論 文 の 内 容 の 要 旨

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論 文 題 目

Nox4 redox regulation of PTP1B contributes to the proliferation and migration of glioblastoma cells by modulating tyrosine-phosphorylation of coronin-1C
(Nox4-PTP1B レドックスシグナルは、coronin-1C のタイロシンリン酸化を介して膠芽腫細胞の増殖と運動 に寄与する)

（論文の内容の要旨）

Glioblastoma multiforme is a common primary brain tumor in adults and one of the most devastating human cancers. Reactive oxygen species (ROS) generated by NADPH oxidase (Nox) 4 have recently been a focus of attention in the study of glioblastomas, but the molecular mechanisms underlying the actions of Nox4 remain elusive. In this study, we demonstrated that silencing of Nox4 expression by Nox4-targeted siRNA suppressed cell growth and motility of glioblastoma U87 cells, indicating the involvement of Nox4. Furthermore, Nox4-derived ROS oxidized and inactivated protein tyrosine phosphatase (PTP):1B: PTP1B in its active form downregulates cell proliferation and migration. By affinity purification with the substrate-trapping mutant of PTP1B, tyrosine-phosphorylated coronin-1C was identified as a substrate of PTP1B. Its tyrosine phosphorylation level was suppressed by Nox4 inhibition, suggesting that tyrosine-phosphorylation of coronin-1C is regulated by the Nox4-PTP1B pathway. Finally, ablation of coronin-1C attenuated the proliferative and migratory activity of the cells. Collectively, these findings reveal that Nox4-mediated redox regulation of PTP1B serves as a modulator, in part through coronin-1C, of the growth and migration of glioblastoma cells, and provide new insight into the mechanistic aspect of glioblastoma malignancy.