Microenvironmental Factors Make Connective Tissue Cells Either Destructive or Productive

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Many of the government-registered intractable diseases belong to those with immunological disturbances. Histological characteristics of such diseases are often granulomatous in nature, consisting of lymphoid cells, macrophages and connective tissue cells. Such granulomas are resistant to cure and destructive to the surrounding tissues, in general. In human cases, destructive synovitis of rheumatoid arthritis and granulomatous arteritis of Kawasaki disease are suitable targets of our analysis.

A typical granulomatous lesion in rheumatoid arthritis is the subcutaneous nodule. In its center the immune complex is localized and it is covered by palisading connective tissue cells and macrophages. A fibrous capsule finishes the nodule into a sphere. The cells comprising the synovitis are a little different from those of subcutaneous nodule. Discovering what cells destroy the osteocartilaginous tissue is the primary goal of our research project.

MRL/Mp- $\frac{1}{8}$ Y mouse is a good animal model for studying the histopathogenesis of destructive granulomatous lesions. According to the results of our research work, angry macrophages, activated under the influence of

Thy 1.2+ Ly5 + T lymphocyte, attack the arterial wall, joint cartilage and even glomeruli.

The last part of our study will be a description of factors controlling the proliferation of myointimal cells in the healing stage of granulomatous arteritis such as Kawasaki disease. PDGF and some myogenic substances seem to stimulate the proliferation and GM 1 ganglioside on the cell surface and GAG surrounding the cells must be the key substance to control the proliferation of connective tissue cells including myocyte.

Thus

various kinds of humoral factors

cell to cell interactions

cell to matrix interactions seem to make the connective tissue cells either destructive or productive depending on the situation.