



NEWS RELEASE

New Data at DDW 2026 Show TissueCypher® Testing Improves Risk Stratification and Drives Risk-Aligned Management in Barrett's Esophagus

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Clinical studies from Mayo Clinic researchers demonstrate the TissueCypher test provides improved risk stratification and influences risk-aligned surveillance decisions in clinical practice, with one study showing changes in surveillance intervals in more than half of patients compared with recommendations guided by traditional histopathology, supporting more personalized, risk-aligned patient management.

FRIENDSWOOD, Texas, May 4, 2026 /PRNewswire/ -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced that new data generated by researchers at Mayo Clinic will be presented at Digestive Disease Week® (DDW 2026), taking place May 2–5 in Chicago. The findings, featured in two poster presentations, demonstrate how molecular risk stratification with the TissueCypher test can refine risk assessment and directly inform real-world management decisions for patients with Barrett's esophagus (BE).

TissueCypher is a molecular test that can predict a patient's personalized five-year risk of progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) based on their underlying disease biology.

"The findings presented at DDW 2026 suggest that relying on traditional clinical risk assessment alone may not fully capture a patient's true risk of progression," said Cadman L. Leggett, M.D., gastroenterologist at Mayo Clinic and senior author on both studies. "Molecular risk stratification with TissueCypher can provide more clinically actionable insights by more accurately identifying which patients are truly at higher or lower risk. And we see that translating into real-world changes in how physicians manage patients."



Poster Presentations at DDW 2026

The following posters are available on the **DDW ePosters site** and to conference attendees in the DDW meeting planner.

- Authors: Cadman L. Leggett, M.D., Wilfor Jhonathan Diaz-Fernandez, M.C., et al., Mayo Clinic
- Session Type: Abstract Poster
- Session Title: Barrett's Esophagus and Esophagogastric Junction Neoplasia: Biomarkers

Poster Sa1092: The Tissue Systems Pathology Test Impacts Barrett's Surveillance Intervals in Clinical Practice

In a multicenter cohort of patients with BE who underwent TissueCypher testing as part of their clinical care, researchers evaluated how molecular risk classification influenced physician-recommended surveillance intervals compared with population risk-guided recommendations. Following testing, physicians modified surveillance intervals in 55% of patients, demonstrating a direct impact on patient management. Physician-recommended surveillance intervals were aligned with TissueCypher risk classification in 79% of cases, and 93% of patients identified as intermediate/high risk were recommended shorter surveillance intervals, reflecting escalation of care based on the test's results. Among patients with non-dysplastic BE, 92% of those identified as intermediate/high risk were recommended shortened surveillance intervals compared with recommendations based on traditional clinical risk assessment, highlighting the ability of the test to identify higher-risk patients within a population traditionally considered lower risk. These findings demonstrate that TissueCypher can directly impact physician decision-making and surveillance strategies in clinical practice, enhancing guideline-based care and enabling more individualized, risk-aligned management, including escalation for higher-risk patients and de-escalation for those at lower risk of progression.

Poster Sa1093: Discordance Between Clinical and Molecular Risk Stratification in Barrett's Esophagus

In a multicenter cohort of patients with BE who underwent TissueCypher testing as part of their clinical care, researchers compared a clinical risk model, the Progression in Barrett's Esophagus (PIB) model, with TissueCypher, which is designed to predict patients' individualized risk of progression independent of clinicopathologic factors. PIB estimates risk based on four traditional clinical factors: sex, smoking history, BE segment length and presence of low-grade dysplasia. TissueCypher classified substantially more patients as low risk (84% vs. 38%) and showed minimal concordance with PIB ($\kappa=0.04$), with most discordance driven by patients identified as intermediate/high risk by clinical factors but low risk by TissueCypher. Patients who scored TissueCypher intermediate/high risk had a predicted progression risk that exceeds the risk associated with low-grade dysplasia, for which guidelines recommend endoscopic eradication therapy (EET) or short interval surveillance. By contrast, a PIB intermediate/high-risk result had a predicted progression risk similar to patients without dysplasia or indefinite for

dysplasia, indicating that PIB lacks utility for identifying higher risk patients who may benefit from escalation of care to prevent HGD/EAC.

These findings demonstrate that molecular-based risk stratification with TissueCypher can inform refined surveillance strategies to support more appropriate, risk-aligned decisions than those guided by traditional clinical and histologic factors alone, including potentially longer surveillance intervals for low-risk patients and escalation of care to EET or short interval surveillance to prevent progression in higher risk patients. Such strategies can enable more effective use of healthcare resources and individualized, risk-aligned management to improve health outcomes for patients with BE.

Visit Castle at DDW 2026

For more information, visit Castle at booth 4828 or view the full schedule of events at info.castlebiosciences.com/ddw2026.

About Digestive Disease Week® (DDW)

Digestive Disease Week (DDW) is the largest international gathering of physicians, researchers, and academics in the fields of gastroenterology, hepatology, endoscopy, and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society for Surgery of the Alimentary Tract (SSAT), DDW is an in-person and online meeting.

About TissueCypher Barrett's Esophagus Test

TissueCypher is a precision medicine test designed and extensively validated to predict a patient's personalized risk of progression from Barrett's esophagus (BE) to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC). Indicated for patients with non-dysplastic BE, indefinite for dysplasia or with low-grade dysplasia, TissueCypher's five-year risk assessment is designed to help physicians tailor care to each patient's risk of developing HGD or EAC.

Backed by more than 17 peer-reviewed publications and studied in biopsies from more than 8,000 patients, TissueCypher has been shown to be the strongest independent predictor of progression compared with traditional histopathological risk assessment. Using an AI-driven spatialomics approach, the test identifies molecular signatures that often precede the development of dysplasia, which can enable earlier identification, treatment, and management of patients at increased risk of cancer. TissueCypher is designed to integrate seamlessly into routine endoscopic practice by analyzing standard esophageal pinch biopsies, delivering actionable insights without requiring additional procedures. Learn more at CastleBiosciences.com/TissueCypher.

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company improving health through innovative tests that

guide patient care. With a primary focus in dermatologic and gastroenterological disease, we develop personalized, clinically actionable solutions that help improve disease management and patient outcomes.

We put people first—empowering patients and clinicians and informing care decisions through rigorous science and advanced molecular tests that support more confident treatment planning. To learn more, visit www.CastleBiosciences.com and connect with us on [LinkedIn](#), [Instagram](#), [Facebook](#) and [X](#).

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Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning: TissueCypher's ability to (i) play an important role in identifying BE patients at higher risk for progression to esophageal cancer and inform real-world management decisions, (ii) provide more clinically actionable insight and translate study results into real-world changes in how physicians manage patients and (iii) enable more personalized surveillance and intervention strategies for BE patients that help prevent cancer. The words "believe," "can," "may" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation: subsequent study or trial results and findings may contradict earlier study or trial results and findings or may not support the results obtained in these studies, including with respect to the discussion of our tests in this press release; actual application of our tests may not provide the aforementioned benefits to patients; and the risks set forth under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2025, and our subsequent Quarterly Reports on Form 10-Q, each as filed or to be filed with the SEC, and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, except as may be required by law.

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