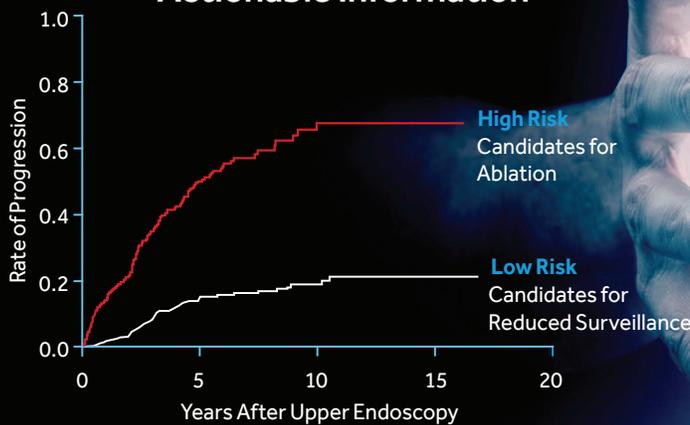
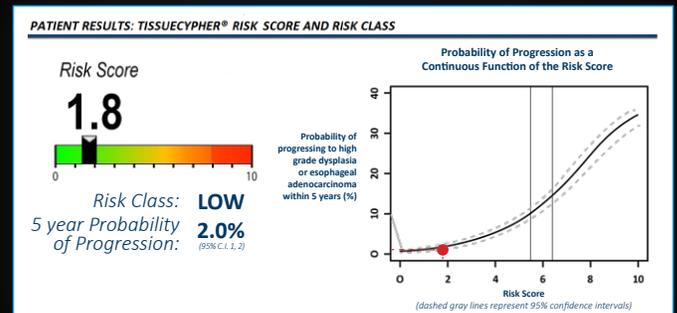
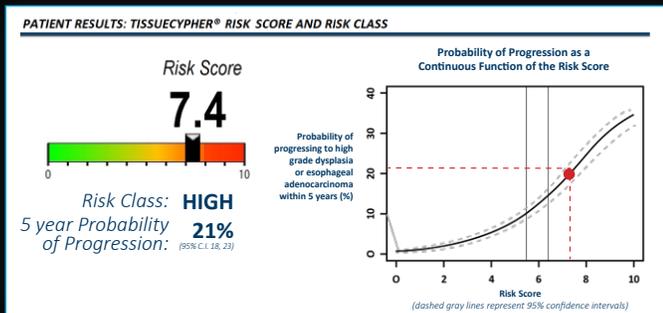
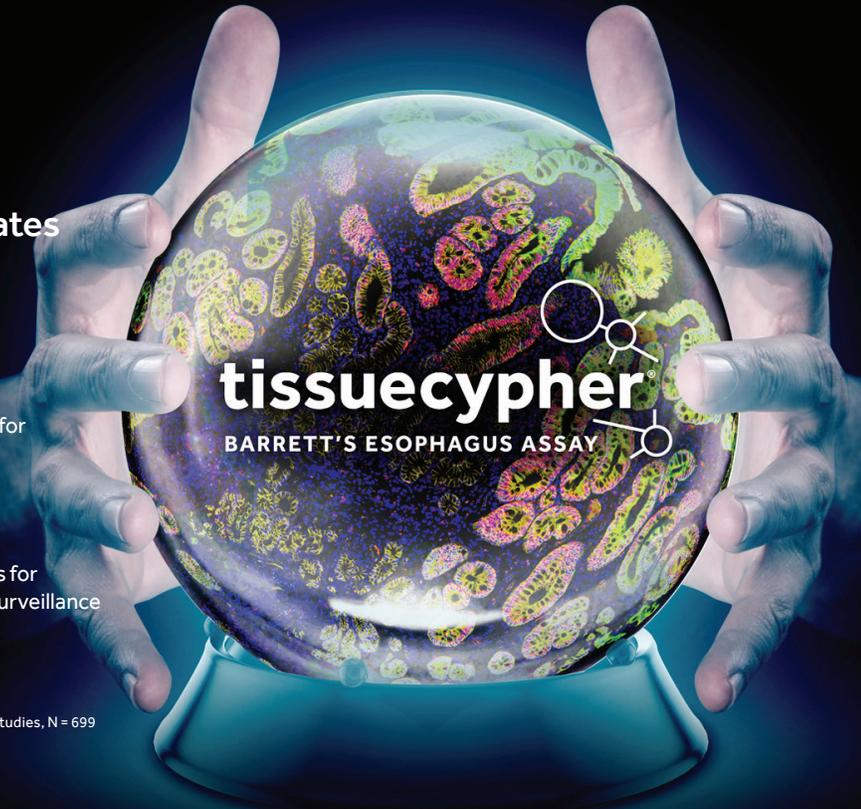


Predict progression to esophageal cancer: What's **your patient's** risk?

