Urokinase-type plasminogen activator receptor (uPAR) in Systemic Sclerosis: from molecular target to diagnostic biomarker Filomena Napolitano and Nunzia Montuori 2335

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Abstract Description:

Urokinase-type plasminogen activator receptor (uPAR) in Systemic Sclerosis: from molecular target to diagnostic biomarker Systemic Sclerosis (SSc) is a heterogeneous autoimmune disease characterized by widespread vasculopathy, the presence of autoantibodies, and progressive fibrosis of skin and visceral organs. There are still many questions about its pathogenesis, particularly in the complex regulation of fibrotic process, and in the factors that trigger its onset. Urokinase-type plasminogen activator receptor (uPAR), a glycosylphosphatidyl-inositol-(GPI) anchored protein formed by three domains (DI-DII-DIII), serves to bind the urokinase plasminogen activator (uPA) and localize the activation reactions in the proteolytic cascade of plasminogen activation system. Our recent studies highlighted the key role of uPAR in the fibrotic phase of the disease. Synthetic compounds targeting uPAR significantly inhibited oxidative stress and SSc fibroblast proliferation, thus suggesting new opportunities for the development of new-targeted therapies in fibrotic diseases. Moreover, after the removal of the GPI anchor by proteases or phospholipases, uPAR shed from the cell membrane and exist as a soluble form (suPAR) that is detectable in various body fluids. The analysis of serum suPAR in SSc patients showed that suPAR could be considered as a novel biomarker for vascular dysfuction in SSc. Finally, uPAR is an emerging biomarker and molecular target in SSc.

Funding Sources: Supported by PRIN: PROGETTI DI RICERCA DI RILEVANTE INTERESSE NAZIONALE – Bando 2022 PNRR Prot. P2022HB33K

Topic Categories: Cellular Adhesion, Migration, and Inflammation (CAM)

Keywords: Diseases - Autoimmunity
Molecules - Adhesion Molecules
Processes - Inflammation
Signal Transduction
Tissues - Skin