# SECTION 1

## INTRODUCTION

# *Introduction*

The house mouse, *Mus musculus* being a premier model organism in biomedical research, its biology and genetics has been extensively studied (Lundrigan *et al.,* 2002; She *et al.,* 1990). Recently, the complete sequence of mouse genome is also known (Church *et al.,* 2009). The genus *Mus* Linnaeus, 1758, includes a group of 38 extant species of mouse belonging to the subfamily Murinae under the family Muridae (Marshall, 1977a, b, 1981, 1998; Musser and Carleton, 1993). Based on morphological characters and diploid chromosome number, Marshall (1977a, b; 1978; 1981; 1998) and Musser and Carleton (1993) recognized four subgenera, *Pyromys, Coelomys, Nannomys and Mus* in the genus *Mus,* the classification has also been supported by Boursot *et al.* (1993). Each of these taxa has been considered either as a subgenus or a genus characterized by distinct morphological and cytogenetical features (Marshall,1977a, b, 1986; Bonhomme *et al.,* 1984; Jotterand-Bellomo, 1984; She *et al.,* 1990; Matsubara *et al.,* 2003). However, the evolutionary relationship among these subgenera is still unclear. In spite of extensive studies on subgenus *Mus*, particularly cosmopolitan and commensal house mouse, *Mus musculus* (Marshall, 1986; Berry, 1995; Berry and Scriven, 2005), the time and place of origin of genus *Mus* is still debated.

Multidimensional studies throughout the world using molecular techniques have shed some lights on the evolution and origin of genus *Mus*. In a report based on electrophoretic, mitochondrial DNA (mtDNA) RFLP and single copy nuclear DNA (scnDNA) hybridization studies, She *et al.* (1990) inferred that the genus *Mus* might have diverged somewhere between 3.7 and 2.4 million years ago (Mya). Chevret and workers (1995, 2002) utilizing a molecular clock for two mitochondrial and one nuclear

genes and two calibration points based on the fossil records estimated that the genus *Mus* diverged from other murine lineages at about 10-8 Mya ago. Chevret and workers in a recent study estimated that the radiation of four subgenera of *Mus* took place between 7.8 and 6.7 Mya (Chevret *et al.,* 2005).

*Pyromys*, Thomas 1911, a subgenus of the genus *Mus*, known as spiny mice with five recognized species is distributed in Indian Subcontinent (Marshall 1977a,b; 1978; 1981). Another subgenus, *Coelomys*, Thomas 1915a, known as shrew mice composed of four recognised species are distributed mainly in the mountain forests of North-East as well as Nilgiri Hills in India and also found in Bhutan, Thailand, Cambodia, Laos, Vietnam, West Sumatra, West Java and Indonesia. The African pygmy mice, Subgenus *Nannomys* with 19 recognised species show extensive differentiation both within and between species and exclusively found in African sub-continent (Musser and Carleton,1993; Veyrunes *et al.,*2004). The subgenus *Mus* is more widespread and more diversified containing the species *M. caroli, M. cervicolor, M. cooki, M. musculus* with more than 8 subspecies and *M. booduga* along with its relatives. The Indian subcontinent represents three subgenera *Pyromys, Coelomys and Mus* with highest diversity in the genus *Mus.* Based on these facts, two hypotheses on the origin and radiation of house mice have been proposed.

The first hypothesis is based on the centrifugal model (Fig. 1.1A) of evolution (Boursot *et al.,* 1993, 1996; Bonhomme *et al.,* 1994; Din *et al.,* 1996; Guenet and Bonhomme, 2003). In this model house mice are proposed to have originated in the northern part of the Indian subcontinent and subsequently an expansion occurred to the West, North and East giving rise to *M. m. domesticus, M. m. musculus and M. m. castaneus,* respectively. Great taxonomic variety of fossil *Mus* recovered from Middle and Late Miocene and Plio- Pleistocene deposits in the Northern region of Indian

subcontinent and its abundance as well as recovery of the fossil of the first known *Mus* species, *Mus auctor* (Jacobs, 1978) from Siwalik deposits indicate that an early diversification event of the genus *Mus* had occurred in this region (Patnaik *et al.,* 1993, Sharma, 1996). It is also evident that house mice in the Indo-Pakistan region have the highest genetic variability (allozyme, nuclear and mtDNA) when compared to surrounding populations (Din *et al.,* 1996; Boursot *et al.,* 1996, Singh and Sharma, 1997). A fourth lineage *M. m. gentilulus* is recognized from the Saudi Arabian Peninsula (Tucker 2007).

