also expressed in SMA patients, however, the expression pattern is different from that of *SMN1*. Most *SMN2* transcripts lack exons 3, 5, or 7, especially exon 7. On the other hand, the *SMN1* gene seems to express mostly, a full-length mRNA.[11-12] Dosage analysis has also shown that the SMN protein is significantly decreased in patients with severe SMA.[13-14]

No specific treatment is currently available for SMA patients. Thus, the development of a suitable animal model for SMA is not only important for understanding the pathophysiology of the disease but also to provide a biological system for use in drug testing or gene therapies. Five years of effort to establish on SMA animal model has passed since the human SMA-determining gene, *SMN*, has been reported in the early of 1995.[7] At least a couple of laboratories in the United States and Europe tried to accomplish this task (personal communication at the Human Genetic Disease Conference in San Francisco, October, 1999). Alternative methods other than traditional knockout of the mouse *Smn* gene must be applied because there is only a single copy of *Smn* gene in the mouse genome and its targeted disruption results in early embryonic lethality[15]. Conditional-knockout with a motor neuron-specific promoter-drived Cre recombinase would be a more straightforward way to prevent early lethality and obtain a mouse model with the muscular degeneraton phenotype. We were failed to obtain the mouse model by deleting the most important exon 7 of the *Smn* gene, although a similar genetic status as in human heterozygous offspring was expected. These heterozygous mice, however, were phenotypically normal, and homozygous mice died during peri-implantation. This result indicates the instability of the exon 7-deficient Smn protein. We thus developed transgenic mouse lines carrying the human *SMN2* gene and crossed them with the *Smn*-deleted heterozygous mice. Introducing the human *SMN2* gene onto the *Smn* null background indeed a correct approach to establish

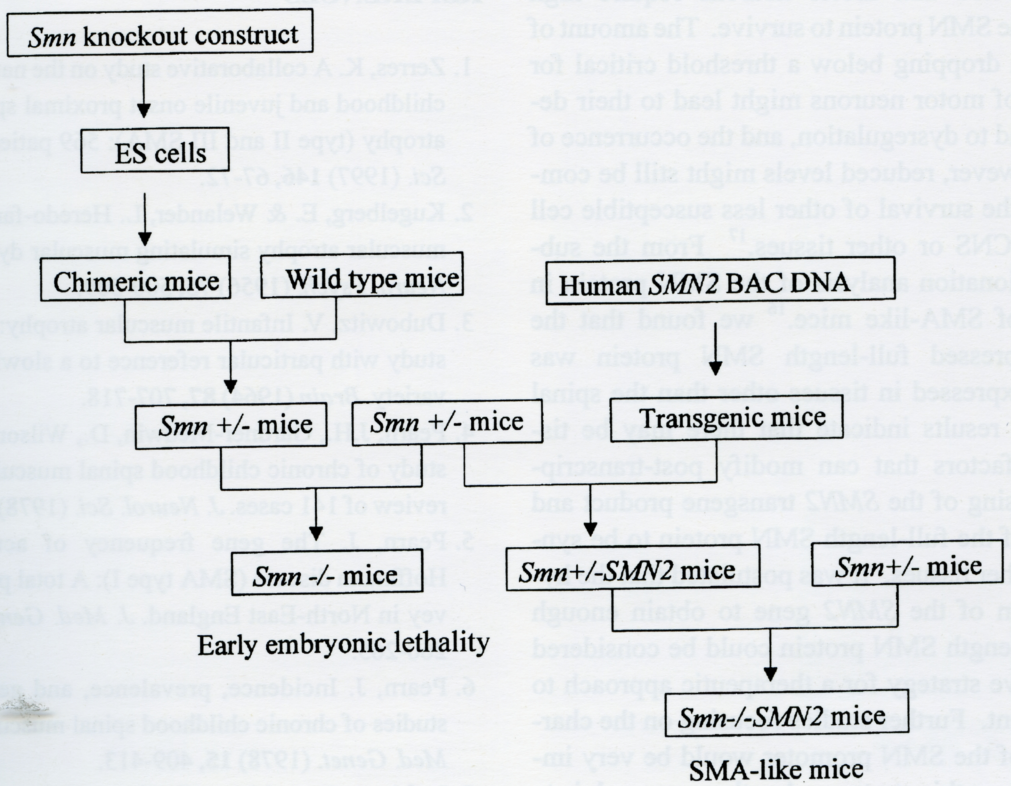

Fig. 1. The flow chart for making SMA-like mice.