# A Recessive Remutation of *Dll3* (*pu-J*) causes Kinked Tails, Rib and Vertebral Deformities, and occasional Paralysis in Homozygous Mice.

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Mutation (allele) symbol: $Dll3^{pu\text{-}J}$

Mutation (allele) name: pudgy Jackson

Gene symbol: *Dll3*

Strain of origin: STOCK Tg(Pfkl)224Yg/J

Current strain name: STOCK Tg(Pfkl)224Yg/J-$Dll3^{pu\text{-}J}$/GrsrJ

Stock #005040 (jaxmice.jax.org)

Phenotype categories: tail, skeletal

**Abstract**
A recessive remutation of *Dll3* named pudgy Jackson results in mice with shortened spines, misaligned and mishapen vertebrae, kinked tails, and occasional paralysis in the rear limbs. This remutation is located on mouse Chromosome 7 and is non-recombinant with *D7Mit57* and *D7Mit341* at 4.0 and 8.0 cM respectively. The chromosomal location and the phenotypic description of this mutant are very similar to the previously described pudgy mutant $Dll3^{pu}$ (MGD 2004, Kusumi et al. 1998)). A test for allelism confirmed this phenotype to result from a remutation to $Dll3^{pu}$.

**Origin and Description**
Pudgy Jackson (*pu-J*) arose spontaneously in 1998 in the Mouse Mutant Resource at The Jackson Laboratory and was discovered by Larry Bechtel. This mutation produces approximately one quarter homozygotes in the maintenance colony of heterozygote mated to heterozygote, as expected for a recessive mutation with full penetrance. Some homozygotes breed, but litter sizes are small and occasionally female homozygotes do not survive birthing. This mutation results in mice with shortened vertebral spines, splayed ribs, and kinked tails. Common clinical characteristics include compression of the cervical, thoracic and lumbar vertebrae plus extreme variability in size, shape, and irregular fusion of tail vertebrae. The description of the original pudgy mutation (Gruneberg, 1961) referred to the spine as "chaotic" and a "jumble of vertebrae"; the skeletons of pudgy Jackson could be simiarly described. As in the original pudgy mutation, the vertebrae of this remutation retains some regional specificity whereby the shape and orientation of the vertebrae within the lower lumbar and sacral regions appear normal. The appendicular skeleton also is relatively normal, although the long bones have a very thin cortical shell and few trabeulae can be seen by 5X magnification x-ray analyses. Occasional paralysis in the rear limbs is observed in pudgy

Jackson. Two other *Dll3* mutations, *oma* (Shinkai et al.) and *tm1Rbe* (Dunwoodie et al. 2002) result in mice with phenotypes very similar to *pu-J.*

**Genetic Analysis**

Using our standard mapping procedures, a female CAST/Ei was mated to a male heterozygote and produced all normal F1 progeny. The F2 progeny did segregate and 19 affected mice were used to determine the chromosomal location of this mutation. A genome scan was started on distal Chr 7 because a mutant with a similar phenotype (*Tbx6*, formerly called rib-vertebrae) maps there. Pudgy Jackson did not map to distal Chr 7, but did map to proximal Chr 7. Linkage was first detected with *D7Mit117* at 11 cM. The individual DNAs were then typed for 8 additional Mit markers. The recombination estimates with the standard errors and the best gene order are centromere - *D7Mit178* - 11.3 +/- 5.9 - [*D7Mit57*, *D7Mit341*, *pu-J*] - 2.8 +/- 2.8- *D7Mit117*-2.8 +/- 2.8 - *D7Mit247*- 5.6 +/- 4.0- *D7Mit345*. We detect no recombination between *pu-J* and *D7Mit431* and *D7Mit57*. A direct complementation test for allelism using a heterozygous female pudgy mated to a heterozygous new mutant male produced 2 affected progeny out of 17 born confirming allelism.

**Pathology**

Histological sections of long bones showed no abnormalities of growth plates of joints. The vertebral bodies were generally enlarged. In older mice the intervertebral disks were often distorted, with proliferative and degenerating cartilage. Some disks had prolapsed causing degeneration of spinal roots and neurogenic atrophy of skeletal muscle fibers.

Fig. 1: Normal growth plates (**GP**), intervertebral discs (**D**) and mature bone (**B**) and marrow (**BM**) at 5 months of age.

