Rodentia embraces the largest number of existing species. The numerous convergences, as well as variations in the rates of morphological evolution among lineages have led to discrepancies between molecular and morphological efforts in respect to their phylogenetic relationships. An improved and deeper characterization of this group is thus essential and can be achieved with Comparative Chromosome Painting that allows the generation of global comparative genome maps, where contiguous chromosome segment combinations are used as phylogenetic characters to infer evolutionary relationships. *Praomys tullbergi* (PTU), a member of the *Praomys* group, belongs to the Muridae family, one of the most diverse and abundant groups of rodents. In this work we performed a high resolution chromosome comparison of *Praomys tullbergi* with the index genome *Mus musculus* (MMU) to decode its genome architecture of and to extend the knowledge of the complex genome restructurings of the Muridae genome during the course of evolution. *Praomys tullbergi* showed to be the highly rearranged rodent genome ever analysed by comparative chromosome painting. PTU genome displays about 65 syntenic segments with *M. musculus*. It was possible making evolutionary inferences about PTU genome and to reconstruct the chromosome evolutionary events that Praomys tullbergi karyotype experienced from the ancestral putative genome, being these mainly tandem fusions and/or or robertsonian translocations accompanied by
centromere repositioning, fissions, and a few inversions. The integration of our data with the published one allowed outlining phylogenetic considerations among Murinae.