Syk tyrosine kinase mediates Epstein-Barr virus latent membrane protein 2A-induced cell migration in epithelial cells

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摘要

Abstract

Although spleen tyrosine kinase (Syk) is known to be important in hematopoietic cell development, the roles of Syk in epithelial cells have not been well studied. Limited data suggest that Syk plays alternate roles in carcinogenesis under different circumstances. In breast cancer, Syk has been suggested to be a tumor suppressor. In contrast, Syk is essential for murine mammary tumor virus-mediated transformation. However, the roles of Syk in tumor migration are still largely unknown. Nasopharyngeal carcinoma, an unusually highly metastatic tumor, expresses Epstein-Barr virus LMP2A (latent membrane protein 2A) in most clinical specimens. Previously, we demonstrated LMP2A triggers epithelial cell migration. LMP2A contains an immunoreceptor tyrosine-based activation motif, which is important for Syk kinase activation in B cells. In this study, we explored whether Syk is important for LMP2A-mediated epithelial cell migration. We demonstrate that LMP2A expression can activate endogenous Syk activity. The activation requires the tyrosine residues in LMP2A ITAM but not YEEA motif, which is important for Syk activation by Lyn in B cells. LMP2A interacts with Syk as demonstrated by coimmunoprecipitation and confocal microscopy. Furthermore, LMP2A-induced cell migration is inhibited by a Syk inhibitor and short interfering RNA. Tyrosines 74 and 85 in the LMP2A immunoreceptor tyrosine-based activation motif are essential for both Syk activation and LMP2A-mediated cell migration, indicating the involvement of Syk in LMP2A-triggered cell migration. The LMP2A-Syk pathway may provide suitable drug targets for treatment of nasopharyngeal carcinoma.