Anatomic pathology selected abstracts

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SATB2 expression in tumors: a tissue microarray study

October 2023—Special AT-rich sequence-binding protein 2, or SATB2, induces local chromatin loops to facilitate transcription. SATB2 immunostaining is commonly used as a marker for colorectal adenocarcinoma and osteosarcoma. The authors conducted a study to better understand the prevalence and diagnostic value of SATB2 expression in cancer by analyzing a comprehensive set of human tumors. SATB2 expression was analyzed in 15,012 tissue samples from 120 tumor types and subtypes and 608 samples from 76 nonneoplastic tissue types using IHC in a tissue microarray format. SATB2 positivity was found in 89 of the 120 (74 percent) tumor types—59 of the 120 (49 percent) had at least one moderately positive tumor and 38 of the 120 (32 percent) had at least one strongly positive tumor. Expression was high in adenomas (n=42 of 44 and 44 of 47; 96 and 94 percent, respectively), adenocarcinomas of the colorectum (1,747 of 2,023; 86 percent), various subtypes of neuroendocrine tumors of the colorectum and appendix (n=3 of 7 and 12 of 12; 43 and 100 percent, respectively), Merkel cell carcinoma (n=25 of 34; 74 percent), osteosarcoma (n=15 of 25; 60 percent), and papillary renal cell carcinoma (n=121 of 235; 52 percent). Associations with clinicopathologic tumor features were assessed in colorectal and kidney cancers. In colorectal cancer, weak SATB2 expression was linked to high pT (P<.001), nodal metastasis (P<.001), right-sided tumor location (P<.001), microsatellite instability (P<.001), and *BRAF* mutations (P=.02). In papillary renal cell carcinoma, low SATB2 expression was associated with high pT (P=.02), distant metastasis (P=.04), and reduced tumor-specific survival (P=.04). In clear cell renal cell carcinoma, low SATB2 expression was linked to high pT (P<.001), high Union for International Cancer Control stage (P<.001), high Thoenes grade (P=.02), and reduced recurrence-free survival (P=.02). The authors concluded that strong SATB2 expression supports a colorectal origin for adenocarcinomas and neuroendocrine neoplasms. Weak SATB2 expression reflects progression and poor prognosis in colorectal and kidney cancers.

Dum D, Kromm D, Lennartz M, et al. SATB2 expression in human tumors: A tissue microarray study on more than 15,000 tumors. *Arch Pathol Lab Med*. 2023;147(4):451–464.

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Impact of p53-abnormal 'fields of dysplasia' in HPV-independent vulvar squamous cell carcinoma

Abnormal p53 IHC staining patterns can be found in vulvar squamous cell carcinoma and differentiated vulvar intraepithelial neoplasia. They can also be found in the adjacent skin that shows morphology that falls short of the traditional diagnostic threshold for differentiated vulvar intraepithelial neoplasia (dVIN). The authors hypothesized that mutation-associated p53 IHC staining in the skin surrounding the vulvar squamous cell carcinoma (VSCC), referred to as the p53-abnormal field of dysplasia, is clinically significant and may explain the high rates of disease recurrence in human papillomavirus (HPV)-independent *TP53*-mutant VSCC. The authors conducted a study in which they selected from their institutional archive vulvectomy specimens containing HPV-independent abnormal p53 (p53abn) VSCC with margins originally reported as negative for invasive and in situ disease. Blocks showing the closest approach of the VSCC to a peripheral surgical margin were stained with p53 IHC stains. The authors assessed the detection of morphologically occult p53abn in situ neoplasia, rates of margin status change after p53 IHC staining, and effect of p53abn IHC staining at margins on two-year local recurrence rates. Seventy-three HPV-independent p53abn VSCCs were included in the study. Half (35 of 73; 48 percent) had an in situ lesion documented in the original report. The use of p53 IHC staining identified 21 (29 percent) additional cases with

p53abn in situ lesions that were originally unrecognized. The histology of in situ lesions in the p53abn field varied and became more subtle (morphologically occult) farther away from the VSCC. Fifteen (21 percent) cases had a morphologically occult and previously unrecognized p53abn in situ lesion present at a resection margin, which conferred an increased risk of local recurrence (five of seven [71.4 percent] versus six of 22 [27.3 percent]; $P = .036$). The p53abn in situ lesions at a margin were confirmed to have *TP53* mutations by sequencing. P53 IHC staining identified morphologically occult p53abn in situ lesions surrounding HPV-independent VSCC. P53abn IHC staining at a margin was associated with a threefold increased risk of local recurrence.