Precision Risk Stratification Generates Actionable Information



TissueCypher® Performance from 5 Independent Validation Studies, N = 699



NDBE patients who progress to EAC?

TissueCypher® identifies patients that progress to EAC at a 5-10x higher rate than current standard of care.

BE with a low risk to progress to EAC?

TissueCypher® can aid physician decision-making to potentially forgo ablation and optimize frequency of endoscopic surveillance.

THE SITUATION

Thousands of people will be diagnosed with Barrett's esophagus each year, yet few of them will progress to esophageal adenocarcinoma (EAC).¹

For those who do progress, EAC is a very deadly disease – a disease which, if caught early, may be effectively managed without risk of progression.²

Couple this conundrum with challenges of thorough and effective biopsy sampling, along with pathologist discordance, and your ability to confidently assess patient risk may be compromised.³

WHY TISSUECYPHER® BARRETT'S ESOPHAGUS ASSAY

TissueCypher® is a deep tissue interrogation supplement to your Barrett's esophagus patient workup. It provides:

- The ability to reprocess biopsy tissue already collected without needing to call a patient back for new samples,
- Stronger predictive power than current clinical variables, including pathologic diagnosis by a GI subspecialist,⁴⁻⁶
- A risk score for future progression from Barrett's esophagus to EAC, and
- Additional decision support that may help overcome limitations of random sampling and subjective diagnosis, potentially enabling earlier detection of HGD and EAC.⁶

TissueCypher® has been independently validated to predict progression to high grade dysplasia and EAC in clinical studies with five leading institutions.⁴⁻⁶

1. Hayeck TJ, Kong CY, Spechler SJ, et al. The prevalence of Barrett's esophagus in the US: estimates from a simulation model confirmed by SEER data. *Dis Esophagus*. 2010 Aug;23(6):451-7.

2. Zakko L, Lutzke L & Wang KK. Screening and Preventive Strategies in Esophagogastric Cancer. *Surg Oncol Clin N Am*. 2017 Apr;26(2):163-178.

3. Vennalaganti P, Kanakadandi V, Goldblum JR, et al. Discordance Among Pathologists in the United States and Europe in Diagnosis of Low-Grade Dysplasia for Patients With Barrett's Esophagus. *Gastroenterology*. 2017 Feb;152(3):564-570.e4.

4. Critchley-Thorne RJ, Duits LC, Prichard JW, et al. A Tissue Systems Pathology Assay for High-Risk Barrett's Esophagus. *Cancer Epidemiol Biomarkers Prev*; 25(6) June 2016.

5. Davison JM, Goldblum JR, Grewal U, et al. Independent Validation of a Tissue Systems Pathology Test to Predict Progression in Barrett's Esophagus Patients. *Am J Gastroenterology*, 2020;115:843-852.

6. Critchley-Thorne RJ, Davison JM, Prichard JW, et al. A Tissue Systems Pathology Test Detects Molecular and Cellular Abnormalities Associated with Prevalent High Grade Dysplasia and Esophageal Cancer in Barrett's Esophagus Patients. *Cancer Epidemiol Biomarkers Prev*. 2017 Feb;26(2):240-248.

TISSUECYPHER® IMAGE ANALYSIS

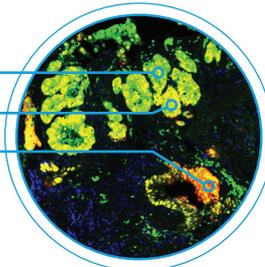
TissueCypher® utilizes a risk prediction model to blend image analysis data on nine biomarkers and changes in size and shape of cellular structures. It offers a unique ability to visualize the simultaneous expression of biomarker results within the same biopsy sample.

