ABERRANT DNA METHYLATION IN LGR5-POSITIVE GASTRIC EPITHELIAL STEM CELLS DURING HELICOBACTER PYLORI-ASSOCIATED GASTRIC CARCINOGENESIS AND ITS PROGNOSTIC VALUE

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Genome-wide DNA methylation analysis of Lgr5-positive gastric stem cells during H. pylori-associated gastric carcinogenesis identified six key differentially methylated genes with prognostic significance, including ADCY1 and SFRP1 as independent prognostic factors.

KEY POINTS

- More than 100,000 differentially methylated sites were identified in Lgr5-positive gastric epithelial stem cells, with 10-fold more in gastric cancer than in intestinal metaplasia.
- Six key differentially methylated genes (GABBR1, GRIA4, ADCY1, CDH2, NRXN2, and SFRP1) showed methylation levels negatively correlated with transcript levels and had prognostic significance in H. pylori-positive gastric cancer.
- A prognostic risk score based on ADCY1 and SFRP1 transcript levels achieved areas under the ROC curve of 0.664, 0.725, and 0.716 for 1-year, 3-year, and 5-year survival prediction, respectively.
- ADCY1 and SFRP1 were identified as independent prognostic factors and showed significantly higher protein expression in tumor tissues compared to paired adjacent mucosal tissues.
- The 139 differentially methylated genes were predominantly involved in Wnt, PI3K-Akt, and cAMP signaling pathways, suggesting these pathways are disrupted during H. pylori-driven malignant transformation.

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