6) Human and mouse SAP cDNAs and genomic DNAs were isolated. The deduced amino acid sequence of human SAP is highly homologous with that of mouse SAP.

7) The level of SAP mRNAs in mouse liver increased up to 60-fold during the first 20 hr after induction of an acute inflammation.

8) Transgenic mice carrying and expressing the human mutant transthyretin gene were constructed. In these mice, human transthyretin and mouse SAP were deposited as amyloid fibrils.

SI-2. MUTATIONS IN COLLAGEN METABOLISM DISORDERS. Hiroshi KONOMI (NCNP-Natl. Inst. Neurosci., Tokyo)

Collagen is one of the major components of extracellular matrix. There are 13 different types of collagen molecules, and at least 24 genetically distinct subunit chains.

Characteristic clinical features of collagen metabolism disorders are deformities of skeleton, bone fracture, fragility and hyperextensibility of skin, joint hypermobility, easy bruisability, venous varicosities, hernia and ocular fragility. Collagen metabolism disorders include Ehlers-Danlos syndrome (ED), osteogenesis imperfecta (OI) and Marfan syndrome (MF). ED and OI show large heterogeneity in clinical manifestations. Recent advances of collagen metabolism revealed that pathogenesis of ED are considered to be abnormalities of biosynthetic processes of type I and III procollagen or that of maturation of type I collagen fibers with a few exceptional variants, and that of OI are type I procollagen gene mutations. On the other hand, in spite of researches about one MF variant who showed insertion of about 20 amino acids in α2(I)-CB5 of type I collagen, underlying defects in connective tissues of MF is still unclear.

One of the characteristic features of osteogenesis imperfecta with collagen gene mutations depend on triple herical structure of type I collagen molecule, which is composed with two α1(I) chain and one α2(I) chain. When cultured fibroblasts from the patients synthesized approximately equal amounts of normal proα1(I) chains and of shortened proα1(I) chains (mutant proteins), one-half of the trimers assembled in cells contained one shortened proα1(I) chains and one-quarter contained two shortened proα1(I) chains. The trimers containing the shortened proα1(I) chains, however, were metabolically unstable. They folded into a triple-helical conformation only at temperatures well below body temperature. The phenomenon, which has been referred to as "protein suicide," created a situation in which the total amount of biologically useful type I procollagen produced by fibroblasts was reduced to one-quarter of the control.

We analyzed collagens produced by skin fibroblasts from a patient with a lethal form variant of osteogenesis imperfecta (OI-type II). They synthesized equal amount of two proα1(I) chain, one was normal and the other was shortened chain. CNBr peptide mapping, animal collagenase digestion revealed that the mutation location of the shortened proα1(I) chain existed in CB8-peptide. In addition to the mutation of proα1(I) chain, there was elevated synthesis of type IV and V collagen. These results indicated that alteration of collagen metabolism occurred in the disease.