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Immunohistochemistry in the Differential Diagnosis of Cutaneous Basal Cell Carcinoma and Squamous Cell Carcinoma

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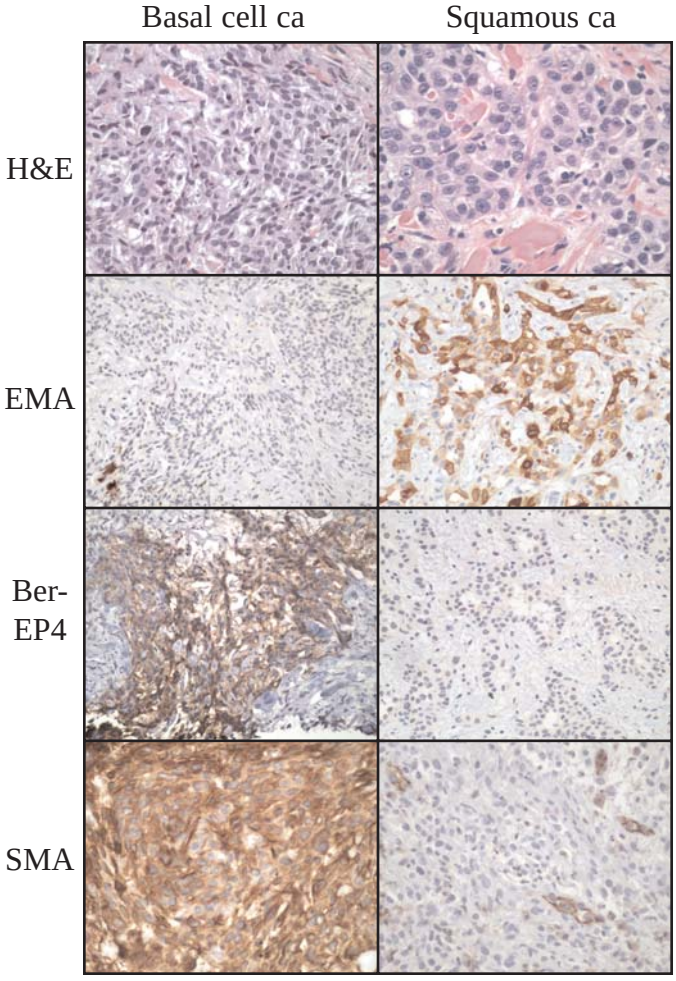
Basal cell carcinoma and squamous cell carcinoma are two of the most common cutaneous tumors seen by pathologists. In the large majority of cases, the distinction between these two tumors is readily made on the basis of standard H&E morphology. However, many of us see cases from time to time that for one reason or another (minuscule biopsy, mishandled specimen, crushed beyond recognition, dryed out, poorly fixed, etc., etc.), it is difficult to know for certain whether one is dealing with a squamous carcinoma or a basal cell carcinoma. This month, we discuss several immunostains that can be of utility in approaching this problem.

It is worth mentioning that both basal cell carcinoma and cutaneous squamous cell carcinoma characteristically express strong and diffuse high molecular weight cytokeratin, cytokeratin 5 (or cytokeratin 5/6) and nuclear p63, so the absence of staining with these markers (assuming adequate tissue and technique of course) should lead you to consider another diagnosis.

EMA is a useful antibody for this problem, since basal cell carcinomas are negative for EMA, although occasionally lumina associated with sebaceous differentiation in these tumors may show EMA positivity. In contrast, most squamous cell carcinomas of the skin will have substantial EMA immunoreactivity.

Ber-EP4 is also a useful marker, as basal cell carcinomas are typically positive for this marker, unlike



cutaneous squamous carcinoma. Interestingly, non-cutaneous squamous carcinomas (e.g., pulmonary squamous carcinoma) may express Ber-EP4, so conceivably reactivity of Ber-EP4 in a known cutaneous squamous tumor might suggest the possibility of metastatic squamous carcinoma, although I do not

know of any published reports that have specifically addressed that question.

Interestingly, **smooth muscle actin** (SMA) has been found to be expressed in a significant number of basal cell carcinomas of the skin (13 of 17 cases in one study). Indeed, we have observed strong SMA reactivity in a number of basal cell carcinomas that we have stained, although the frequency of reactivity is not as high in our hands as in some published series. Cutaneous squamous carcinomas are negative for SMA.

BCL-2 has been reported by some authors to be useful in this situation, since basal cell carcinomas are typically diffusely positive for this marker. Cutaneous squamous cell carcinomas are generally negative, although some authors describe focal positivity enough to 26% of cutaneous squamous carcinoms.

In summary, when faced with the differential diagnosis of cutaneous basal cell carcinoma versus cutaneous squamous carcinoma, a reasonable first approach would be to employ immunostains for EMA and Ber-EP4. If these results are not diagnostic, immunostains for SMA and BCL-2 would be worth a try. Again, if the tumor in question does not show strong high molecular weight cytokeratin, cytokeratin 5, cytokeratin 5/6, and nuclear p63, consideration of another diagnosis would be prudent. Results of expected staining in these tumors are listed in table below.

Expected Immunophenotype:

	EMA	Ber-EP4	SMA	BCL-2
Basal Cell ca	-	+	+ or -	+
Squamous ca	+	-	-	- or focal+

REFERENCES:

1. Wick MR: Practical immunohistology of cutaneous neoplasms: an update. Presentation at the American Society of Dermatopathology Companion Meeting, 2004 Annual Meeting of the United States and Canadian Academy of Patholgy, Vancouver, BC, March 7, 2004.

2. Jimenez FJ et al: Ber-EP4 immunoreactivity in normal skin and cutaneous neoplasms. Mod Pathol 8(8): 854-858, Oct 1995.

3. Peterdy G et al: Immunohistochemical separation of microcystic adnexal carcinoma from basal cell carcinoma and squamous cell carcinoma. Mod Pathol 14(1):72A (abstract # 407), Jan 2001.

4. Varma M et al: Expression of smooth muscle antigens in basal cell carcinomas of skin. Mod Pathol 12(1):65A (abstract # 365), Jan 1999.

5. Williams GA et al: Immunoreactivity for alpha-smooth muscle actin aids in the separation of basal cell carcinoma from both squamous cell carcinoma and trichoepithelioma. Lab Investig 78(1):54A (abstract # 303), Jan 1998.

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