Response of B6C3F1 Mice Continuously Irradiated with Low-dose-rate Gamma-rays to Transplanted Tumor Cells

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Abstract

Transplantability of a murine ovary granulosa cell tumor cell line was significantly enhanced in syngeneic B6C3F1 mice continuously irradiated with low-dose-rate (20 mGy/22h/day) gamma-rays to a total accumulated dose of 8000 mGy. Since the enhancement may be due to a chemokine/chemokine receptor system, we examined RNA expressions of chemokine receptors in blood cells of age-matched irradiated and non-irradiated control mice. Expression of chemokine receptor Ccr5 gene was reduced in irradiated mice, and the low expression level of Ccr5 may result in enhanced tumor transplantability. The reduced expression of Ccl8, known as a ligand of Ccr5, in the tumor cells enhanced the tumor transplantability. The alteration in chemokine axis of chemokine receptor Ccr5 and its ligand Ccl8 may play several important roles in the response to low-dose-rate and continuous gamma-ray irradiation.

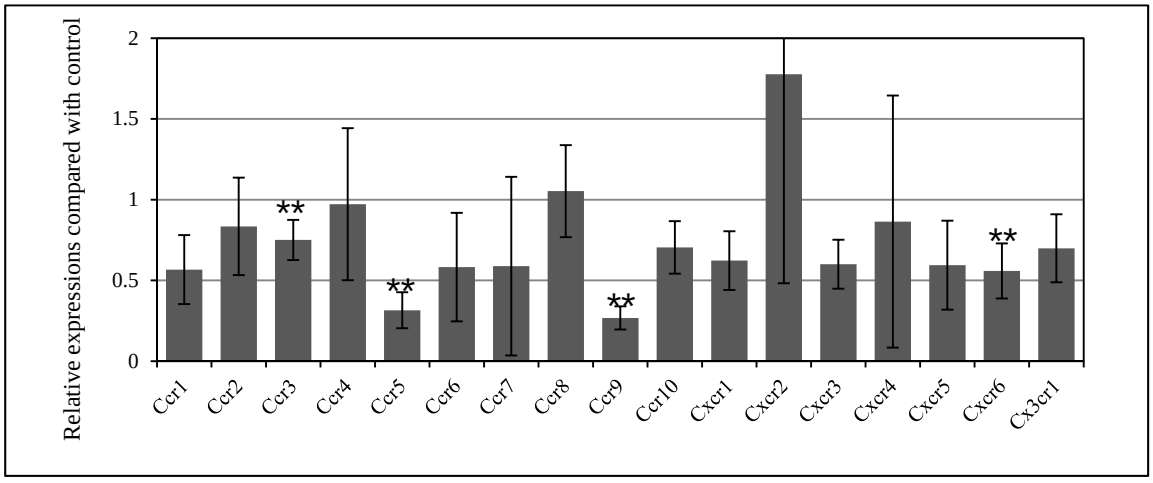


Fig. 1 Relative expressions of chemokine receptors in irradiated mice compared with non-irradiated control mice. RNAs were purified from peripheral blood cells of mice. Expressions were measured using real time quantitative RT-PCR. Error bars indicate mean ± S.D. ***P*<0.01.

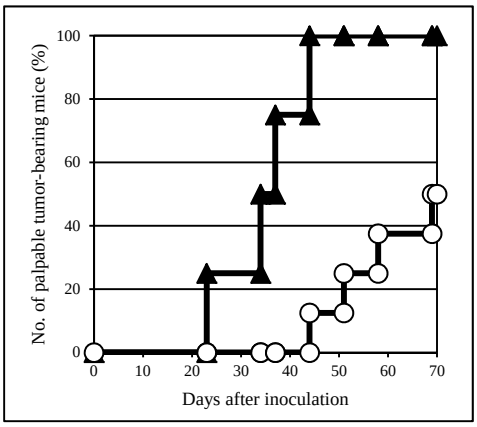
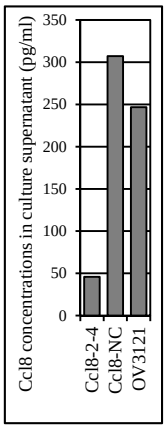
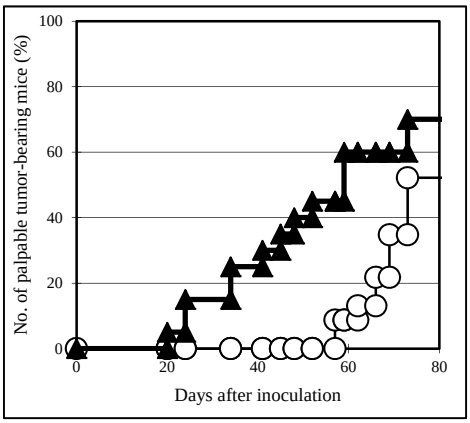


Fig. 2 Comparison of tumor transplantability. 5.0 x 10^5 OV3121 cells were inoculated into mice with high expression of Ccr5 (○) and mice with low expression of Ccr5 (▲). The number of tumor-bearing mice, wherein a palpable tumor was detected, was counted to assess transplanted tumor formation.



A



B

Fig. 3 Down-regulation of Ccl8 in OV3121 cells.
A, SureSilencing shRNA Plasmid for Mouse CCL8 was introduced into OV3121 cells. Concentrations of Ccl8 in culture supernatant were measured using ELISA. B, 1.0 x 10^5 of Ccl8-2-4 cells (▲) and Ccl8-NC cells (○) were inoculated into mice. The number of tumor-bearing mice, wherein a palpable tumor was detected was counted to assess transplanted tumor formation.