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Production of the Novel Disease Animal Model by Used Tet-off System

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The activation of protooncogenes or the inactivation of their gene products may be a specific and effective functional study for human neoplasia. To examine this possibility, we have used the tetracycline regulatory system to generate transgenic mice that conditionally express the HccR-2 protooncogene in vivo. The new *human cervical cancer protooncogene* (HccR-2) was detected from cervical cancer cell line. To elucidate its biological functions, we generated transgenic mice that expressed the HccR-2 gene. The sustained expression of the HccR-2 transgene culminated chronic neutrophilic leukemia (CNL).

CNL is a rare chronic myeloproliferative disorder that presents as a sustained, mature neutrophilic leukocytosis with few or no circulating immature granulocytes, the absence of peripheral blood monocytosis, basophilia, or eosinophilia, and infiltration of neutrophils at the liver, spleen and kidney. Mice expressing the HccR-2 and tetracycline-transactivating protein (tTa) transgene were found to have altered myeloid development that was characterized by increased percentages of mature neutrophil and band form neutrophil in the peripheral blood, liver and spleen. Activation of the transgene causes CNL. In our model, expression of HccR-2 transgene mice was similar in many respects to the human CNL. This model will be valuable not only for investigating the biological properties of the HccR-2 and other protooncogenes in vivo but also for analyzing the mechanism involved in the progression of CNL.

Key words) ***HccR-2, Transgene mice, CNL***