HHEX suppresses lung cancer cell migration by regulating the RHOA/CDC42–CFL1 axis

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Abstract

The protein HHEX plays multiple roles in development, gene expression, and cancer suppression. For example, it can inhibit breast cancer and prostate cancer cell migration and invasion, which are important processes for cancer spread, but whether and how HHEX affects lung cancer cell motility remain unknown. To learn more, a new study investigated HHEX's functions in human non-small cell lung cancer cells and control cells. According to an analysis of published datasets, HHEX expression was reduced in lung cancer cells, and low HHEX expression was associated with reduced overall survival in patients. In lung cancer cell lines, silencing HHEX accelerated wound gap closure and increased protrusion formation, indicating increased migration ability, while HHEX overexpression had the opposite effects. HHEX interacted with the cell movement-related proteins RHOA and CDC42, inhibiting their activation in cancer cells and maintained the motility-suppressing protein CFL1 in an active state by reducing p-CFL1 levels in cooperation with RHOGDIA, HHEX also enhanced RHOGDIA–RHOA/CDC42 interaction. Although the exact mechanisms are unclear, the results show that HHEX suppresses lung cancer cell migration by regulating the RHOA/CDC42–CFL1 axis, indicating the potential diagnostic and prognostic value of HHEX.