Synopsis of Original Research Paper

# The research to establish the drug for white skin through analysis of melanin production

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Malignant melanoma is one of the most aggressive tumors. Incidence of melanomas is increasing by upregulation of ultraviolet irradiation. Therefore, it is necessary to establish a new drug for preventing against and curing melanoma though the clarification of its mechanism. We established the RET-transgenic mouse line (304/B6), in which spontaneously develops benign melanocytic tumor(s) without exception. About 70% of the benign tumors will be changed to malignant melanomas. We investigated the role of c-Kit in the hereditary melanoma developed in the RET-transgenic mice (line 304/B6). In $W^V/W^V$-RET (304/B6)-transgenic mice, in which c-Kit function was severely impaired, development of melanoma was strongly suppressed. Whereas 31 of the 44 original RET-transgenic mice died of rapidly growing melanoma within 12 months after birth, only 8 of the 44 $W^V/W^V$ -RET-transgenic mice developed slowly-growing melanocytic tumors with a greatly prolonged mean tumor-free period, two of which died of melanoma at a late stage. Even $W^V$ /+-RET-transgenic mice had a clearly prolonged tumor-free period and a definitely reduced frequency (6/61) of tumor death within 12 months after birth. Melanin production in the skin of these mice was not strongly impaired, suggesting that c-Kit affects the development of melanomas in these mice with only minor effects in melanin production. More importantly, a single injection of anti-c-Kit antibody (ACK2) into RET-transgenic mice soon after birth caused a surprisingly long-lasting suppression of development of melanoma, greatly prolonging the tumor-free period, and none of the 28 ACK2-treated RET-transgenic mice had died from tumors at 12 months of age. The c-Kit function needed for melanin production was also suppressed for an unusual long time in ACK2-treated RET-transgenic mice. These results suggest that c-Kit can be a unique target molecule to prevent against melanoma. In the next step, we should clarify whether c-Kit can be a target of therapy for the developed melanoma or not.