Establishment of a neuroblastoma mouse model by subcutaneous xenograft transplantation and its use to study metastatic neuroblastoma

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ABSTRACT. The aim of this study was to establish a metastatic human neuroblastoma (NB) mouse model by xenograft in order to study the metastatic mechanisms of NB. A human NB cell line was obtained from a 5-year-old patient and cultured *in vitro*. A suspension of these cells was subcutaneously inoculated into nude mice at the right flank next to the forelimb. The biological characteristics of the developed subcutaneous and metastatic tumors were analyzed by hematoxylin and eosin staining. The expression of the tumor marker neuron-specific enolase was determined by immunohistochemistry, and the invasive ability of metastatic tumors

was examined by a Matrigel invasion assay. DNA microarray analyses were performed to examine the metastasis-related gene expression. Our results showed that tumors grew in 75% of the mice injected with NB cells and the rate of metastasis was 21%. The xenograft tumors retained the morphological and biological characteristics of the NB specimen from the pediatric patient. Neuron-specific enolase was highly expressed in both subcutaneous and metastatic tumors. The metastatic tumor cells possessed a higher invasive capability than the primary NB cells. The expression of 25 metastasis-related genes was found to be significantly altered in metastatic tumors compared to primary tumors, including RECK, MMP2, VEGF, MMP3, and CXCL12. In conclusion, we successfully established a human NB xenograft model with high tumor-bearing and metastatic rates in nude mice, providing an ideal animal model for the *in vivo* study of NB.

Key words: Neuroblastoma; Metastasis; Nude mice; Xenograft; Neuron-specific enolase

