data).

In this study, CKs were also confirmed to be expressed in normal sweat glands. However, they showed different distribution in the secretory and ductal portions. Moreover, different immunoreactivity was noted in the luminal and basal cells of eccrine ducts. There were also some differences of immunophenotypes between the acrosyringium and the dermal ducts.

Based on the previous observations, the immunophenotypes of CKs in eccrine poroma can be summarized thus: 1) the poroma cells were stained positively with RCK102 (against CKs 5 and 8) and AE3 (against CKs 1 to 8), weakly with 34BE12 (against CKs 1, 5, 10, and 11), and occasionally with AE1 (against CKs 10, 14 to 16, and 19). 2) With 34BE12 (against CKs 1, 5, 10, and 11), RCK102 (against CKs 5 and 8), AE1 (against CKs 10, 14 to 16, and 19), and 170.2.14 (against CK 19), intense staining was observed in the luminal cells not only of the cystic spaces, but also of sweat-ductlike lumina. 3) The luminal cells of some cystic spaces were stained with KL1 (against CK 11), 35BH11 (against CK 8), 4.1.18 (against CK 8), CAM5.2 (against CKs 8 and 18), NCL5D3 (against CKs 8, 18, and 19), and PKK1 (against CKs 8, 18, and 19). 4) Some cystic spaces revealed staining similar to that of sweatductlike lumina.

Comparative observations of immunohistochemical staining in eccrine poroma and normal eccrine glands revealed that the poroma cells expressed immunophenotypes similar to those of the basal cells of eccrine gland dermal ducts. Therefore, poroma cells seem to be most closely related to the basal cells of eccrine gland dermal ducts, being in no way analogous to the acrosyringium.

Eccrine poroma was originally regarded as a benign neoplasm of the acrosyringeal portion of the epidermis. This belief, however, is improbable, because the acrosyringium was negative for RCK102, despite its positive reactivity in eccrine poroma.

In normal skin, CKs of simple epithelium recognized by CAM5.2, 35β H11, and NCL5D3 antibodies are present exclusively in the eccrine secretory elements. The existence of these secretory cell-specific antigens in the luminal cells of some cystic spaces indicates that some of these cystic structures differentiating toward eccrine secretory are elements. Sweat-ductlike structures were also present within the tumor, and these were intensely stained with 34BE12, AE1, 170.2.14, and RCK102. Because these staining patterns were also observed in the inner cells of dermal eccrine ducts, it is speculated that these small ductal structures are differentiating toward the inner cells of eccrine ducts. Some cystic spaces, especially those directly lined by smooth-surfaced cells, revealed similar reactivity to sweat-ductlike structures. These cysts, therefore, may be considered to be formed by the cystic dilatation of these structures.

We can speculate from the previously cited data that eccrine poroma originates *via* the proliferation and expansion of the basal cells of eccrine ducts. Furthermore, some of the tumor cells (so-called poroma cells) may differentiate toward inner cells of the eccrine ducts, forming ductal lumina, whereas other tumor cells differentiate toward eccrine secretory portions, forming some cystic spaces.

It is very difficult, if not impossible, to prove the histogenesis of skin tumors, because it is likely that neoplastic growth would have altered patterns of keratinization. However, analysis of CKs can complement and significantly extend data obtained by established techniques such as light and electron microscopy as well as histochemistry. The specificity of these antibodies for the eccrine sweat apparatus, observed in this study, will make them potentially useful for the analysis of epidermal neoplasms with differentiation toward eccrine glands and differentiation from other tumors of epidermal appendage.

