Modern Pathology (2022) 35, 1138–1139

INSIDE THE USCAP JOURNALS

https://doi.org/10.1038/s41379-022-01140-5

MODERN PATHOLOGY

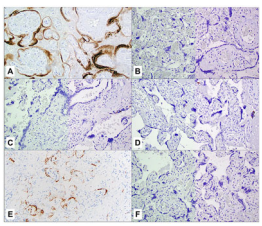
Deep learning can assist pathologists without displacing them

https://doi.org/10.1038/s41379-022-01073-z

Acknowledging that deep learning will not replace the knowledge base of pathologists, Ba et al. performed a multi-reader multi-case study of deep learning assistance to pathologists' diagnosis of gastric cancer. Using 110 whole-slide images, 16 board-certified pathologists made their analysis with or without deep learning assistance. Deep learning-assisted pathologists achieved higher area under receiver operating characteristics curve (ROC-AUC) values than those who were unassisted. These pathologists also demonstrated higher sensitivity in detection of gastric cancer than those without deep learning assistance (90.63%), and the average time to draw a conclusion fell from 26.37 seconds to 22.68 seconds. The group prefaces the study with the observation that deep learning is typically pitted against the pathologist and that this is an unlikely scenario. When asked to evaluate their experience, the majority of the pathologists confirmed that the presence of deep learning improved their performance. The data support the use of deep learning assistance to increase accuracy and efficiency in gastric cancer diagnosis.

SARS-CoV-2 mRNA vaccine is safe in pregnancy

https://doi.org/10.1038/s41379-022-01061-3

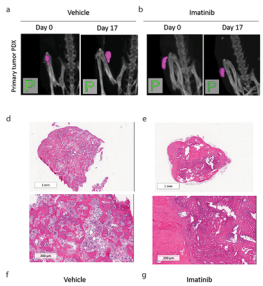


The pregnant population remains a vulnerable group in public health efforts to control the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Hesitancy toward vaccination persists in the general population and is heightened in pregnancy due to uncertainty regarding the presence of the SARS-CoV-2 spike protein (or the RNA encoding it) in the developing placenta following vaccination. Santos et al. set out to determine the validity of this concern using in situ hybridization (ISH). Their test population included 48 patients receiving one or two doses of vaccine during gestation, 1 known case where the protein was present as a positive control, and, as negative controls, 7 term placentas from prior to the emergence of SARS-CoV-2. Eighty-one percent of patients in the study group underwent a third-trimester delivery, and most patients (63%) had their latest dose of vaccine within 15 days before delivery. All the placentas in both the negative-control group and the study group were negative for SARS-CoV-2 on ISH analysis, suggesting that the mRNA vaccines would be unable to reach significant concentrations in the placenta because the spike protein does not accumulate there. The authors conclude that this evidence supports the safety of mRNA vaccines during pregnancy.

LABORATORY INVESTIGATION

Preclinical models of mesenchymal chondrosarcoma sensitive to imatinib mesylate

https://doi.org/10.1038/s41374-021-00704-4

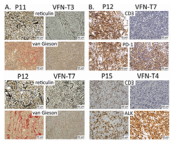


Mesenchymal chondrosarcoma (MCS) is an aggressive malignancy representing 2–9% of chondrosarcomas, and HEY1-NCoA2 gene fusion is the driver in the vast majority of cases. There is a shortage of MCS samples and biological models, making it challenging to collect preclinical data to develop effective therapeutics. Tepes et al. developed two independent in vitro and in vivo models of HEY1-NCoA2-driven MCS for application in therapeutic strategies to combat them. The in vitro model was characterized by RNA sequencing and successfully mimicked relevant MCS features. Imatinib mesylate demonstrated highly selective cytotoxic effects targeting the HEY1-NCoA2 fusion-driven cellular model. For the in vivo model, patient-derived xenografts were developed from primary tumors as well as distant metastases. In these models too, imatinib was able to

reduce tumor growth compared with controls. The group propose additional study of imatinib as a possible therapeutic for HEY1-NCoA2-driven MCS.

