OLFM4 Promotes Intestinal Metaplasia Progression via Activation of the MYH9/GSK3β/β-Catenin Pathway

Hongfa Wei, Wenchao Li and Leli Zeng, Mol Cancer 23, 124 (2024)

Presenter: Yu, Sun **Date/Time**: 2025/05/22, 15:20-16:10

Commentator: Dr. Hsiu-Chi, Cheng **Location**: Room 601, Med College Building

Background:

Intestinal metaplasia (IM), especially its incomplete subtype (IIM), is a critical precursor to intestinal-type gastric cancer, associated with a 4- to 11-fold increased risk of malignancy. However, existing diagnostic markers like CDX2 and MUC2 lack sufficient specificity and sensitivity for identifying IIM. OLFM4, a glycoprotein linked to stem cell maintenance and tumorigenesis, has been reported to be overexpressed in several cancers, yet its role in the early stages of gastric carcinogenesis and in IIM has not been clearly defined.

Objective:

This study aimed to evaluate OLFM4 as a biomarker for IIM and investigate its role in promoting IM progression through the MYH9/GSK3β/β-catenin signaling pathway.

Results:

OLFM4 was significantly overexpressed in IIM tissues, showing superior diagnostic accuracy compared to CDX2 and MUC2. In both patient samples and organoid models, OLFM4 expression correlated with proliferative and invasive phenotypes. Mechanistically, OLFM4 was found to interact with MYH9, enhancing the ubiquitination and degradation of GSK3β, thereby stabilizing β-catenin and activating the Wnt signaling pathway. Functional experiments in GES-1-derived PLGC cells and MNNG-induced animal models confirmed that OLFM4 upregulation promoted malignant features, whereas its knockdown suppressed tumor-like behavior.

Conclusion:

OLFM4 is a promising biomarker for IIM and facilitates its malignant progression via the MYH9/GSK3β/β-catenin pathway, offering a potential target for early diagnosis and treatment in gastric cancer.