CÁNCER GÁSTRICO

Early detection of gastric cancer using global, genome-wide and IRF4, ELMO1, CLIP4 and MSC DNA methylation in endoscopic biopsies.

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Abstract

Clinically useful molecular tools to triage gastric cancer patients are not currently available. We aimed to develop a molecular tool to predict gastric cancer risk in endoscopy-driven biopsies obtained from high-risk gastric cancer clinics in low resource settings.We discovered and validated a DNA methylation biomarker panel in endoscopic samples obtained from 362 patients seen between 2004 and 2009 in three high-risk gastric cancer clinics in Lima, Perú, and validated it in 306 samples from the Cancer Genome Atlas project ("TCGA"). Global, epigenome wide and gene-specific DNA methylation analyses were used in a Phase I Biomarker Development Trial to identify a continuous biomarker panel that combines a Global DNA Methylation Index (GDMI) and promoter DNA methylation levels of IRF4, ELMO1, CLIP4 and MSC.We observed an inverse association between the GDMI and histological progression to gastric cancer, when comparing gastritis patients without metaplasia (mean = 5.74, 95% CI, 4.97-6.50), gastritis patients with metaplasia (mean = 4.81, 95% CI, 3.77-5.84), and gastric cancer cases (mean = 3.38, 95% CI, 2.82-3.94), respectively ($p < 0.0001$). Promoter methylation of IRF4 ($p < 0.0001$), ELMO1 ($p < 0.0001$), CLIP4 ($p < 0.0001$), and MSC ($p < 0.0001$), is also associated with increasing severity from gastritis with no metaplasia to gastritis with metaplasia and gastric cancer.Our findings suggest that IRF4, ELMO1, CLIP4 and MSC promoter methylation coupled with a GDMI>4 are useful molecular tools for gastric cancer risk stratification in endoscopic biopsies.