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Immunohistochemistry

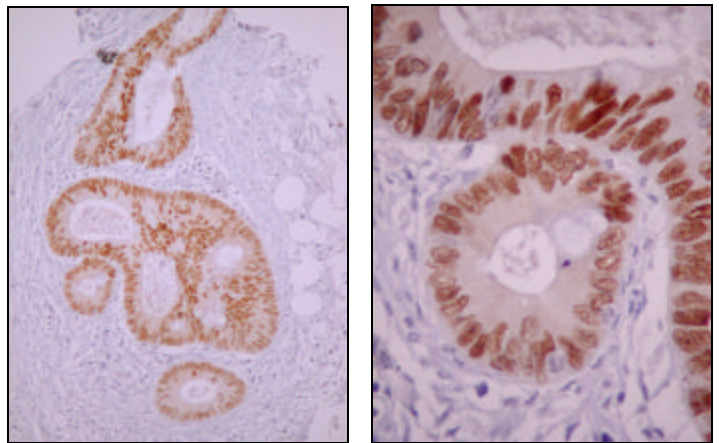
CDX2

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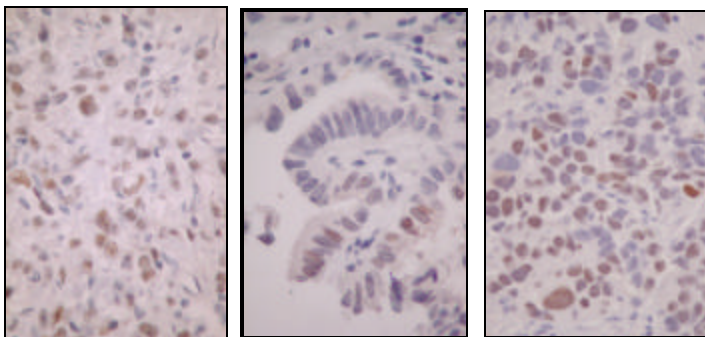
CDX2 is a transcription factor expressed in the nuclei of gastrointestinal epithelial cells, primarily from the duodenum to colorectum. Because of its reported specificity for gastrointestinal (GI) epithelium, antibodies to CDX2 have been investigated as a potential marker of GI origin in metastatic carcinomas of unknown primary site. At the 2002 United States and Canadian of Pathology meeting, Murer et al. reported their studies on the use of CDX2 in 68 cases of primary and metastatic lung adenocarcinoma. They noted that this marker was strongly positive in the nuclei of all primary colonic carcinomas studied (n=20), but was negative in all other tumors studied, including primary pulmonary adenocarcinomas (n=20), mucinous bronchoalveolar carcinomas (n=8), non-mucinous bronchoalveolar carcinomas (n=7), mixed mucinous/non-mucinous bronchoalveolar carcinomas (n=3), breast carcinomas (n=5), and kidney carcinomas (n=5).

In a recent newsletter, Drs. Gown and Werling of PhenoPath Laboratories reported their experience using CDX2 in a study of 476 tumors. Tumors studied included 189 from the colon and duodenum, 95 tumors from other GI sites (including esophagus, stomach, pancreas, and bile ducts), and a number of others including carcinomas from the female genital tract, genitourinary tract, head and neck, breast, and lung. They found that 188 of 189 colonic and duodenal tumors showed strong uniform expression of CDX2 in the nuclei of the neoplastic cells. Non-colorectal carcinomas (including pancreatic and gastric carcinomas) showed heterogeneous expression, but they noted that hepatomas and carcinomas from the genitourinary tract, female genital tract, breast, lung, and head and neck were essentially negative.

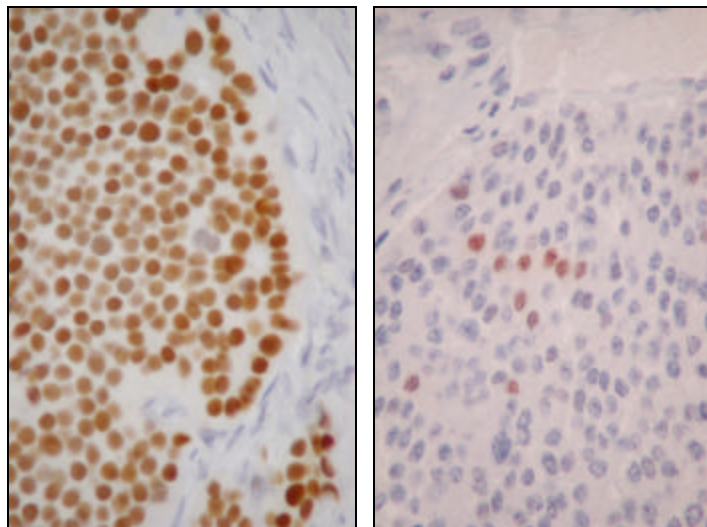


CDX 2 immunostain on colonic adenocarcinoma, showing the uniform and diffuse strong nuclear staining characteristic of colonic and duodenal tumors.

Studies of CDX2 expression in tumors present in ProPath's multitumor sandwich block (which contains 80 tumors of many different types) as well as studies on cases referred to our laboratory for immunophenotyping have mostly agreed with the findings reported above, with several exceptions. We have identified significant nuclear immunostaining with CDX2 in several unequivocal pulmonary carcinomas, particularly bronchoalveolar carcinomas, although most of the non-bronchoalveolar pulmonary carcinomas that we have studied have been negative. In addition, we have observed variable CDX2 immunostaining (ranging from scattered cells to strong uniform positivity) in a number of neuroendocrine tumors, including GI carcinoids, islet cell tumors of the pancreas, and large cell neuroendocrine carcinomas. We also found CDX2 immunostaining in rare vascular smooth muscle cells, focal weak staining in a mucinous ovarian carcinoma, and focal staining in a yolk sac tumor.



CDX2 immunostain on a poorly differentiated gastric carcinoma (left) shows patchy weak to moderate nuclear staining. Focal fairly weak staining is present in a bronchoalveolar carcinoma of the lung (middle). Although CDX2 staining in lung tumors is reported by other authors to be rare, we have seen it on several occasions at ProPath. The right frame shows CDX2 immunostaining in a high grade transitional cell carcinoma of the bladder.



CDX 2 may also be observed in neuroendocrine tumors, as shown by the strong and diffuse staining of a carcinoid tumor (left) and the focal patchy staining of a pancreatic islet cell tumor (right).

Those of us who frequently phenotype metastatic carcinomas of unknown primary site realize that the "cytokeratin 7 positive, cytokeratin 20 negative, villin positive" phenotype is a common one that includes many non-colorectal GI tract tumors, pancreatic and bile duct tumors, as well as some lung tumors. It was my hope that CDX2 might allow distinction of pulmonary adenocarcinoma (ideally CDX2 negative) from GI, pancreas, or bile duct tumors (ideally CDX2 positive), but in light of the identification of a number of CDX2-positive lung carcinomas in our laboratory, it remains to be seen whether CDX2 will be useful in separating all cases of pulmonary adenocarcinoma from GI tract or pancreaticobiliary tract tumors. Undoubtedly, we will be reading more in the surgical pathology literature about this marker as additional data is reported by other investigators.

CDX2 is now available in the ProPath Immunohistochemistry Laboratory.

REFERENCES

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4. Bai YQ, Yamamoto H, Akiyama Y, et al: *Cancer Lett* 176 (1):47-55, 2002.

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