Patient-derived xenografts may not replicate the primary lymphoma microenvironment

https://doi.org/10.1038/s41374-022-00784-w



Translational research into preclinical in vivo validation of experimental approaches for lymphoma is commonly carried out using patient-derived xenografts (PDXs). PDXs have been shown to keep most somatic mutations with the lymphoma samples from which they were derived; however, the composition of the PDX tumor microenvironment is largely unexplored. Jakša et al. studied 15 PDX models from patients with various types of non-Hodgkin lymphoma (NHL). Whole-exome sequencing (WES) was implemented in the 13 with available DNA, and immunohistochemistry (IHC) was used to explore cellular composition. While WES data confirmed genetic heterogeneity with the original lymphoma within the PDX, the IHC data revealed alterations in composition. The findings indicate that even with the same genetic profiles, PDX models of aggressive NHL do not replicate the microenvironment of the original lymphomas. This leads to concerns about the continued relevance of PDX models in preclinical research. Better models with more fidelity may be needed, taking into consideration potential histopathological discrepancies between the model and primary lymphoma.

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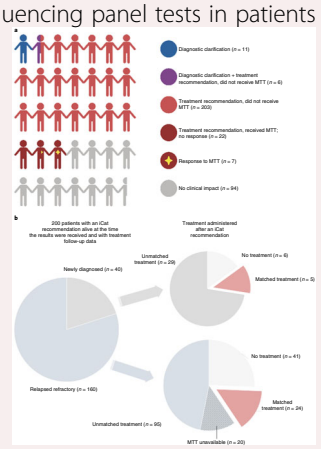
Molecular profiling is beneficial in pediatric solid cancers

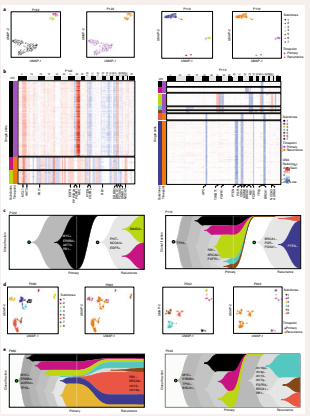
Church et al. conducted a large-scale multicenter study evaluating the clinical impact of molecular tumor profiling (MTP) with targeted sequencing panel tests in patients with extracranial solid tumors. Of the 345 patients evaluated, 298 (86%) had samples with at least one alteration with the potential to impact care. Genomic alterations with either diagnostic, prognostic, or therapeutic significance were present in 61, 16, and 65% of patients, respectively. Two hundred forty patients exhibited an alteration that could be linked to a molecularly targeted therapeutic, and 24% of patients who received this medication exhibited an objective response or durable clinical benefit. Of the alterations identified, 77% were gene fusions, indicating that MTP platforms weighted toward gene fusion detection could significantly impact the identification of clinical therapeutic strategies in young patients with these solid tumors. The study is ongoing, and additional data will be reported as they are analyzed.



Nature Medicine, published online 23 June 2022; https://doi.org/10.1038/s41591-022-01856-6

Clonal relationships of ductal carcinoma and recurrent invasive breast cancer

Lips et al. explored a fundamental question about the pathogenesis of ductal carcinoma in situ (DCIS). DCIS is the most common form of preinvasive breast cancer. Despite treatment, 5–10% of patients will develop subsequent invasive disease. The target question was whether the initial DCIS has invasive properties or unrelated disease explains the invasion in this small population. Genomic analysis of initial DCIS lesions and paired invasive recurrent cells in 95 patients was performed. In 75% of cases, the invasive recurrence was clonally related to the initial DCIS (indicating that the cells simply were not eliminated by the initial treatments). A small proportion, 18%, were clonally unrelated to the initial DCIS—i.e., new independent lines—and 7% were ambiguous. This indicates the need to maintain aggressive strategies for the initial treatment of DCIS, to avoid missing invasive cells, and also to identify predictive biomarkers that might distinguish the few cases where independent metastases may occur.



Nature Genetics 2022;54:850–860; https://doi.org/10.1038/s41588-022-01082-3

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