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**Extracellular Vesicle–Derived lncRNA Signature Enables Early, Non-Invasive Detection of Early-Onset Gastric Cancer**

Guo X, Wang W, Cheng X, *et al.* Diagnostic efficacy of an extracellular vesicle-derived lncRNA-based liquid biopsy signature for the early detection of early-onset gastric cancer. Gut 2025; 74(8): 1209-1218. doi: 10.1136/gutjnl-2024-333657.

Early-onset gastric cancer (EOGC), defined as gastric cancer occurring in individuals under 50 years old, carries high morbidity and often presents at an aggressive stage. Existing diagnostic biomarker, such as CEA (carcinoembryonic antigen), Helicobacter pylori serology, and pepsinogens, perform poorly in younger populations, and delayed detection can critically limit curative treatment options.

In this study, Guo *et al.* developed a non-invasive liquid biopsy signature based on three extracellular vesicle derived long non coding RNAs (EV lncRNAs): NALT1 (NOTCH1 Associated LncRNA In T Cell Acute Lymphoblastic Leukaemia 1), PTENP1 (Phosphatase and tensin homolog pseudogene 1), and HOTTIP (HOXA transcript at the distal tip). Through an integrated discovery phase using genome wide transcriptomics from tissue samples (43 EOGC, 31 late onset GC, and 37 controls), they identified candidate EV lncRNAs. These were then validated by qPCR across a large training cohort (299 patients) and two independent external validation cohorts (Xi’an, n=462; Beijing, n=438).

The three-component signature achieved strong diagnostic performance: AUC (area under the curve) = 0.924 (95% CI 0.889–0.953) in the training cohort and maintained high accuracy in both validation cohorts—AUC = 0.911 in Xi’an and AUC = 0.932 in Beijing. Importantly, the signature effectively identified resectable early stage (stage I/II) EOGCs from precancerous lesions, outperforming traditional biomarkers. Levels of these EV lncRNAs dropped after surgical resection, and were low or absent in other gastrointestinal cancers, supporting specificity to gastric cancer and responsiveness to tumour burden.

This EV lncRNA biomarker panel represents a promising, minimally invasive tool for early detection of EOGC, especially in resectable stages where curative treatment is possible. Guo *et al.* suggest potential clinical utility in screening young patients at risk, pending further prospective studies and broader validation.