Add TissueCypher® to your management protocol and identify patients at high risk for progression within five years for whom eradication therapy may be beneficial.⁴⁻⁶

BIOMARKERS AND THEIR PURPOSES

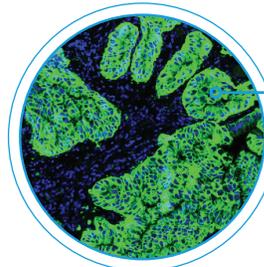
Measures loss of tumor suppression and cell cycle control

p53
p16
AMACR*



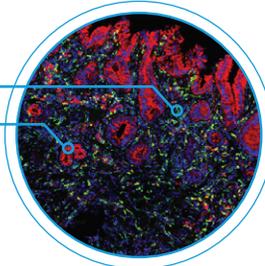
Measures cancer growth and cell transformation

HER-2, K20



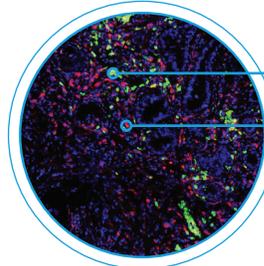
Measures immune and inflammation markers

CD68
COX2



Measures connective tissue markers

HIF1alpha
CD45RO



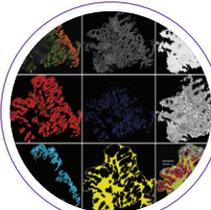
TISSUECYPHER® WORKFLOW

Immunofluorescence Slide Labeling



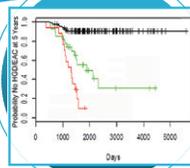
Whole Slide Fluorescence Scanning

TissueCypher® Image Analysis



Extract quantitative feature data

TissueCypher® Classifier

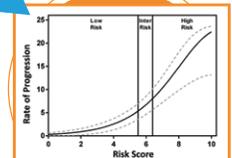


INPUT
Features & Coefficients

COX MODEL

OUTPUT
Probability & Risk Class

Report to Physician



TISSUECYPHER® PATIENT REPORT



Cernostics, Inc.
235 William Pitt Way, Pittsburgh, PA 15238 USA
(412) 820-3050 | www.cernostics.com

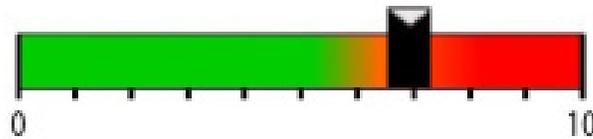
BARRETT'S ESOPHAGUS PATIENT REPORT

Patient Name:	Patient3, Demo	Date Biopsy Collected:	6/29/2017
Medical Record #:	345678	Date Received:	7/10/2017
Cernostics ID:	20170712002A	Ordering Institution:	Demo Clinic
Date of Birth:	8/10/1944	Ordering Physician:	Dr. Gastro
Sex:	Female	Submitting Pathologist:	Dr. Path
Specimen #:	S20-345678	Number of Levels/Blocks Submitted:	1
Specimen Type:	Esophageal Pinch Biopsy (Part B)	Number of Levels/Blocks Tested:	1
Other Comments/Reason for Ordering Test: History of HGD, now with LGD after ablation			

PATIENT RESULTS: TISSUECYPHER® RISK SCORE AND RISK CLASS:

