conferenceseries.com

9th European Immunology Conference Associated with Antibody Engineering Meeting

June 14-16, 2018 | Rome, Italy

Anti-carbamylated and anti-citrullinated LL37 antibodies are present in psoriatic arthritis (PsA) patients and are potential markers of disease together with GM-CSF and IFN-α

Loredana Frasca¹, Roberto Lande¹, Raffaella Palazzo¹, Maria Sole Chimenti², Elisabetta Botti³, Simone Auteri⁴, Francesca Spadaro¹, Stefano Alivernini⁵, Barbara Tolusso⁵, Barbara Marinari³, Immacolata Pietraforte¹, Francesca Romana Spinelli⁴, Tania Colasanti⁴, Guido Valesini⁴, Fabrizio Conti⁴, Antonio Costanzo⁶ and Roberto Perricone²

¹Istituto Superiore di Sanità (ISS), Italy

²University of Rome Tor Vergata, Italy

³Sapienza University of Rome, Italy

⁴University La Sapienza, Italy

⁵Catholic University of the Sacred Heart, Italy

⁶Humanitas Clinical and Research Center, Italy

 \mathbf{P} soriasis is a chronic inflammatory and immune-mediated skin disease of unclear etiology, affecting 2-3% of individuals in Europe. A third of patients develop psoriatic arthritis (PsA), an inflammatory arthritis associated with psoriasis. The exact mechanisms that lead to development of PsA in psoriasis patients are elusive. We previously uncovered that the antimicrobial peptide LL37, that is over-produced by keratinocytes in psoriasis skin, plays a crucial role in sustaining inflammation in the skin by binding to nucleic acids and stimulating plasmacytoid and myeloid dendritic cells (pDC, mDCs) to release IFN-a and other pro-inflammatory factors production. In psoriasis, LL37 also becomes the target of autoimmune T cells with a Th1/ Th17 phenotype. On the other hand, anti-LL37 antibodies are frequently detected in systemic lupus erythematosus, a systemic autoimmune disease characterized by increased neutrophil NETosis in target tissues. Furthermore, it is known that LL37 is the substrate for irreversible post-translational modifications (PTM), such as citrullination or carbamylation. In these work we showed the presence of native and modified LL37 and related anti-LL37 antibodies both in circulation and synovial fluids of psoriasis and PsA subjects as compared to healthy donors (HD) and osteoarthritis (OA) patients by ELISA. Moreover, we found the presence of inflammatory factors that can either recruit neutrophils and/or induce neutrophil activation/degranulation or NETosis, or citrullination of proteins (GM-CSF, C5a, IFN-a). In synovial biopsies from very early and untreated PsA patients, expression of the IFN-related gene MX1 is highly up-regulated in close proximity of myeloperoxidase and LL37 staining. Synovial anti-LL37 autoantibodies recognizing the citrullinated form of LL37 correlate with IFN-α expression, and both anticitrullinated and anti-carbamylated LL37 do correlate with GM-CSF. These results suggest that serum IFN-a, GM-CSF and anti-LL37 antibodies, especially those directed to carbamylated LL37 are potential disease markers in PsA.

Biography

Loredana Frasca obtained her Biological Science degree in 1992 and her PhD in Cellular Immunology in 1996. She has expertise in cellular immunology with particular focus on T-cells, antigen presentation and T-cell tolerance. She has also expertise in innate immunity, in particular in regulation of dendritic cells functions. In the last ten years she worked on activation and homeostasis of T-cells and dendritic cells in normal responses and autoimmunity. Most recent research is focused towards the identification of pathogenic pathways that activate both innate and adaptive immunity in autoimmune diseases such as psoriasis, lupus, systemic sclerosis and arthritis.

Loredana.frasca@iss.it