The other hypothesis explaining the origin and radiation of mice as sequential or linear model (Fig. 1.1B)(Prager *et al.,* 1998) is based on additional sampling and the use of mtDNA trees to infer the relative ages of house mice lineages. According to this model the possible site for the origin of house mice is the West Central Asia, the current range of *M. m. domesticus* and the Southern Arabian Peninsula giving rise to *M. m. gentilulus*. From the Arabian Peninsula migration had taken place eastward and northward into South Central Asia giving rise to *M. m. castaneus* and then moved northward into North Central Asia giving rise to *M. m. musculus.*

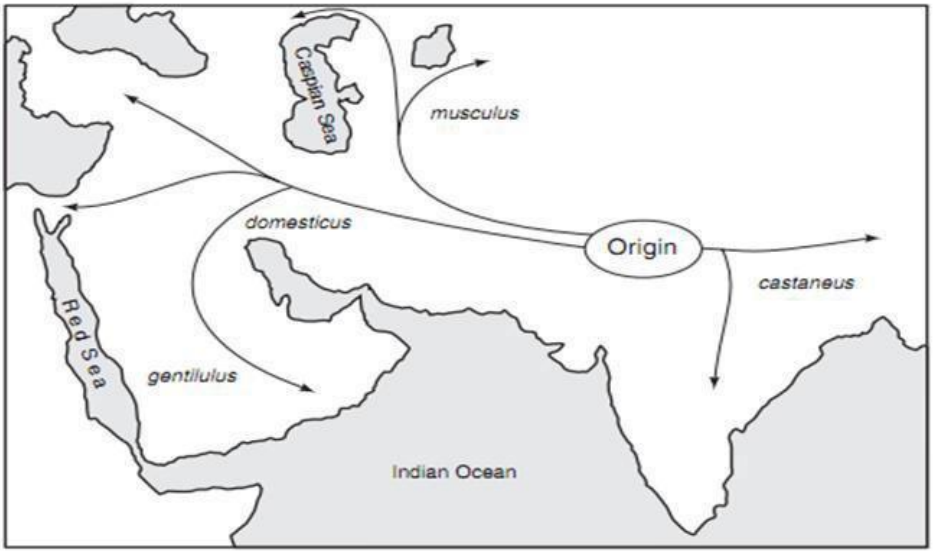
*M. m. musculus* and *M. m. domesticus* are hypothesized to have independently colonized in Europe (Auffray *et al.,* 1990; Cucchi *et al.,* 2005). These two taxa presently form a narrow zone of hybridization through Central Europe. Recent studies of mitochondrial and nuclear genes ( Lundigran *et al.,* 2002; Chevret *et al.,* 2003, 2005; Tucker *et al.,* 2005) and data based on greater taxonomic sampling (Chevret *et al.,* 2005) support the monophyletic origin of the genus *Mus* and each of the four subgenera (Fig. 1.2).

Being widely distributed and diversified, a general interest grew to know the evolutionary status of house mice and the related taxa of *Mus.* The finding of the first

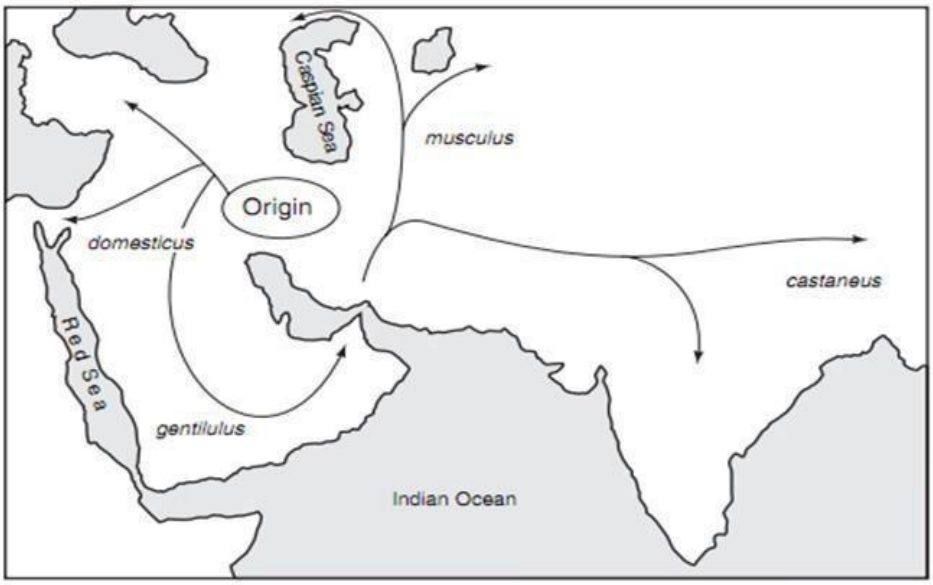
fossil *Mus* from the deposits of Siwalik range in Indo-Pakistan region (Jacobs, 1978) initiated an evolutionary study in this direction and the subsequent studies showed the occurrence of largest number of species, both extinct as well as extant of genus *Mus* in the Indian subcontinent indicating this region as the cradle of the origin of genus *Mus* (Patnaik *et al.,* 1993, Boursot *et al.,* 1996 and Din *et al.,* 1996).

