Identification of the genomic mutation in *Epha4*$^{rb\text{-}2J/rb\text{-}2J}$ mice

ABSTRACT

The EphA4 receptor tyrosine kinase is involved in numerous cell-signalling activities during embryonic development. EphA4 has the ability to bind to both types of ephrin ligands, the ephrinAs and ephrinBs. The C57BL/6J-*Epha4rb-2J*/GrsrJ strain, denoted *Epha4*$^{rb\text{-}2J/rb\text{-}2J}$, is a spontaneous mouse mutant that arose at The Jackson Laboratory. These mutants exhibited a synchronous hind limb locomotion defect or "hopping gait" phenotype, which is also characteristic of *EphA4* null mice. Genetic complementation experiments suggested that *Epha4*$^{rb\text{-}2J}$ corresponds to an allele of *EphA4*, but details of the genomic defect in this mouse mutant are currently unavailable. We found a single base-pair deletion in exon 9 resulting in a frame shift mutation that subsequently resulted in a premature stop codon. Analysis of the predicted structure of the truncated protein suggests that both the kinase and sterile α motif (SAM) domains are absent. Definitive determination of genotype is needed for experimental studies of mice carrying the *Epha4*$^{rb\text{-}2J}$ allele, and we have also developed a method to ease detection of the mutation through RFLP. Eph-ephrin family members are reportedly expressed as numerous isoforms. Hence, delineation of the specific mutation in *EphA4* in this strain is important for further functional studies, such as protein–protein interactions, immunostaining and gene compensatory studies, investigating the mechanism underlying the effects of altered function of Eph family of receptor tyrosine kinases on phenotype.

Keyword: EphA4; Hopping gait; Spontaneous mutation; Knockout mouse; rb-2J strain