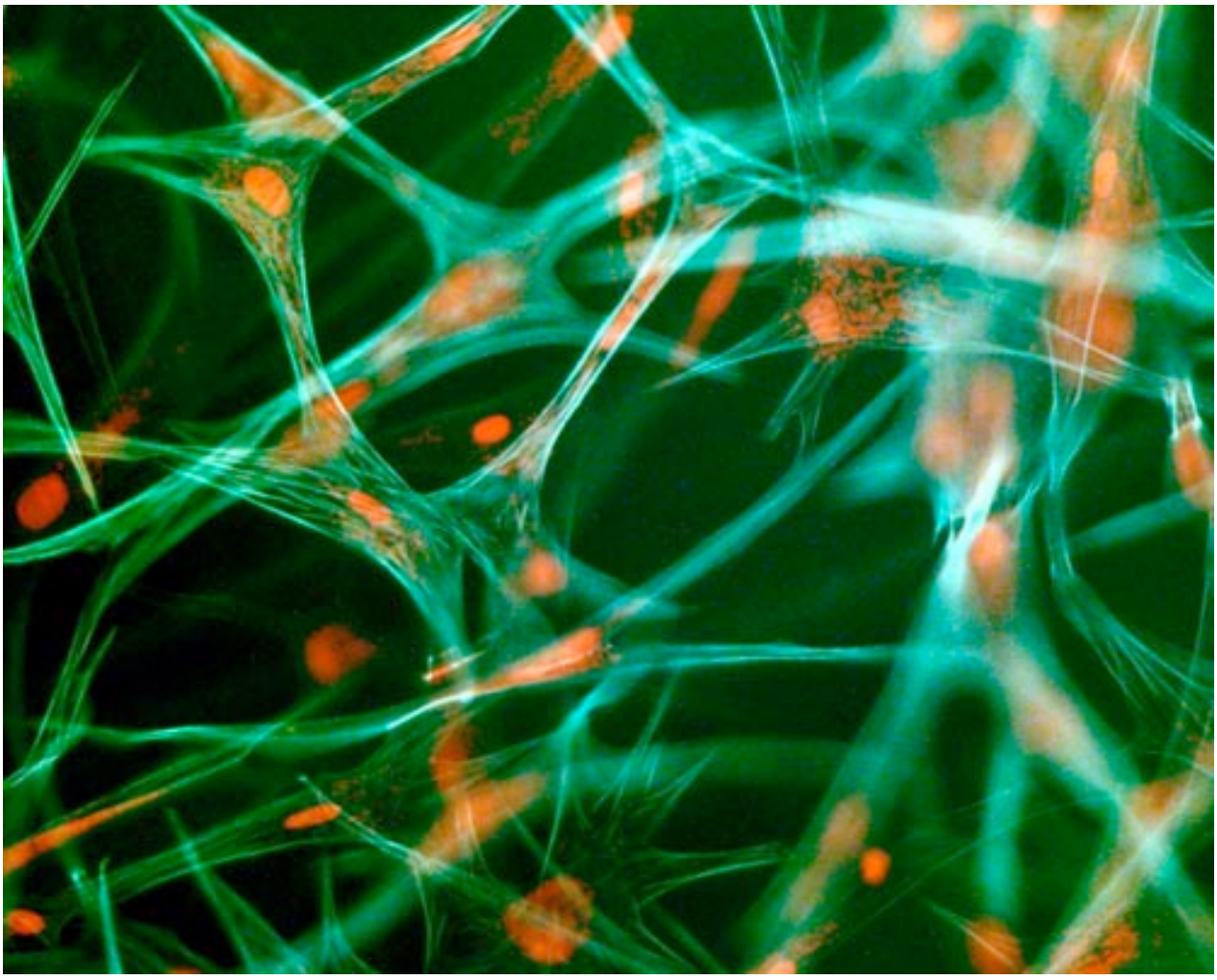
Lecture 25. Scleroderma and Other Fibrosing Diseases

Learning Objectives and Summary



Fluorescence micrograph of myofibroblasts stained for α-smooth muscle cell actin (*green*), and nuclei (*red*) embedded in a collagen gel. The myofibroblast, whose phenotype is an amalgam between fibroblasts and smooth muscle cells, is one of the principal cell types that produces excessive ECM proteins in fibrosing diseases.

Lecture 25. Scleroderma and other fibrosing diseases

Learning Objectives

1. To appreciate the clnical manifestations of the major subtypes of scleroderma
2. To understand the role of B cells and autoantibodies in the pathogenesis of scleroderma
3. To understand the therapeutic approaches to the treatment of scleroderma
4. To develop a conceptual framework for fibrosing diseases, in general.
5. To learn about specific growth factors that contribute to the development of fibrosis
6. To appreciate the origins of mesenchymal cells in fibrosing diseases

Summary

1. Scleroderma is an autoimmune disease involving multiple organs. It is characterized by a vasculopathy, varying degrees of inflammation, and fibrosis. Several major clinical variants of scleroderma have been described.

2. Pulmonary complications of scleroderma are common and severe in substantial minority. Death is due to severe pulmonary hypertension, pulmonary fibrosis, or both, ultimately leading to cor pulmonale.

3. Autoantibodies play an important role in the pathogenesis to scleroderma. Agonistic autoantibodies against the PDGFR have been isolated from patients with scleroderma.

4. Various theories of fibrogenesis have been proposed. Regardless of the precise etiology, fibrosis is due to the excessive deposition of ECM by the major collagen-producing cells in the body, fibroblasts and myofibroblasts.

5. Fibroblasts arise from a combination of local proliferation of resident mesenchymal cells, EMT, and influx of fibroblast precursors from the bone marrow.

6. Among the various pro-fibrogenic growth factors, TGF-β usually plays an important role in fibrosis. TGF-β triggers increased production of ECM proteins, induces EMT, and typically induces proliferation (rather than cell cycle arrest) in fibroblasts.