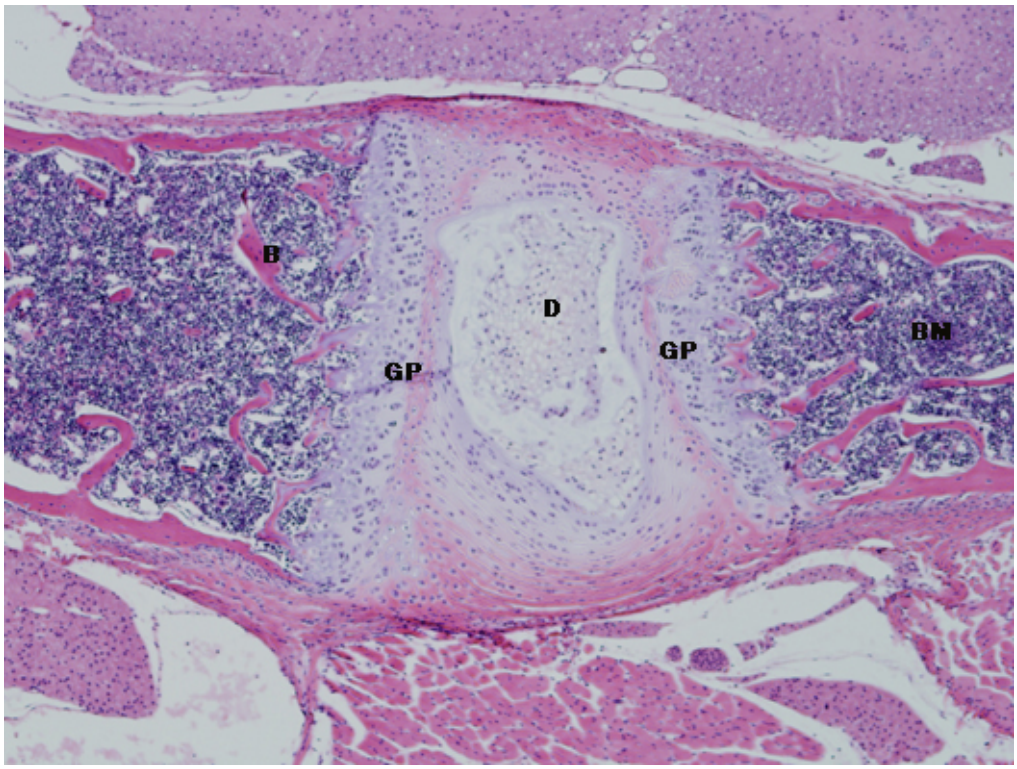


Fig 2: A disorganized mixture of disc, cartilage (**C**), bone and marrow in an affected animal at 11 months of age.

