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General Summary

Cancer is the leading cause of death in Japan. More than 300,000 people die of cancer every year. With the goal of conquering cancer, a state anticancer policy was established out in 2007. Under such a situation, we are studying to develop innovative therapeutic methods.

Research Activities

Exploring the etiology of human leukemia

Two groups of genes are involved in the pathogenesis of leukemia. One group of genes regulates the growth of hematopoietic cells, and the other controls the differentiation of cells. These genes co-operate to develop leukemias. Both megakaryocytic and erythroid leukemias are thought to originate from megakaryoerythroid progenitor cells, but the clinical characteristics of the leukemias differ markedly. Moreover, the molecular mechanism of lineage shifting remains largely unclear. We recently established a megakaryoerythroid leukemia cell line, JAS-R, whose cells show a lineage shift depending on culture conditions. The interaction between fibronectin and integrin elicits the megakaryocytic phenotype and leads to the loss of erythroid characteristics in JAS-R cells. Expression profiling analysis revealed that several transcription factors changed during lineage shifting. Of these genes, FLI1 was considered to be responsible for the expression of the megakaryocytic phenotype. These results are useful for understanding normal hematopoiesis and the treatment of leukemia.

Pharmacology of anticancer drugs

Several lines of evidences demonstrate that telomerase is a promising molecular target for cancer therapy. 5,10,15,20-Tetra-(N-methyl-4-pyridyl)porphyrin (TMPyP4) is a compound that binds to telomere DNA stably and tightly and blocks telomerase activity *in vitro*. Thus, we studied the anticancer activity of TMPyP4 using K562 leukemic cells and found that TMPyP4 directly inhibits the growth of K562 cells. We also studied whether TMPyP4 functions as an anticancer agent for other cancer cells. Two retinoblastoma cell lines, Y79 and WERI-Rb1, were studied. Apoptosis was induced in both cell lines by short-term exposure to TMPyP4. This apoptosis was associated with the phosphorylation of P53 and the activation of mitogen-activated protein kinase. Furthermore, pretreatment of Y79 cells with TMPyP4 increased radiation-induced cell death. These findings show that TMPyP4 is a potential anticancer agent and may be applicable for some patients with retinoblastoma who require radiation therapy.

Publications

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