

Update on Immunohistochemistry of Germ Cell Tumors:

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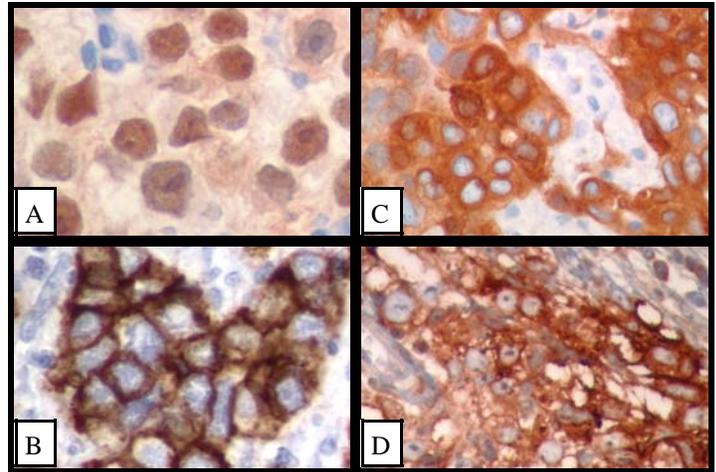
by Rodney T. Miller, M.D., Director of Immunohistochemistry

Germ cell neoplasms can show a bewildering array of appearances, and there may be significant morphologic overlap among subtypes. For this reason, immunohistochemistry is often performed to assist in accurately assessing the types and extent of germ cell elements present within a tumor. This month, we discuss our current approach to analyzing problematic germ cell neoplasms, employing some newer (and better) markers than those available to us in the past.

Low molecular weight cytokeratin (CK-lmw) is performed on all of our germ cell tumors. Embryonal carcinoma, yolk sac tumor, and choriocarcinoma are always positive for CK-lmw. Classical seminoma and spermatocytic seminoma may be negative, or sometimes show scattered positive cells, often with a perinuclear dot-like pattern of reactivity.

OCT3/4 is a superb nuclear marker of classical seminoma and embryonal carcinoma, and has been previously discussed in the May 2004 issue of our newsletter. It has excellent sensitivity and specificity for these two tumors, and can be effectively used as the "screen" for these neoplasms when dealing with a metastatic tumor of unknown origin.

D2-40 (also known as **podoplanin**) has also been previously discussed in the October 2005 issue of the "Focus", where we addressed its utility as a marker of lymphatics, mesothelial cells, heman-gioblastoma, certain vascular tumors, and cutaneous adnexal tumors. At that time, we noted that it stained cases of classical seminoma strongly, and there have been a number of recent publications attesting to the utility of D2-40 as a marker of classical seminoma. In contrast to the strong diffuse staining observed with D2-40 in classical seminoma, embryonal carcinoma is typically negative or only shows



A: OCT 3/4 nuclear staining in embryonal carcinoma. B: Strong membranous D2-40 in classical seminoma C: HLA-G highlights the intermediate trophoblasts in a metastatic choriocarcinoma. D: Glypican 3 stain of yolk sac tumor

focal weak reactivity. Other germ cell tumors have been found to be negative for D2-40.

CD30 has been used for some time as a marker of embryonal carcinoma, since it is typically positive in that tumor but negative in other germ cell tumors.

AFP is useful in identifying foci of yolk sac tumor, as it is negative in other tumors, although some authors report focal reactivity in some embryonal carcinomas.

In the December 2006 issue of the *American Journal of Surgical Pathology*, **Glypican 3 (GPC 3)** was reported as a useful marker for the classification of germ cell tumors. Specifically, GPC 3 stained all cases (24/24) of yolk sac tumor, and typically in a strong fashion. Additionally, 7 of 7 cases of choriocarcinoma were GPC 3 positive, where it stained the syncytiotrophoblasts strongly with weaker staining of cytotrophoblasts. Overall however, the staining was weaker than that noted in yolk sac tumor. Some of

	Classical Seminoma	Spermatocytic Seminoma	Embryonal Carcinoma	Yolk Sac Tumor	Choriocarcinoma
CK-LMW	- / focal dots	- / rare dots	+	+	+
OCT4	+ (strong)	-	+ (strong)	-	-
D2-40	+ (strong)	-	- or focal wk +	-	-
CD30	-	-	+	-	-
AFP	-	-	- (rare + cell?)	+ (often focal)	-
GPC3	-	-	- (8% weak +)	+	+
HCG	- (foc+ if ST GC)	-	-	-	+ (ST)
HLA-G	-	-	-	-	+ (IT)

the immature elements within teratomas reacted with GPC 3, including primitive stroma, neuroepithelium, fetal-type glands, primitive tubules, and cartilage anlage. 35 of 37 (92%) of cases of embryonal carcinoma were negative for GPC 3, with the positive cases showing only focal staining. All classical seminomas (n=42) and mature teratomas (n=20) were negative for this marker.

HCG is well known as a marker of syncytiotrophoblasts in choriocarcinoma, although it will also stain isolated syncytiotrophoblastic giant cells in classical seminoma.

HLA-G is an excellent marker of intermediate trophoblastic lesions, and is very useful in highlighting the intermediate trophoblast component of choriocarcinoma. Parenthetically, p63 can be useful to highlight the cytotrophoblast component of choriocarcinoma.

All of the above antibodies are available at ProPath. The table above summarizes the expected findings in germ cell tumors. Use of these selected markers can assist greatly in accurately characterizing these tumors, providing the basis for optimal therapy.

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Rodney T. Miller, M.D., Director of Immunohistochemistry

After completing an AP/CP residency and Surgical Pathology Fellowship, Dr. Miller spent 10 years in hospital-based Pathology, and set up and directed several hospital IHC labs. He joined ProPath in 1993, and developed a large, sophisticated, and thriving IHC lab and IHC consultation service. He is a nationally and internationally recognized expert in the field, and has lectured on the subject numerous times. He has authored multiple scientific articles on IHC, and is a member of the Editorial Board of The American Journal of Clinical Pathology.

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