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References

- 1. Pinkus H, Rogin JR, Goldman P: Eccrine poroma. Arch Dermatol 1956, 74:511–521
- 2. Sanderson KV, Ryan EA: The histochemistry of eccrine poroma. Br J Dermatol 1963, 75:86–88
- Hashimoto K, Lever WF: Eccrine poroma. Histochemical and electron microscopic studies. J Invest Dermatol 1964, 43:237–247
- 4. Hashimoto K, Lever WF: Histogenesis of skin appendage tumors. Arch Dermatol 1969, 100:356–369
- 5. Hu CH, Marques AS, Winkelmann RK: Dermal duct tumor. Arch Dermatol 1978, 114:1659–1664

- Battifora H: Recent progress in the immunohistochemistry of solid tumors. Sem Diagn Pathol 1984, 1:251– 271
- Shi S-R, Goodman ML, Bhan AK, Pilch BZ, Chen LB, Sun T-T: Immunohistochemical study of nasopharyngeal carcinoma using monoclonal keratin antibodies. Am J Pathol 1984, 117:53–63
- Debus E, Moll R, Franke WW, Weber K, Osborn M: Immunohistochemical distinction of human carcinomas by cytokeratin typing with monoclonal antibodies. Am J Pathol 1984, 114:121–130
- Gown AM, Vogel AM: Monoclonal antibodies to human intermediate filament proteins. II. Distribution of filament proteins in normal human tissues. Am J Pathol 1984, 114:309–321
- Van Muijen GNP, Ruiter DJ, Ponec M, Huiskens-Van der Mey C, Warnaar SO: Monoclonal antibodies with different specificities against cytokeratins: An immunohistochemical study of normal tissues and tumors. Am J Pathol 1984, 114:9–17
- Hsu SM, Raine L, Fanger H: Use of an avidin-biotinperoxidase complex (ABC) in immunoperoxidase techniques. A comparison between ABC and unlabelled antibody (PAP) procedures. J Histochem Cytochem 1981, 29:577–580
- Smith JLS, Coburn JG: Hidroacanthoma simplex. Br J Dermatol 1956, 68:400–418
- Winkelmann RK, McLeod WA: The dermal duct tumor. Arch Dermatol 1966, 94:50–55
- Cooper D, Schermer A, Sun T-T: Classification of human epithelia and their neoplasms using monoclonal antibodies to keratins: Strategies, applications, and limitations. Lab Invest 1985, 52:243–256
- Broers JLV, Carney DN, Rot MK, Schaart G, Lane EB, Vooijs GP, Ramaekers FCS: Intermediate filament pro-

teins in classic and variant types of small cell lung carcinoma cell line: a biochemical and immunochemical analysis using a panel of monoclonal and polyclonal antibodies. J Cell Sci 1986, 83:37-60

- Makin CA, Borrow LG, Bodmer WF: Monoclonal antibody to cytokeratin for use in routine histopathology. J Clin Pathol 1984, 37:975–983
- Miettinen M, Virtanen I, Talerman A: Intermediate filament protein in human testis and testicular germ-cell tumors. Am J Pathol 1985, 120:402–410
- Viac J, Reano A, Brochier J, Staquet M-J, Thivolet J: Reactivity pattern of a monoclonal antikeratin antibody (KL1). J Invest Dermatol 1983, 81:351–354
- Moll R, Achtstatter T, Becht E, Balcarova-Stander J, Ittensohn M, Franke WW: Cytokeratins in normal and malignant transitional epithelium: Maintenance of expression of urothelial differentiation features in transitional cell carcinomas and bladder carcinoma cell culture lines. Am J Pathol 1988, 132:123–144
- Watanabe S, Wagatsuma K, Ichikawa E, Takahashi H: Abnormal distribution of epidermal protein antigens in psoriatic epidermis. J Dermatol 1991, 18:143–151
- Staquet MJ, Viac J, Thivolet J: Keratin polypeptide modifications induced by human papilloma viruses. Arch Dermatol Res 1981, 271:83–90
- Moll R, Franke WW, Volc-Platzer B, Krepler R: Different keratin polypeptides in epidermis and other epithelia of human skin: A specific cytokeratin of molecular weight 46,000 in epithelia of pilosebaceous tract and basal cell epitheliomas. J Cell Biol 1982, 95:285–295
- Woodcock-Mitchell J, Eichner R, Nelson WG, Sun T-T: Immunolocalization of keratin polypeptides in human epidermis using monoclonal antibodies. J Cell Biol 1982, 95:580–588