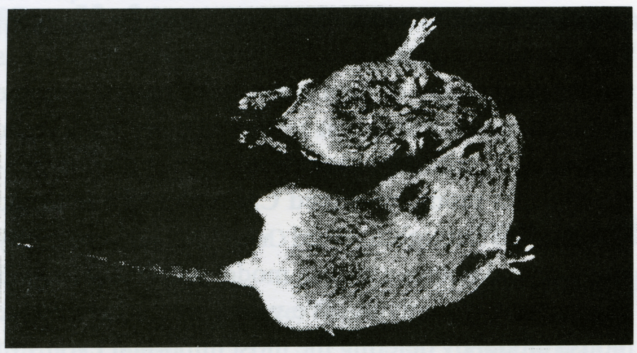

Fig. 2. The phenotypes of SMA-like mice are similar to findings in human SMA patients. A type II SMA-like mouse (bottom) shows paralysis in the hindlimbs. The mouse on the top is the control littermate.

the SMA mouse model since the transgene/knockout resulted mice are both genotypically and phenotypically mimic human SMA patients.[16] (Fig. 1 and 2).

SMN protein is widely expressed in the central nervous system as well as in various non-neural tissues.[17] It was suggested that motor neurons require high amounts of the SMN protein to survive. The amount of SMN protein dropping below a threshold critical for the survival of motor neurons might lead to their degeneration and to dysregulation, and the occurrence of apotosis. However, reduced levels might still be compatible with the survival of other less susceptible cell types in the CNS or other tissues.[17] From the subcellular fractionation analysis of the SMN protein in three types of SMA-like mice.[16] we found that the transgene-expressed full-length SMN protein was abundantly expressed in tissues other than the spinal cord. These results indicate that there may be tissue-specific factors that can modify post-transcriptional processing of the *SMN2* transgene product and allow more of the full-length SMN protein to be synthesized in other tissues. It was postulated that the hyper-expression of the *SMN2* gene to obtain enough level of full-length SMN protein could be considered as an attractive strategy for a therapeutic approach to SMA treatment. Further studies focusing on the characterization of the SMN promoter would be very important to pursue this strategy. Another approach is to change the alternative splicing pattern to result in production of greater quantities of the full-length SMN protein from the *SMN2* gene. Characterization of the tissue distribution of alternative-splicing involving factors would be an important step to understand alternative splicing mechanism of the *SMN2* gene and further provide the basis for the therapeutic strategies.

In conclusion, this mouse model was established and characterized through the collaboration of molecular biologists and clinicians from different institutions in Taiwan.[16] Our success indicated that scientists in Taiwan are becoming competitive with scientists of developed countries. The characterization of the SMA-like mouse model suggested potential therapeutic strategies, for example, hyper-expression of intact SMN proteins from *SMN2* in affected patients. The SMA-like mice produced in this study thus present a model which will be useful to explore theoretical understanding of the SMN involved in SMA and therapeutic strategies for SMA.

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