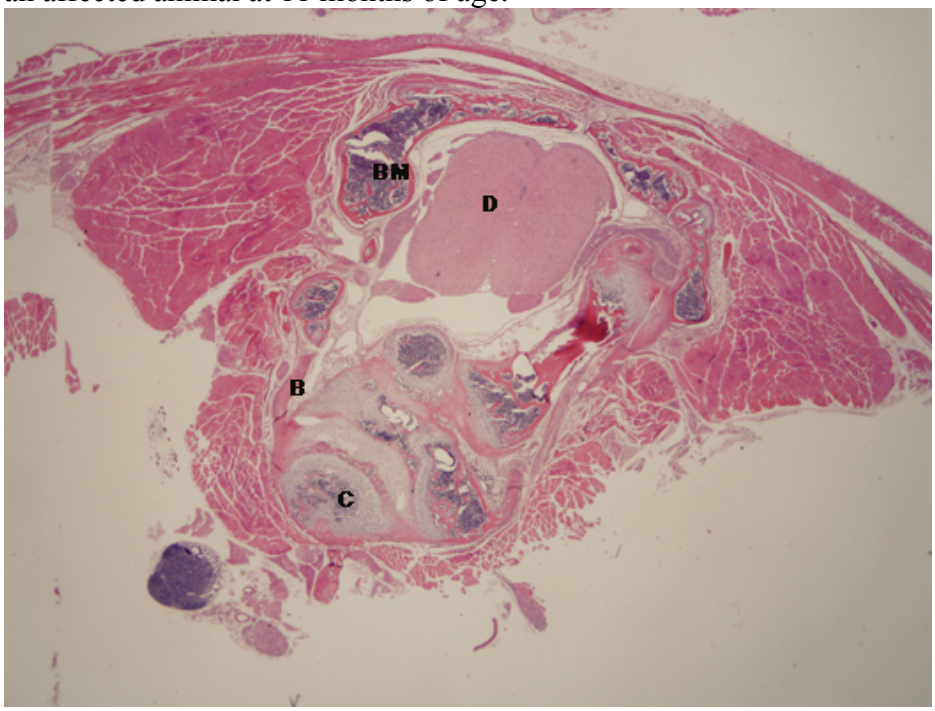
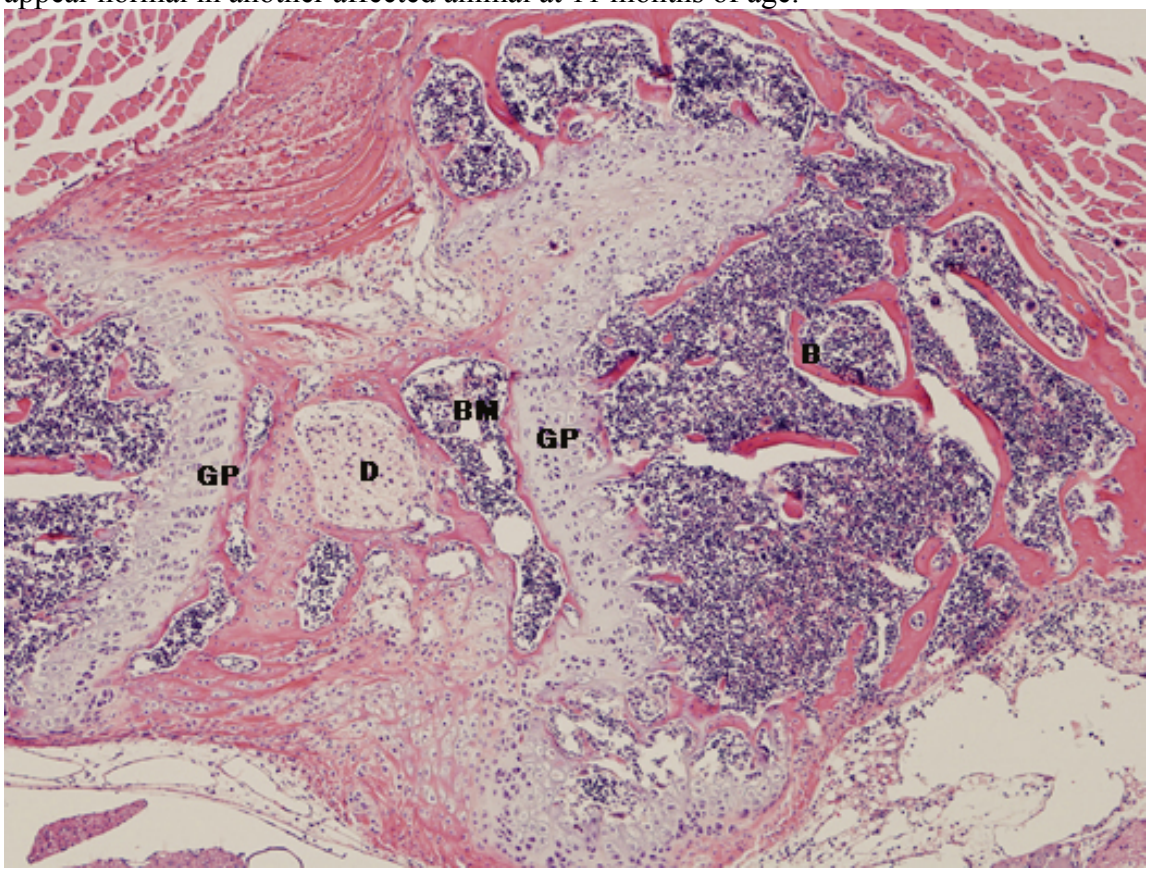



Fig. 3: Irregular clumps of cartilage are mixed with bone and bone marrow, but growth plates appear normal in another affected animal at 11 months of age.



Three homozygotes and one heterozygote were tested for auditory-evoked brain stem response and all had good hearing. The eyes of 1 control and 3 mutant mice were examined with an ophthalmoscope and were determined to be normal.

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**References**

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