PROPATH
THE FOCUS
Immunohistochemistry

Oct3/4: A New Marker of Embryonal Carcinoma and Seminoma

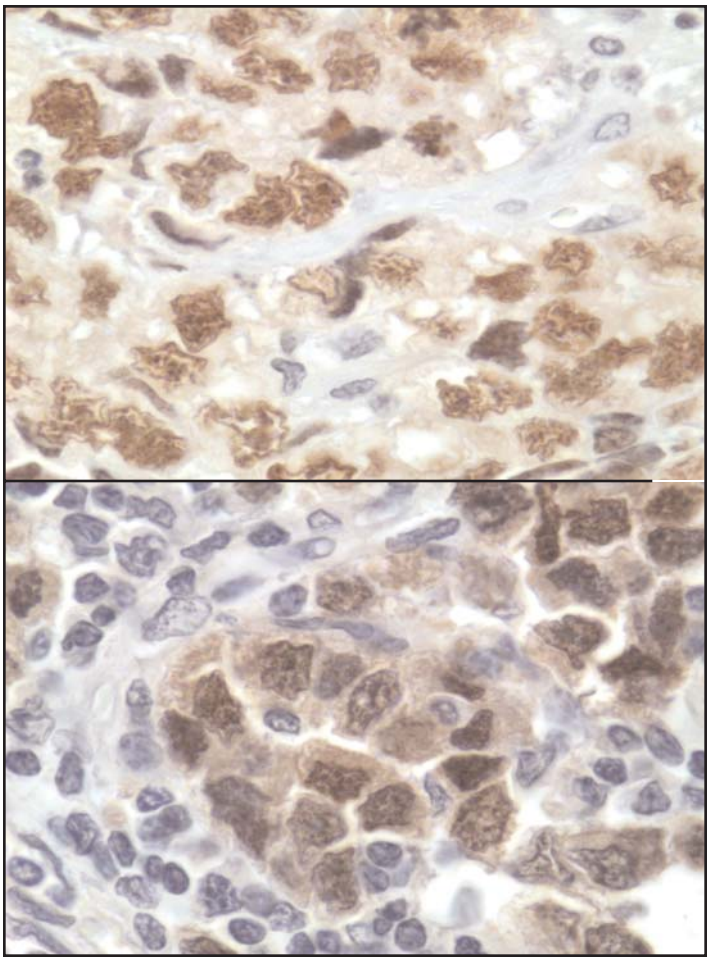
May 2004

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

As always, the United States and Canadian Academy of Pathology Meeting (USCAP), held last March in Vancouver, contained numerous items of interest to pathologists. This month, we review some of the information presented at that meeting regarding the utility of OCT3/4, a novel marker with excellent sensitivity and specificity for embryonal carcinoma, seminoma, dysgerminoma, and intratubular germ cell neoplasia.

OCT3/4 (also known as POU51) is a nuclear transcription factor containing the POU homeodomain that is expressed by early embryonic cells, germ cells, and stem cells. It is an important regulator of tissue specific gene expression, and a critical amount of OCT3/4 is required to maintain stem cell replication. The gene that codes for this transcription factor is located on human chromosome 6p21.3.

In a May 2003 paper in Cancer Research, Looijenga and associates performed an immunohistochemical study of over 3500 individual tumors, of more than 100 different tumor categories. Nuclear expression of OCT3/4 was consistently identified in intratubular germ cell neoplasia, gonadoblastoma, seminoma/germinoma/dysgerminoma, and embryonal carcinoma, including all of 84 cases of seminoma and embryonal carcinoma. However, no other form of invasive germ cell tumor showed reactivity (including cases of spermatocytic seminoma, teratoma, and yolk sec tumor). Of 3439 non-germ cell tumors in the microarrays, only 3 other tumors stained positively, including 1 of 50 conventional clear cell renal cell carcinomas, 1 of 50 pulmonary squamous carcinomas, and 1 of 47 pulmonary large cell carcinomas.



Photomicrographs (1000x) of metastatic embryonal carcinoma (top) and metastatic seminoma (bottom) showing strong nuclear staining with OCT3/4.

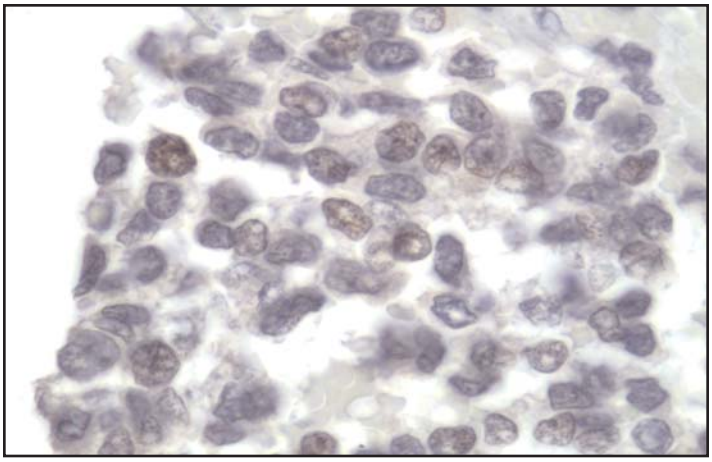
Dr. Thomas Ulbright and colleagues from Indiana University School of Medicine presented 4 different abstracts at the USCAP meeting that confirmed the above findings. In a study of 44 cases of intratubular germ cell neoplasia, OCT3/4 stained the nuclei of >90% of the dysplastic cells in all cases. 27 of these cases were also stained with PLAP, and the staining results with OCT3/4 were easier to interpret than those obtained with PLAP. In addition, 10 orchiectomy specimens from prostate cancer patients and 10 testes from autopsy patients were stained with OCT3/4, and all were negative.

