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**BIOCHEMISTRY OF WOUND HEALING: FROM BENCH TO BED SIDE****Ferdinando Mannello<sup>a</sup>, Daniela Ligi<sup>a</sup> and Lidia Croce<sup>a</sup>**<sup>a</sup>University of Urbino, Italy

**Statement of the Problem:** Chronic venous diseases are widespread in Western countries, and their main complication (i.e., venous leg ulcer) is involved in more than half of lower extremity wounds, with prevalence up to 15% in the aged population; it represents a chronic recurrent problem inducing decreased quality of life as well increased morbidity and healthcare costs. The purpose of this study is to describe our experience in wound translational medicine, characterizing early biomolecular pathways of healing/non-healing processes and developing novel targeted therapies.

**Methodology & Theoretical Orientation:** Based on the exhibition in chronic wounds of both inflammatory and proteolytic altered metabolisms, as well as extracellular and endothelial dysfunctions, we analyzed soluble and membrane-bound biomolecules released in venous leg ulcer fluids as a mirror of wound microenvironment in healing and non-healing phases, with and without pharmacologic treatments.

**Findings:** The biochemical profiles (e.g., IL-1beta, CXC-8, VEGF, TGF-beta3, MMP-9 and MMP-12) in inflammatory wounds were found statistically different from those granulating ulcers, as well as significantly altered respect to plasma profiles. On the other hand, granulating healing wounds showed significantly increased levels of IP-10, CCL-5 and PDGF-bb. Finally, in vitro studies highlighted that pharmacologic treatments (e.g., glycosaminoglycan and flavonoid) significantly down regulated the release of peculiar soluble and membrane-bound inflammatory mediators (e.g. IL-12, VEGF, TNF-alfa, MMP-2 and TIMP).

**Conclusions:** Our studies revealed different biochemical microenvironments in both non-healing and healing venous leg ulcers, pinpointing their role of inflammatory and proteolytic hallmarks in wound healing. Moreover, the ability of glycosaminoglycan to counteract the inflammatory and degradative processes in non-healing wound provides a biochemical tool for developing a targeted therapy.