

Mechanisms of homeostasis of blood coagulation factors

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We recently reported the first molecular mechanisms of age-related regulation of human factor IX (Science 1999; 285: 739-43) and also showed the fundamental functional universality with human protein C (J. Biol. Chem. 2002; 277: 4532-40). Through systematic studies with transgenic mice, we now have established the key roles of ASE, one of the two genetic elements, ASE and AIE, in the unique puberty-onset amelioration of hemophilia B Leyden as well as in determining the strict tissue specific expression of genes. These observations suggest that a temporal and a spatial regulation of gene expression may have a commonality, suggesting a new concept. The functional ASE is strictly specific in its nucleotide sequence among the Ets family consensus sequences, and all other similar sequences are not functional in age-regulation of gene expression. Further characterization of ASE and AIE, and their binding nuclear proteins are in progress. These results will be presented in a comprehensive way, revealing the highly dynamic molecular mechanisms underlying the homeostasis (slow dynamic process) of blood coagulation.

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