Indian subcontinent has been proposed as the land of the origin of genus *Mus* with high genetic polymorphism (Din *et al.,* 1996) including earlier offshoot of this genus, *M. booduga and M. dunni* (*=M. terricolor*) from India (Bonhomme *et al.,* 1984, Chatterjee *et al.,* 1994), therefore a phylogenetic study of Indian species of *Mus* using multidimensional approaches will be highly interesting.

The common pygmy field mouse, *Mus terricolor* is the indigenous species of India and was known as *M. dunni* until Musser and Carleton (1993) replaced the nomenclature with the original one. The species has reddish brown dorsal fur and white underparts fur in gray bases. Body length of matured mice including tail is 13.5 inches. Tail is about 6 inches long (Fig. 1.3). They infest mainly paddy and wheat fields and coexist with its sibling species, *Mus booduga* (Gray, 1837). Although both the species coexist in the same habitat, they show a difference in site preference for burrows. *Mus terricolor* prefers the highest position in the field, the earthen dykes raised for holding water in cultivated fields, whereas *Mus booduga* makes nest at the lowest position of the field that is in the flat portion of the field (Cheong, 1986; Singh *et al.,* 2009). Before the report of Matthey and Petter (1968), these two species were considered as conspecific due to their similar morphology. However, *M. booduga* has white under parts as compared to white fur with gray bases in *M. terricolor*. They also differ in the shape of the first upper molar which has been confirmed by Marshall (1977b). Both these species constitute the lineage of Indian pygmy field mice and are




**A.**




**B.**

**Figure 1.1** Two models of the origin and expansion of house mouse, *Mus musculus*. **A**. The centrifugal model **B.** The sequential or linear model (adopted from "The mouse in Biomedical Research, Diseases. Second Edition").

