Collagen Disorders

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There is increasing success in studying collagen disorders in cell culture. Fibroblasts make both types I and III procollagen, secrete these proteins, convert a portion of the protein to collagen, assemble the molecules into fibers and crosslink them. In certain recessive forms of the Ehlers-Danlos syndrome (type IV-VII) defects in collagen synthesis have been identified. Type III collagen is not synthesized by patients with the EDS IV syndrome. Patients with EDS V-VII syndromes have defects altering the crosslinking of collagen either by affecting lysyl oxidase or by otherwise affecting the crosslinking of type I collagen. The manner in which these defects present appears to depend in part on the tissue distribution of these collagens. For example, decreased crosslinking of type I collagen primarily affects tendon and skin while the lack of type III collagen primarily weakens blood vessels and internal organs.

We have found that the collagen produced by EDS I cells is more extractable than normal, presumably due to decreased crosslinking. Since this is a dominant disorder, we suspect that these patients have amino acid substitutions in type I collagen. Other dominant disorders such as osteogenesis imperfecta presumably also represent amino acid substitutions in type I collagen but not those altering crosslinking. Osteogenesis imperfecta encompasses marked heterogeneity, and many different defects may produce related symptoms.

Most recently, Werb et al. and Eisen and associates have found that fibroblasts in culture produce collagenase in an inactive form. Neutral proteases activate the enzyme. Altered levels of collagenase have been observed in cells from patients with certain malignant and inflammatory diseases.

Such studies can now be extended to other types of cultured cells making still other types of collagen.