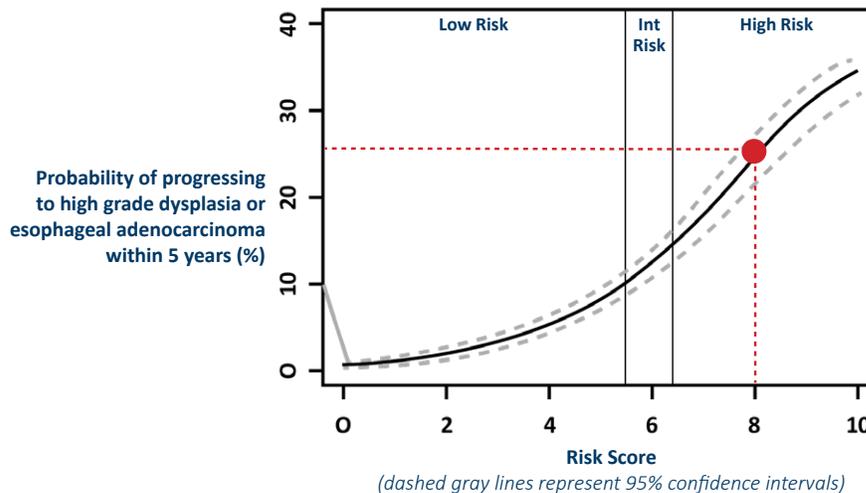
RISK SCORE: **8.0**

RISK CLASS: **HIGH**



5 YEAR PROBABILITY OF PROGRESSION: **25%** (95% C.I. 21, 27)

Probability of Progression as a Continuous Function of the Risk Score



Patient: Patient3, Demo
Date of Birth: 8/10/1944
Specimen ID: S20-345678

CLIA#: 39D2110302 Form#: TCBEAv5-0720
Laboratory Director: Marvin A. Lessig, D.O., FCAP
Email: customer.service@cernostics.com

