Pathnostics
Moving Care Forward

# The Role of AMACR Expression to Identify Dysplasia of Barrett's Esophagus

## AMACR to Detect Dysplasia

Increased levels of AMACR (P504S) protein concentration and activity are typically associated with prostate cancer, used widely as a biomarker in prostate biopsy tissues. In recent years, many studies have also identified AMACR as a useful biomarker in detecting dysplasia in Ulcerative Colitis, Crohn's Disease and Barrett's Esophagus.

## Clinical Significance of AMACR in Barrett's Esophagus

Identifying dysplasia in Barrett's Esophagus patients can be challenging. It has been estimated that endoscopic surveillance protocols that utilize four-quadrant biopsies are limited and may lead to false negative pathology results or to understaging. Forceps biopsies have been show to pick up only 40% of dysplastic cases in the esophagus, as most early neoplastic lesions of the esophagus are focal and not visible to the endoscopist.

Biomarkers that are helpful in differentiating true dysplasia from reactive changes and for grading of dysplasia can significantly contribute to screening in Barrett's Esophagus by identifying those with potential of progression to adenocarcinoma. One such biomarker is AMACR.

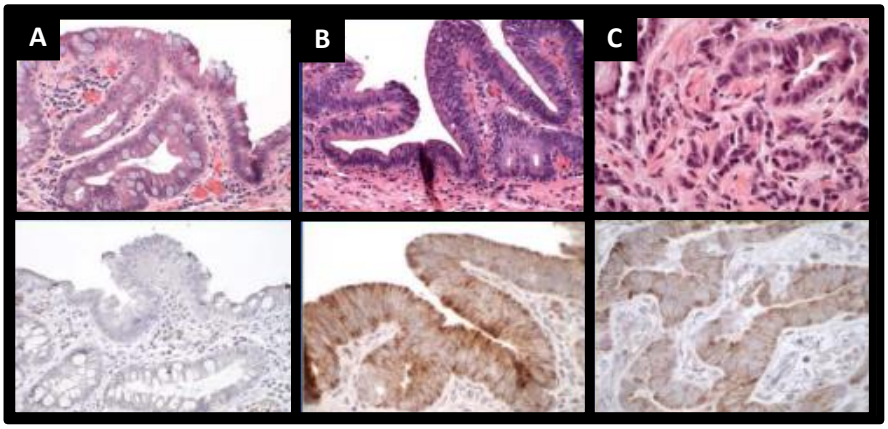
Results of the following studies show that the AMACR biomarker may be useful to detect neoplastic epithelium in patients with Barrett's Esophagus. The following table shows % AMACR expression in Barrett's Esophagus patients classified as negative for dysplasia (BE), indefinite for dysplasia (IND), low-grade dysplasia (LGD), high-grade dysplasia (HGD), and adenocarcinoma (Adeno):

**% AMACR Expression in Barrett's Esophagus Patients**

| Study | BE | IND | LGD | HGD | Adeno |
|---|---|---|---|---|---|
| Dorer (2006) | 0% | 21% | 38% | 81% | 72% |
| Lisovsky (2006) | 0% | 0% | 11% | 64% | 75% |
| Scheil-Bertram (2008) | 0% | 27% | 91% | 96% | 96% |
| Shi (2008) | 12% | 47% | 54% | 93% | 96% |
| Sonwalker (2010) | 0% | 22% | 18% | 60% | 67% |
| Biermann (2013) | * | 49% | 63% | 91% | 77% |

** The Biermann study combines BE and IND in the total 49%*

**AMACAR Expression in Barrett's Esophagus Patients**




*AMACAR expression in Barrett's esophagus without dysplasia (A), with high-grade dysplasia (B), and invasive adenocarcinoma (c).*

**Pathnostics' CBEST™ - Comprehensive Barrett's Esophageal Test**

Pathnostics developed the CBEST brush cytology test method to distinguish patient chromosomal alterations with regard to level of dysplasia and adenocarcinoma earlier than with traditional diagnostic methods by utilizing cytology, IHC Biomarkers and FISH testing.

A 2010 study of 1266 patients showed that the addition of brush cytology to forceps biopsy increased the detection of esophageal dysplasia by 87.5%. Our method allows for the whole surface area of the Barrett's mucosa to be sampled, potentially reducing sampling error vs. forceps biopsy alone. Additionally, brush cytology may detect relevant abnormalities, as dysplastic cells shed easier than normal epithelial cells.

In addition to AMACR, the **CBEST** panel of biomarkers that have known associations with dysplastic changes of Barrett's Esophagus includes:

- **DNA Ploidy** - Abnormalities in DNA ploidy generally correlate well with conventional histologic diagnoses of dysplasia and carcinoma.
- **p53** – The study of p53 expression by immunohistochemistry is of interest in those patients with a mucosa indefinite for dysplasia or with LG.
- **Ki-67** – Immunohistochemical staining for MIB-1, the Ki-67 proliferation antigen, shows gradually increasing expression in the Barrett's esophagus-dysplasia-adenocarcinoma sequence.

Our **Barrett's FISH** testing identifies genetic abnormalities in patients with Barrett's Esophagus and provides an indication of progression requiring additional procedures and specific management. Utilizing a four-probe panel to detect gains and losses of **MYC** (8q24), **p16** (CDKN2A at 9p21), **HER2** (ERBB2 at 17q12), and **ZNF217** (20q13) associated with higher-risk disease, our Barrett's FISH panel offers:

- Differentiation between patients with low-grade dysplasia and high-grade dysplasia.
- Histology confirmation when results are concordant, and suggests further investigation is needed when results differ from histology.
- Support of aggressive treatment decisions based on positive test results together with concordant morphology.