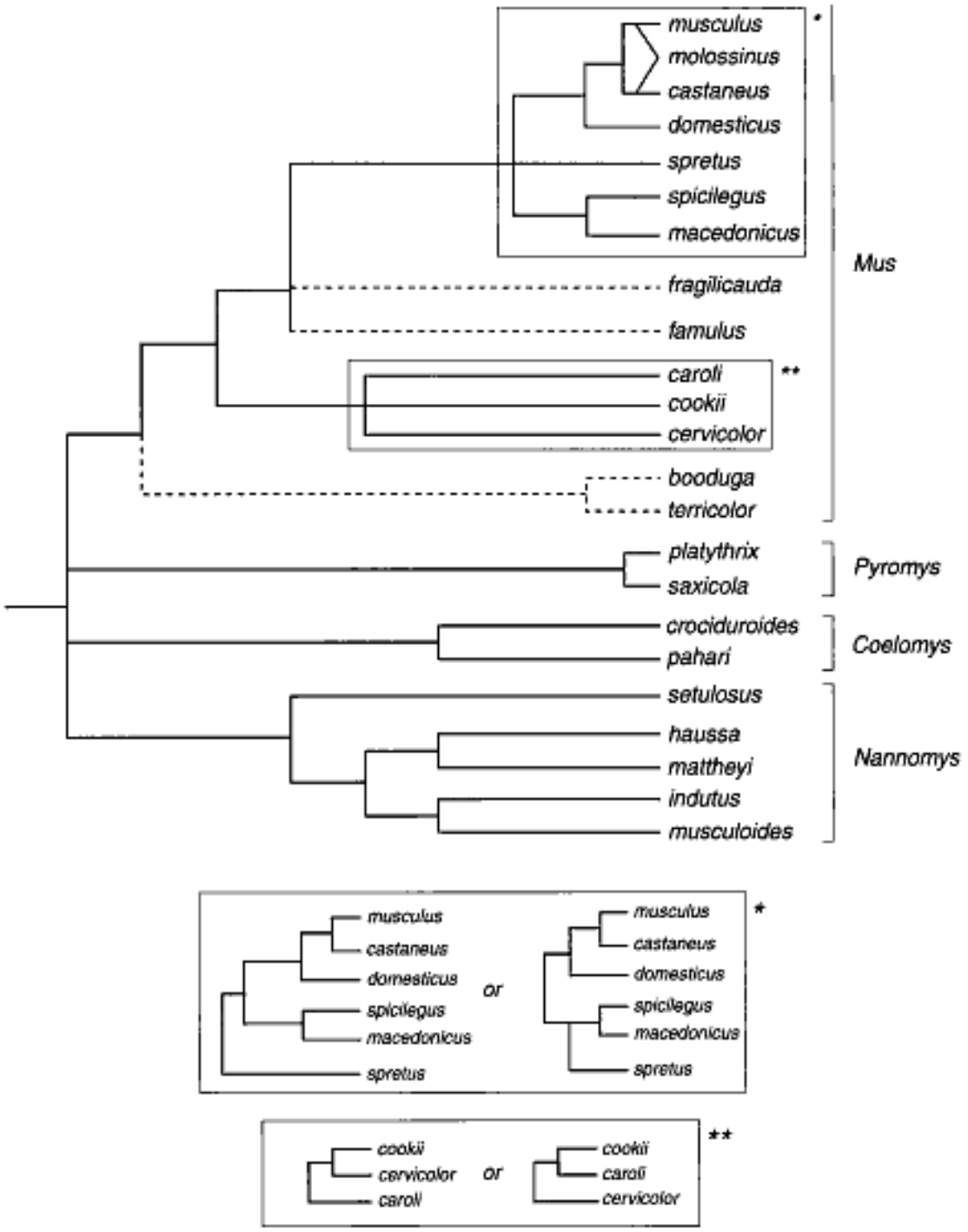



**Figure 1.2** The phylogenetic relationship of different subgenera of the genus *Mus*. Species belonging to the four subgenera are bracketed. The phylogeny adopted from ("The Mouse in Biomedical Research, Diseases. Second Edition").

closely related to *Mus musculus* which can be distinguished only on the basis of average characters (Ellerman, 1961). The diploid number in both the species is 2n=40 chromosomes. The karyotype of *M. booduga* is identical to that of *M. musculus* with all acrocentric chromosomes except a smaller Y chromosome in *M. booduga*. But *M. terricolor* drew special attention owing to the presence of unusually large submetacentric X and a large acrocentric Y-chromosome. Extensive chromosomal studies of the Indian pygmy field mice, *M. terricolor* have been carried out by many workers like Sharma and Garg (1975), Markvong *et al*. (1975), Manjunatha and Aswathanarayana (1979), Sen and Sharma(1983), Sharma *et al.* (1986), Bahadur and Sharma (1995) and Bahadur (1995), which revealed. chromosomal variation in this species due to the presence of variable number of heterochromatic short arms on the autosomes. Studies by Sharma and groups revealed the presence of three distinct chromosomal populations designated as types, I, II and III (Fig. 3.2) with apparently non-overlapping habitat in the population (Sharma *et al.,* 1986;1990).

The *M. terricolor* type I distributed in Northern India, Goa, Pune and Kolhapur in Western India, Jhansi in the Central India and from as far as Alipurduar in Eastern India, has all acrocentric autosomes with minute C-band positive short arms. The chromosomal type II has been shown to be distributed in Mysore and Erode possessing two submetacentric autosome pairs 1and 3 with C-band positive short arms, while the other autosomes are either telocentric or acrocentric with C-band positive minute arms. The populations of *M. terricolor* from Madras, Tirupati, Pondicherry and Madurai are chromosome type III having autosome pairs 1, 3 and 6 with C-band positive short arms. The large submetacentric X and the large acrocentric Y are identical in all populations (Cheong, 1986; Sharma *et al.,* 1990; Bahadur and Sharma, 1995; Bahadur, 1995).