cernostics
PROVIDING DEEPER TISSUE INSIGHTS

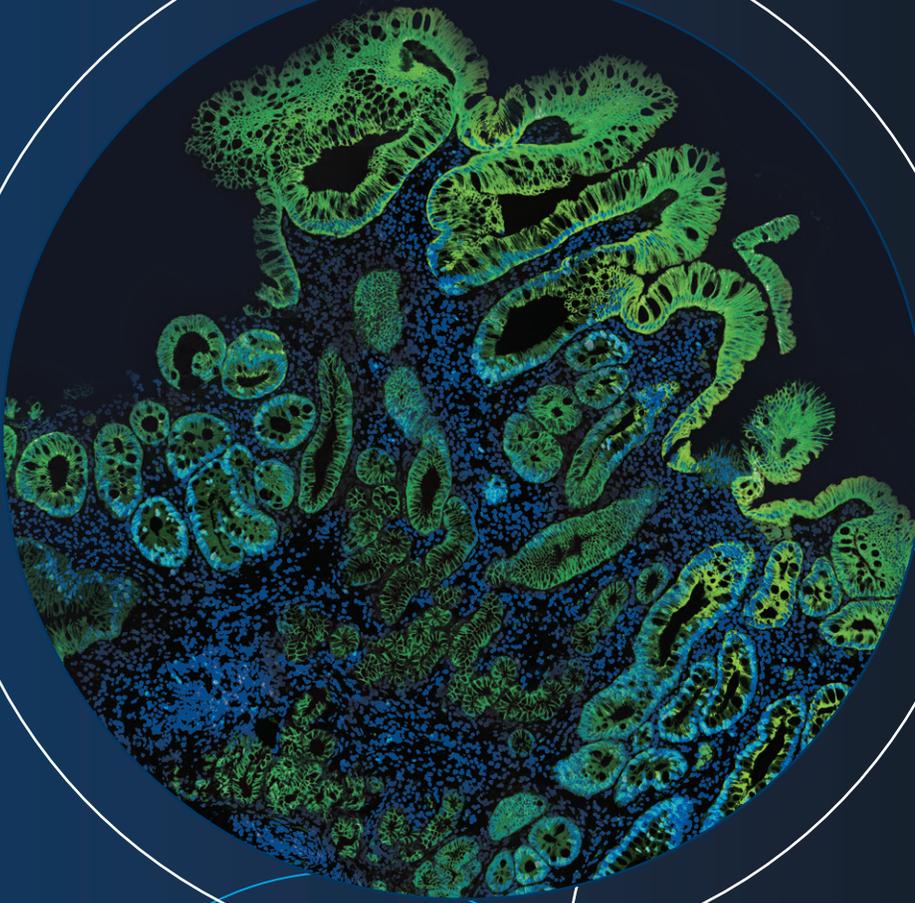
STUDY	KEY FINDINGS	STUDY CATEGORY & LEVEL OF EVIDENCE (LOE) ¹	REFERENCE
GAPP1 Study	<ul style="list-style-type: none"> Clinical validation demonstrating TissueCypher® predicts risk of future progression to HGD or EAC in Barrett's patients with baseline histologic diagnosis of ND, IND or LGD 	Category D, LOE IV	Critchley-Thorne RJ, et al. A tissue systems pathology assay for high-risk Barrett's esophagus. <i>Cancer Epidemiol Biomarkers Prev.</i> 2016 Jun;25(6):958-68.
GAPP2 Study	<ul style="list-style-type: none"> Clinical validation of locked assay to detect prevalent HGD/EAC missed by standard white light endoscopy and histology in patients with Barrett's esophagus 	Category D, LOE IV	Critchley-Thorne RJ, et al. A tissue systems pathology test detects abnormalities associated with prevalent high-grade dysplasia and esophageal cancer in Barrett's esophagus. <i>Cancer Epidemiol Biomarkers Prev.</i> 2017 Feb;26(2):240-248.
CC/UP Study	<ul style="list-style-type: none"> Independently validated the ability of TissueCypher® to predict risk of future progression to HGD/EAC within 5 years in BE patients with ND, IND or LGD Demonstrated that TissueCypher® identifies an "at-risk" subset of patients with ND BE who progress at a higher rate than patients with expert-confirmed LGD 	Category C, LOE II	Davison JM, Goldblum J, Grewal US, McGrath K, Fasanella K, Deitrick C, DeWard AD, Bossart EA, Hayward SL, Zhang Y, Critchley-Thorne RJ, Thota PN. Independent validation of a tissue systems pathology test to predict progression of Barrett's esophagus patients. <i>American Journal of Gastroenterology.</i> 2020;115:843-852.
CE Study	<ul style="list-style-type: none"> Demonstrated cost-effectiveness of TissueCypher®-directed management versus standard of care-directed surveillance and treatment Indicated change in healthcare utilization and potential improvement in patient outcomes associated with TissueCypher®-directed management 	LOE Quality A/B	Hao J, Critchley-Thorne RJ, Diehl DL, Snyder SR. A Cost-Effectiveness Analysis of an Adenocarcinoma Risk Prediction Multi-Biomarker Assay for Patients with Barrett's Esophagus. <i>Clinical Economics and Outcomes Research.</i> 2019;11:623-635.
AMC Spatial and Temporal Study	<ul style="list-style-type: none"> Confirmed ability of TissueCypher® to predict incident progression in ND BE patients Confirmed ability of TissueCypher® to identify ND BE patients that progress at a higher rate than patients with expert-confirmed LGD Demonstrated that evaluation of additional spatial and temporal specimens increases the predictive performance of TissueCypher® 	Category C, LOE II	Frei NF, Konte K, Bossart EA, Stebbins K, Zhang Y, Pouw RE, Critchley-Thorne RJ, Bergman JJ. Independent Validation of a Tissue Systems Pathology Assay to Predict Future Progression in Non-Dysplastic Barrett's Esophagus: A Spatial-Temporal Analysis. <i>Clinical and Translational Gastroenterology.</i> 2020; Oct 11(10).
SURF Biomarker Study	<ul style="list-style-type: none"> LOE I study (retrospective analysis of completed prospective RCT)² Independently validated the ability of TissueCypher® to predict risk of progression to HGD/EAC in patients with community practice diagnosis of LGD 	Category B, LOE I	Frei NF, Khoshiwal AM, Konte K, Bossart EA, Stebbins K, Zhang Y, Pouw RE, ten Kate FJW, Seldenrijk CA, Meijer SL, Critchley-Thorne RJ, Bergman JJ. A Tissue Systems Pathology Test Objectively Risk Stratifies Barrett's Esophagus Patients with Low-grade Dysplasia. <i>American Journal of Gastroenterology.</i> 2020; Nov 18.
Geisinger Decision Impact Study	<ul style="list-style-type: none"> TissueCypher® changed the management plan for 55% of BE patients studied at an expert center TissueCypher® led to upstaging of management plan in 21.7% of patients, indicating potential to improve outcomes TissueCypher® led to downstaging of management plan in 33.4% of patients, supporting surveillance rather than therapy 	LOE II	Diehl DL, Khara HS, Akhtar N, Critchley-Thorne RJ. The TissueCypher Barrett's Esophagus Assay Impacts Clinical Decisions in the Management of Patients with Barrett's Esophagus. <i>Endoscopy International Open.</i> 2021; 09(03): E348-E355.

1 Based on guidance in J. Natl. Cancer Inst., 101 (2009), pp. 1446-1452 (for clinical studies) and Value in Health 2010 Dec;13(8):952-7 and PLoS ONE10(12): e0144892 (for cost-effectiveness study).

2 Phoa et al., Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial. *JAMA* 2014;311:1209-17.

For links to these studies and more, please scan this code





Cernostics, Inc.
(412) 820-3050
235 William Pitt Way
Building B1
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