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JWA gene based targeting peptide inhibits melanoma proliferation and metastasis

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Cancer metastasis is still the biggest challenge to cancer patients worldwide. Melanoma is the most malignant tumor due to its rapid metastatic capacity and shorter survival rate. The JWA gene, also known as *ARL6IP5*, is initially cloned from a retinoid acid induced cell differentiation cell culture model in HBE (human bronchial epithelial) cells. JWA is also identified as an multi-functional protein in both normal and cancer cells. In normal cells, JWA works as an active ROS (reactive oxygen species) response gene and DNA repair protein; however, in cancer cells, JWA exerts a tumor suppressor role to inhibit cell migration, proliferation, angiogenesis and chemoresistance in some cancers including melanoma and gastric cancer. Here, we have developed a JWA gene based polypeptide (PJP1-RGD) which is able to specifically target overexpressed integrin αvβ3 on membrane of melanoma cells by its RGD linker. Our data showed 50 mg.kg/day of PJP1-RGD could effectively inhibit xenograft tumor growth of both B16H10 and A375 melanoma cells in mice, suppressed its metastasis and improved mice survival. The anticancer effect of PJP1-RGD is comparable to 80 mg.kg/day Dacarbazine, a first line drug for clinical melanoma chemotherapy. More importantly, a synergistic role was observed between PJP1-RGD and Dacarbazine in the treatment of melanoma. The combined use of PJP1-RGD (50 mg.kg/day) and Dacarbazine (40 mg.kg/day) indicated an enhanced inhibitory effects but less side effects of Dacarbazine. In conclusion, PJP1-RGD targeting peptide might be an useful anti-cancer metastasis candidate and with translational significance in drug development.

Recent Publications:

1. Wang S Y et al. (2009) JWA regulates XRCC1 and functions as a novel base excision repair protein in oxidative-stress-induced DNA single-strand breaks. Nucleic Acids Res. 37(6):1936-1950.
2. Bai J et al. (2010) JWA regulates melanoma metastasis by integrin αvβ3 signaling. advance online publication. Oncogene. 29(8):1227-1237.
3. Wang S et al. (2012) Prognostic and predictive role of JWA and XRCC1 expressions in gastric cancer. Clin. Cancer Res. 18(10):2987-2996.
4. Lu J et al. (2013) JWA inhibits melanoma angiogenesis by suppressing ILK signaling and is an independent prognostic biomarker for melanoma. Carcinogenesis. 34(12):2778-2788.
5. Qiu D et al. (2018) RNF185 modulates JWA ubiquitination and promotes gastric cancer metastasis. Biochim Biophys Acta. 1864(5 Pt A):1552-1561.

Biography

Jianwei Zhou has his expertise in research on DNA damage and repair, cancer initiation, metastasis and drug resistance. Based on the mechanistic discovery of JWA gene in anticancer and neuroprotection, he has developed anticancer polypeptides and small molecular compounds and these will can be potentially used as neurodegenerative protection and cancer metastasis therapeutic agents.

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