The "BEGINNINGS" OF MATRIX BIOLOGY

Jerome Gross, Cutaneous Biology Research Center, Department of Dermatology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA 02129, USA

The subject has a long history dating back to the early Greeks who prepared and used gelatin for glue and the many ancient cultures who prepared leather from hides. The science of the connective tissues (cell plus matrix) may be conveniently divided into 'pre-modern' and 'modern' periods. The pre-modern era might include the years of the late 1800's with rapid advances in histologic and cytologic studies, embryology and even amino acid analyses of semi purified components. This highly productive period extended to a sharp transition point in 1942. In that year the modern era began with the first papers published on the axial periodic and lateral ultrastructure of collagen fibrils as defined by electron microscopy and X-ray crystallography, simultaneously from the United States and Germany. From then on progress was rapid with the development and use of biochemical, physical chemical, ultrastructural and cell biological techniques. Exploitation of the self assembling properties of dissolved collagen fibrils using the new methodologies led to an explosion of our understanding of collagen structure, fibrillogenesis, metabolism, biosynthesis, degradation, crosslinking, molecular enzymatic processing, molecular heterogeneity, genetic structure and regulation, genetic diseases and interactions with cells. There was a simultaneous, equally active expansion of our knowledge of the important extra collagenous components of the matrix, including glycosaminoglycans, proteoglycans, elastin and other fibrous and nonfibrous constituents. Some puzzling current questions will be briefly discussed.

The biological mechanism of collagenolysis in vivo and in tissue culture became a major area for study in the Developmental Biology Laboratory at the Massachusetts General Hospital in the late 1950's, beginning with my effort to understand the early biochemical and cellular mechanisms of amphibian limb regeneration, particularly the very early event of dedifferentiation. Collagenolysis was clearly a critical and necessary process. Its study in the frog tadpole led to the discovery and characterization of the animal collagenases. Yutaka Nagai, at that time a post doctoral fellow in the laboratory, played a key role in purifying the enzyme and characterizing its specific mode of action on native collagen molecules. These studies are fundamental to all the subsequent work done on the mammalian metalloproteases, collagenase in particular, and established some of the basic analytic methods. It will be my great pleasure to recall for you Dr. Nagai's accomplishments and try to peer into the future.