Thompson EF, Wong RWC, Trevisan G, et al. p53-abnormal "fields of dysplasia" in human papillomavirus-independent vulvar squamous cell carcinoma impacts margins and recurrence risk. *Mod Pathol*. 2023;36(2). https://doi.org/10.1016/j.modpat.2022.100010

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Liver injury after SARS-CoV-2 vaccination: clinical features, treatment response, and outcome

A few cases of autoimmune hepatitis–like liver injury following SARS-CoV-2 vaccination have been reported. The authors assembled a large case series to evaluate clinical features, treatment response, and outcomes of liver injury in patients following such vaccination. They collected data from patients in 18 countries. The R-value was used to assess the type of liver injury. The study population was categorized according to features of immune-mediated hepatitis (positive autoantibodies and elevated immunoglobulin G levels) and use of corticosteroid therapy for liver injury. The authors identified 87 patients (63 percent of whom were female), who were a median age of 48 years (range, 18–79 years) at presentation. Liver injury was diagnosed a median of 15 days (range, 3–65 days) after vaccination. Fifty-one (59 percent) cases of liver injury were attributed to the Pfizer-BioNTech (BNT162b2) vaccine, 20 (23 percent) to the Oxford-AstraZeneca (ChAdOX1 nCoV-19) vaccine, and 16 (18 percent) to the Moderna (mRNA-1273) vaccine. Liver injury was predominantly hepatocellular (84 percent), and 57 percent of patients showed features of immune-mediated hepatitis. Corticosteroids were more often given to patients who had grade 3–4 liver injury than to those who had grade 1–2 liver injury (88.9 versus 43.5 percent; $P=.001$). They were also more often given to patients who had immune-mediated hepatitis than to those who did not (71.1 versus 38.2 percent; $P=.003$). Liver injury was resolved in all patients, except one (1.1 percent) man who developed liver failure and underwent liver transplantation. Steroid therapy was withdrawn during the observation period for 12 (26 percent) patients after complete biochemical resolution. None of the patients relapsed during follow-up. The authors concluded that SARS-CoV-2 vaccination can be associated with liver injury. Corticosteroid therapy may benefit those with immune-mediated features or severe hepatitis. Overall outcome was generally favorable, but vaccine-associated liver injury led to fulminant liver failure in one patient.

Efe C, Kulkarni AV, Terziroli Beretta-Piccoli B, et al. Liver injury after SARS-CoV-2 vaccination: Features of immune-mediated hepatitis, role of corticosteroid therapy and outcome. *Hepatology*. 2022;76(6):1576–1586.

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Comparison of malignant rhabdoid tumors of the vulva to epithelioid sarcomas

It has been suggested that most, if not all, extrarenal rhabdoid tumors of the vulva represent proximal-type epithelioid sarcomas. To better understand rhabdoid tumors of the vulva, the authors studied the clinicopathologic, IHC, and molecular features of eight such tumors and 13 extragenital epithelioid sarcomas. IHC analysis for cytokeratin AE1/AE3, epithelial membrane antigen, S100, CD34, ERG, smooth muscle actin, desmin, and SMARCB1 (INI1) was performed. An ultrastructural study of one vulvar rhabdoid tumor was conducted. Next-generation sequencing of the *SMARCB1* gene was performed in all cases. The eight vulvar tumors occurred in adult women (mean age, 49 years). The tumors were poorly differentiated neoplasms with a rhabdoid morphology. The ultrastructural study showed large amounts of intermediate filaments (10 nm). All cases had loss of expression of

INI1 and were negative for CD34 and ERG. One case showed two *SMARCB1* mutations: c.592C>T in exon 5 and c.782delG in exon 6. Follow-up revealed that four patients died of disease, one was alive with disease, and three were alive without evidence of disease. Epithelioid sarcomas occurred in young adults (mean age, 41 years), most of whom were men. Seven tumors arose in the distal extremities, and the other six tumors had a proximal location. The tumors showed the characteristic granulomatous arrangement of neoplastic cells. The recurrent tumors were more proximal and often showed a rhabdoid morphology. All cases had loss of expression of INI1. CD34 and ERG were expressed by eight (62 percent) and five (38 percent) tumors, respectively. No *SMARCB1* mutations were encountered. Follow-up revealed that five patients died of disease, one was alive with disease, and seven were alive without evidence of disease. The authors concluded that, based on the difference in their morphology and biological behavior, rhabdoid tumors of the vulva and epithelioid sarcomas are different diseases with distinct clinicopathologic features. Undifferentiated vulvar tumors with rhabdoid morphology should be classified as malignant rhabdoid tumors rather than proximal-type epithelioid sarcomas.

Espinosa I, D'Angelo E, De Brot L, et al. Malignant rhabdoid tumors of the vulva versus epithelioid sarcomas: a clinicopathologic, immunohistochemical, and molecular genetics study. *Hum Pathol*. 2023;135. https://doi.org/10.1016/j.humpath.2023.02.006

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