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CANCER RESEARCH

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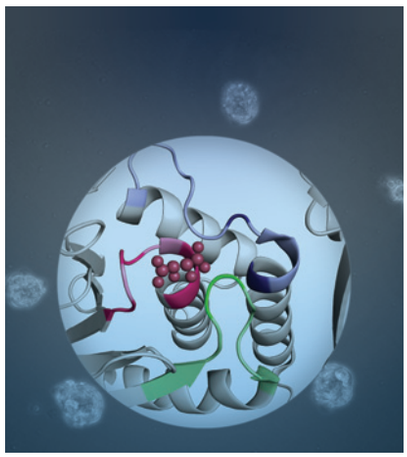
## ABOUT THE COVER



Most germline and somatic cancer variants cannot be annotated due to lack of supporting evidence and are designed as variants of uncertain significance (VUS), confounding diagnosis and treatment. Chao and colleagues developed a cancer variomics approach for annotating variants of the tumor suppressor gene PTEN. They functionally assessed PTEN variants using a clinically relevant 3D tumor cell spheroid assay and reclassified variants with a machine learning model. This integrated approach reassigned many PTEN VUS into actionable classifications, which should allow clinicians to better consolidate data, improving diagnosis and treatment. For details, see article by Chao and colleagues on page 2775.