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Inhibition of Eva1 degrade the formation and development of glioblastomas

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Research focused on the property and targets of cancer stem cells, which have tumorigenicity and treatment-resistant, may contribute to the discovery of new therapeutic and diagnostic strategies. We have previously established mouse glioma-initiating cell (mGIC) lines from normal neural lineage cells, analyzed their gene expression profile and reported functions of GIC-specific genes. We further focused on GIC-specific membrane proteins and found uncharacterized cell-membrane protein Eva1. Here we show the characterization of Eva1 in GIC: Eva1 is highly expressed in mouse GIC line, NSCL61 and human glioblastoma (GBM, WHO grade IV)-derived floating spheres, whereas it is not expressed in normal adult mouse and human brain. Eva1 expression is correlated with the malignancy of glioma. Indeed, we found that Eva1+ cells disseminate in human GBM tissue. Moreover, knockdown of Eva1 inhibited cell proliferation and tumorigenicity in mGIC and hGIC. Forced-expression of Eva1 enhanced malignancy of Low-grade human glioma (Diffuse Astrocytoma: DA, WHO grade II). The combination of polyclonal anti-Eva1 antibody and cytotoxic factor Saporin kills GIC, therefore it promised as a new target of antibody preparation. Using gene expression profiles between mGIC and Eva1-knockdown mGIC, we further found Eva1 signal pathway. Eva1 induced GIC proliferation through the activation of the RelB-dependent noncanonical NF-kB pathway by recruiting TRAF2 to the cytoplasmic tail. This signal pathway is important for human GBM formation. Taken together, these findings suggest that Eva1 is a potential target for immunotherapy.

Biography

Naoki Ohtsu is interested in stem cell biology and tumorigenesis from stem cells. Based on Cancer stem cell theory, they are searching for cells with high tumorigenicity and membrane proteins intensely expressed in the cells. Currently, he focus on glioblastoma, a malignant brain tumor, and analyze membrane proteins that are molecular targets of antibody drugs. Using induced cancer stem cells derived from neural stem cells as model cells, strongly expressed membrane proteins were searched for multiple candidate proteins. This presentation introduces the molecules whose function and molecular mechanism are clarified among the obtained candidate.

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