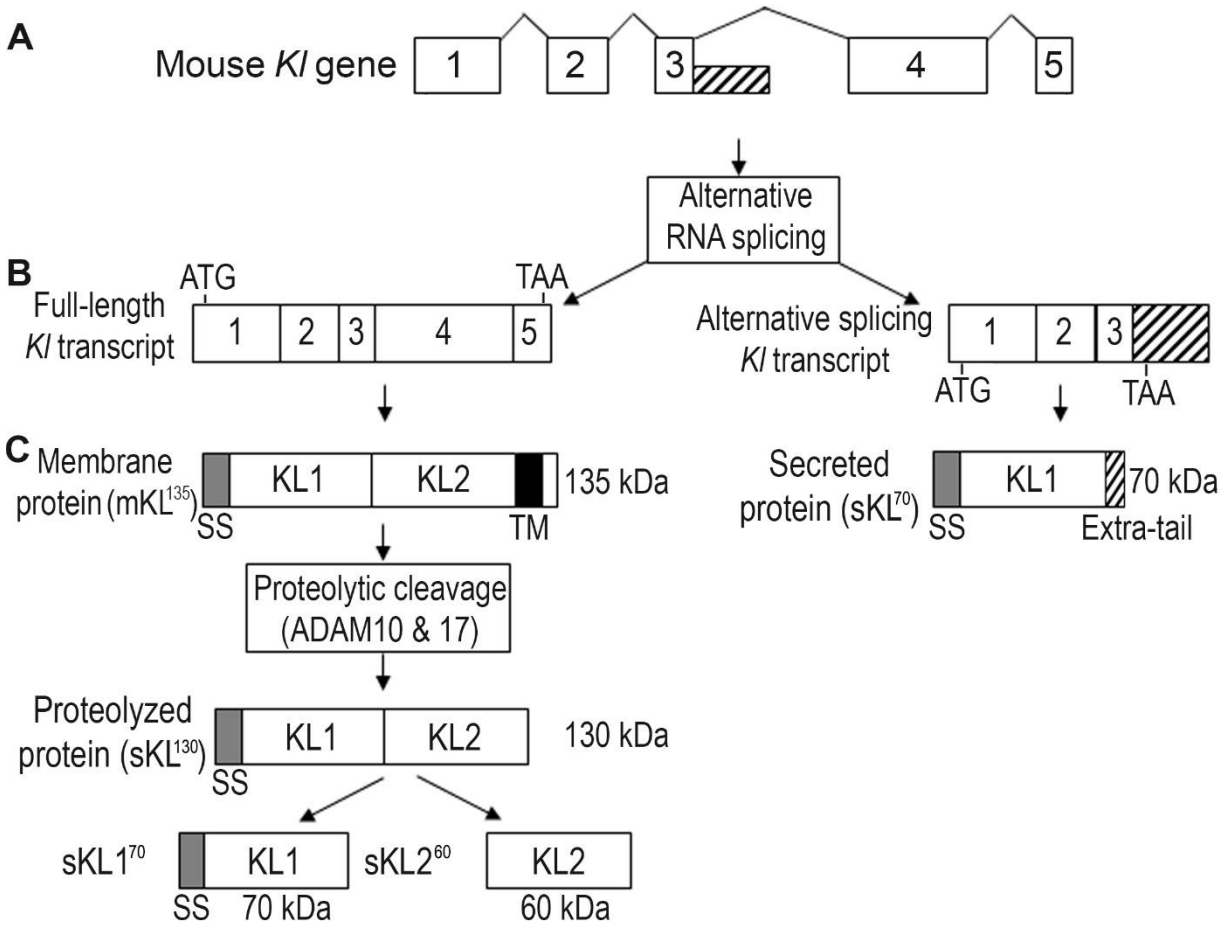
**Supplemental Data**

The nomenclature for the multiple Klotho isoforms generated from alternative transcripts and post-translational processing has not been standardized. Here we use modifications of terminology proposed by Forster et al and Massó et al (89, 90) that considers the molecular weight of the different protein isoforms. $mKL^{135}$ stands for the full-length, transmembrane form; $sKL^{130}$ stands for ectodomain shed Klotho containing the KL1 + KL2 domains, $sKL1^{70}$ and $sKL2^{60}$ respectively represent the further processing of $sKL^{130}$; and $sKL^{70}$ generated by alternative splicing (Supplementary Figure 1). The alternative spliced mRNA includes a specific secretion signal consisting of a 15 amino acid tail that is not found in the full-length *α-Klotho* transcript that can be used to distinguish between them.




**Supplemental Figure 1. Structure of the mouse α-*Klotho* gene, its two transcripts, and several protein isoforms.** (**A**) The α-*Klotho* (*KL*) gene. (**B**) The *KL* mRNA transcripts. (**C**) The membrane (mKL$^{135}$), secreted (sKL$^{70}$), and proteolyzed KL (sKL$^{130}$) protein that contains both KL1 and KL2 domains. sKL1$^{70}$ and sKL2$^{60}$ respectively represent the further processing of s-KL$^{130}$. Open boxes represent exons and the thick line represents introns. The diagonal box represents the continuation of exon 3 in the secreted isoform. The translation start codon and the termination codon are shown above the transmembrane form and under the secreted form transcripts, respectively. Black box represents transmembrane domain (TM) and grey boxes represent signal sequence (SS).