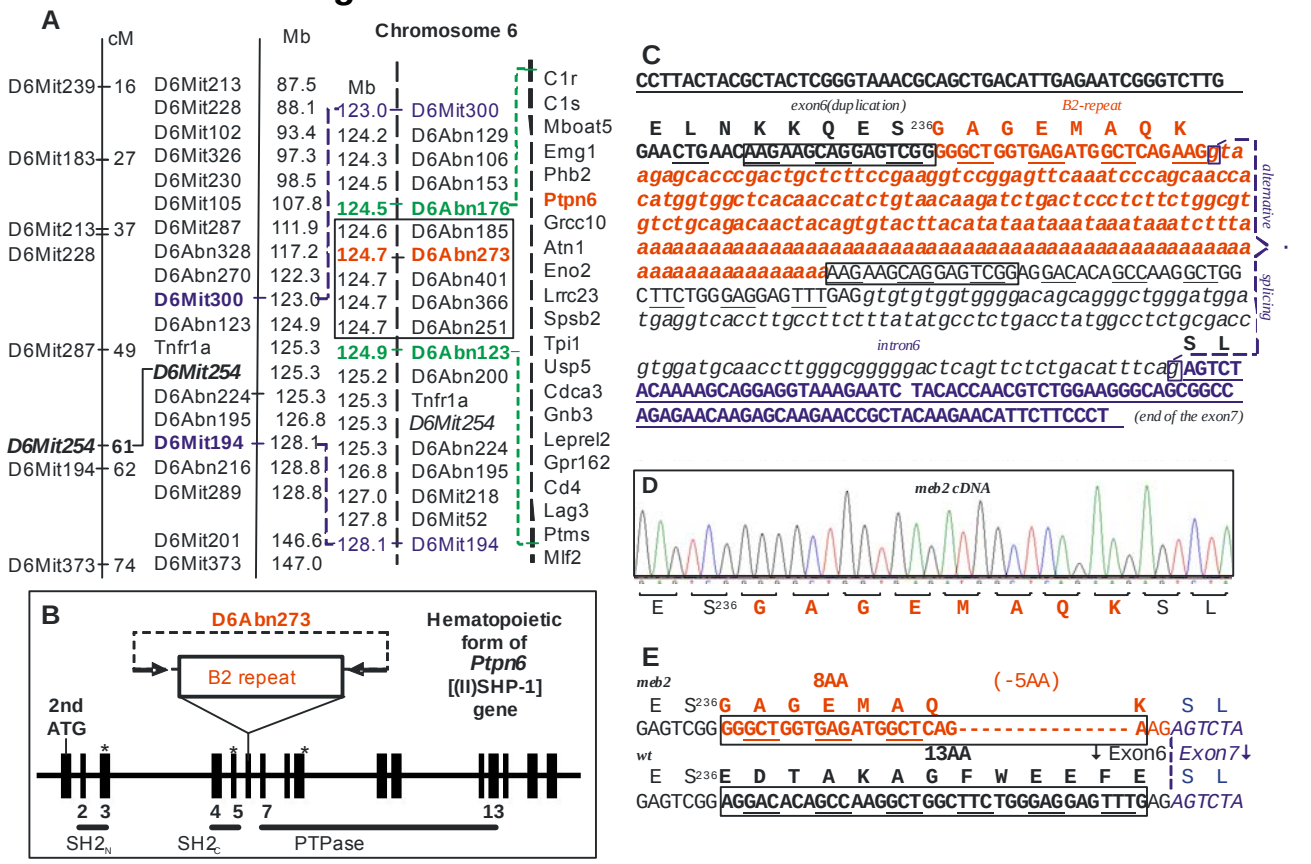
SUPPLEMENTAL Figure 1S



Supplemental Figure 1. Positional cloning of the NDLD locus on mouse chromosome 6, and identification of the insertion of the B2-repeat in the mouse *Ptpn6* gene (*Ptpn6*^{meB2}). (**A**) The locus associated with marker **D6Mit254** was selected after the primary genome-wide scan. The *NDLD* locus was narrowed to 5.1 Mbp and identified with the flanking markers **D6Mit300** and **D6Mit194**. Additional recombination events further narrowed the *NDLD* locus to 0.4 Mbp between markers **D6Abn176** and **D6Abn123**, a chromosome region that contains 20 genes. GeneBank symbols are listed from C1r (Complement C1r-A subcomponent precursor) to Mlf2 (Myeloid leukemia factor 2 or Myelodysplasia-myeloid leukemia factor 2). (**B**) Marker **D6Abn273** flanks the B2-repeat insertion in exon 6 (numbering is from exon-1b of the hematopoietic *Ptpn6* transcript). The 273 bp in the wild-type gene is replaced with the mutant 535-bp fragment (B2-element). This new mutation in the *Ptpn6* gene is designated **'meB2'**. Vertical bars represent exons, and the horizontal line shows intronic regions. Asterisks (*) show the locations of other mutations that cause the "motheaten" (*me*) phenotype (see Supplemental Table 1). (1) A single nucleotide deletion in exon 3 coding for the first SH2 domain ($SH2_N$, exon 2-3) in ***me*** mice; (2) a spontaneous mutation in exon 5 leads to the Y208N amino acid change in the second SH2 domain ($SH2_C$, exon 4-5) in ***spin*** mice; (3) insertion of a B2 element/repeat in exon 6 (**'meB2'**; our colony); and (4) a T→A substitution at the beginning of intron 9 that results in two splice variants carrying an altered sequence within the PTPase domain (exons 7-13) in ***mev*** **(***me-viable,* ***me-v)*** mice. In fact, there are big differences in the clinical phenotypes of the four homozygous *Ptpn6* mutant mice, although all of them exhibit hyperproliferative-like bone marrow, splenomegaly, and extensive extravasation of PMN leukocytes into the skin and various organs. (**C**) The genomic DNA sequence of Ptpn6 exons 6-7, where the B2 element, flanked with 16-nucleotide tandem repeats at both ends, has been incorporated. Consequently, (**D**) a 24-nucleotide sequence (8 amino acids) replaces the 39-bp-long cDNA sequence maintaining the frame in Ptpn6 transcript (**E**). However, the 'meB2' cDNA is 5 amino acids shorter than the normal variant. The homozygous combination of the 'meB2' genotype results in a far less severe phenotype than either the homozygous me or *me-v* genotypes, but it may be more severe than the homozygous 'spin' phenotype.