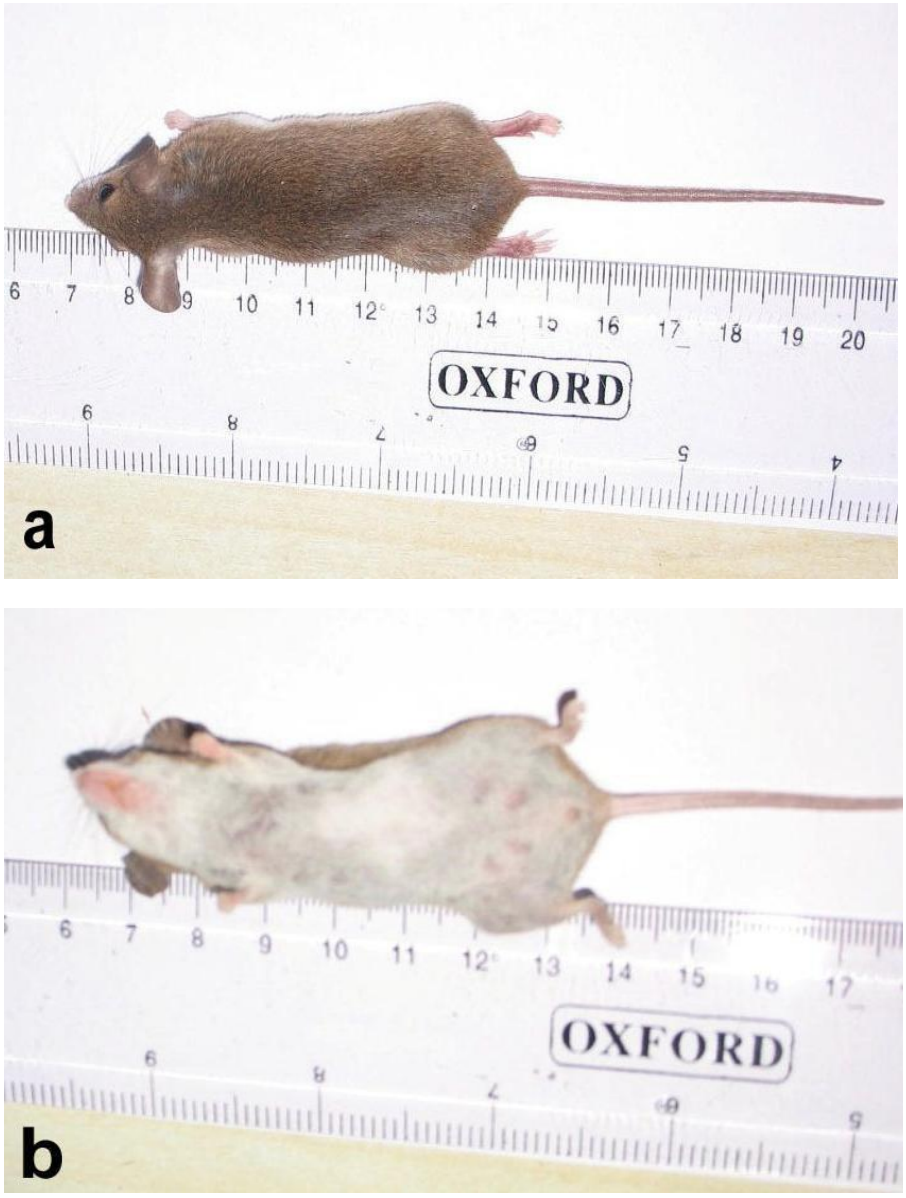



**Figure 1.3** Dorsal (a) and Ventral (b) view of *Mus terricolor.*

The phylogenetic relationship of the genus *Mus* (Fig. 1.2) proposed in "The mouse in Biomedical Research, Diseases. Second Edition"(Tucker 2007) the position of Indian pygmy field mice, *M. terricolor* complex and *M. booduga* (shown by dashed line) is in controversy due to lack of substantial molecular data. The following phylogeny was based on recent studies using different combinations of molecular characters (Lundrigan *et al.,* 2002; Chevret *et al.,* 2003; Auffray *et al.,* 2003; Chevret *et al.,* 2005; Tucker *et al.,* 2005).

Sharma *et al.* (1986; 1990) considered *M. terricolor* chromosomal complex as an incipient species while Chatterjee *et al.* (1994) have shown the recency of evolutionary diversification of this group. Therefore, *M. terricolor* complex provide an opportunity to study the processes of speciation and dynamics of population structure in this species.

The present study investigates the extent of genetic polymorphism based on chromosomal, biochemical and molecular techniques among different population of *Mus terricolor* type I from Terai and the Dooars regions of northern part of West Bengal.