Abstract:
Lx in SHR.Lx rat manifests in homozygotes as hindlimb preaxial polydactyly.
We showed that a 2,964-bp deletion in Plzf (Promyelocytic leukemia zinc finger) intron 2 is the only candidate for Lx. The deletion removes the most deeply conserved CNE with putative regulatory influence on Plzf expression. Using in situ hybridization we found reduced expression pattern of Plzf in Lx/Lx limb and anterior expansion of expression domains of Plzf targets Hoxd10–13 genes and Bmp2, in the absence of ectopic Shh expression.
Rat hd manifests in homozygotes as reduction or loss of digits II and III on both hind and forelimb and impairment of spermatogenesis leading to male infertility. We showed that hd mutation is caused by an insertion of an endogenous retrovirus into intron 10 of the Cntrob gene resulting in the translation of a truncated protein. In situ hybridization showed that expression of cartilage condensation marker Sox9, and Bmp receptor Bmpr1b is absent from the distal parts of the digit condensations II and III. Studying spermatogenesis we showed that centrobin (protein of Cntrob) localizes to the centrosome, manchette, and the marginal ring of the spermatid acroplaxome. Mutant spermatids show a disruption of head-tail coupling apparatus leading to spermatid decapitation .
We demonstrated distinct expression pattern of c-myb in developing limbs. The pattern was robust at stages 13,5 dpc and 14,5 dpc alongside of prospective digit anlagen of both limbs, probably in developing perichondrium. Studying c-myb -/- limb phenotype of stages 12,5-14,5 dpc we did not observe any phenotypical difference in comparison to WT controls indicating that c-myb is dispensable for this stage of limb development.