In a study of 64 cases of mixed germ cell tumor, all cases that had elements of embryonal carcinoma and seminoma stained with OCT3/4, with >90% nuclear staining of these elements. There was no staining of other germ cell tumor elements, including yolk sac tumor (n=38), mature (n=31) or immature (n=31) teratoma, and choriocarcinoma (n=15). The following tumors were negative for OCT3/4: spermatocytic seminoma (n=5), Leydig cell tumor (n=8), Sertoli cell tumor (n=6), unclassified sex-cord stromal tumor (n=4), adenomatoid tumor (n=2), testicular tumor of the adrenogenital syndrome (n=1), and granulosa cell tumor (n=1). In a similar study of ovarian tumors, OCT3/4 stained the nuclei of all cases of dysgerminoma (n=22), and gonadoblastoma (n=2), but was negative in 49 cases of non-dysgerminoma, including mature teratoma (n=12), yolk sac tumor (n=3), Sertoli-Leydig cell tumor (n=4), granulosa cell tumor (n=11), Brenner tumor (n=2), carcinoid tumor (n=4), fibroma (n=5), thecoma (n=1), diffuse large B-cell lymphoma (n=1), follicular lymphoma (n=1), Burkitt lymphoma (n=1), metastatic melanoma (n=1), metastatic carcinoid (n=2), and metastatic small cell carcinoma (n=1).

In another study, material from retroperitoneal lymph node dissections from 56 patients with testicular germ cell tumors were immunostained with OCT3/4, to assess the utility of this antibody in recognizing metastatic germ cell tumor. Another group of tumors included in the study consisted of 33 metastatic lesions in retroperitoneal lymph nodes taken from male patients with non-germ cell metastatic lesions. As might be expected from the foregoing results, all embryonal carcinomas (n=29) and all seminomas (n=12) showed strong nuclear reactivity in the metastatic deposits. However, all yolk sac tumors (n=12), choriocarcinomas (n=4), mature teratomas (n=16), and primitive neuroectodermal tumors (n=5) were negative. Malignant lymphomas (n=4), metastatic melanomas (n=5), and metastatic carcinomas from the prostate (n=5), colon (n=6), pancreas (n=4), and bladder (n=5) were negative for OCT3/4.

When tested on the ProPath multitumor tissue array block (which contains 80 tumors of all different types), as expected the seminomas and embryonal carcinomas stained nicely. The only other tumor that showed nuclear staining was an Ewing's sarcoma, and the staining was focal and relatively weak.

OCT3/4 is now available in the ProPath immunohistochemistry laboratory for pathologists who would like to take advantage of this useful marker of embryonal carcinoma, seminoma, gonadoblastoma, and intratubular germ cell neoplasia.



When staining the ProPath multitumor tissue array (which contains 80 tumors), the only tumor other than seminoma and embryonal carcinoma that showed staining was 1 case of Ewing's sarcoma (above), and reactivity was focal and relatively weak.

References:

1. Looijenga LH, Stoop H, de Leeuw HP et al: POU5F1 (OCT3/4) identifies cells with pluripotent potential in human germ cell tumors. Cancer Research 63:2244-2250, 2003.
2. Jones TD, Ulbright TM, Eble JN, Cheng L: OCT4 immunostaining is useful in the diagnosis of intratubular germ cell neoplasia. Modern Pathology 17: Supplement 1, page 161A, abstract 672, January 2004.
3. Jones TD, Ulbright TM, Eble JN, Cheng L: OCT4 is a sensitive and specific marker for testicular seminomas and embryonal carcinoma. Modern Pathology 17: Supplement 1, page 160A, abstract 670, January 2004.
4. Thomas A, Roth RM, Abdul-Karim FW, Zheng W, Michael H, Cheng L: OCT4 is a specific biomarker for dysgerminoma of the ovary. Modern Pathology 17: Supplement 1, page 215A, abstract 905, January 2004.
5. Cheng L: Diagnosing metastatic germ cell tumors using OFT4 immunohistochemistry. Modern Pathology 17: Supplement 1, page 145A, abstract 60, January 2004.

Rodney T. Miller, M.D.
Director of Immunohistochemistry
214-237-1631 • Fax 214-237-1770
rmiller@propathlab.com

Prior Editions are available for download on our website.

PROPATH
8267 Elmbrook Dr, Ste 100 • Dallas, Texas 75247-4009
(214) 638-2000 • Fax: (214) 905-3457
www.propathlab.com