


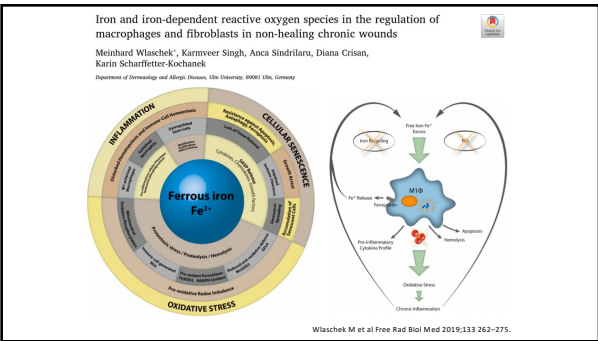
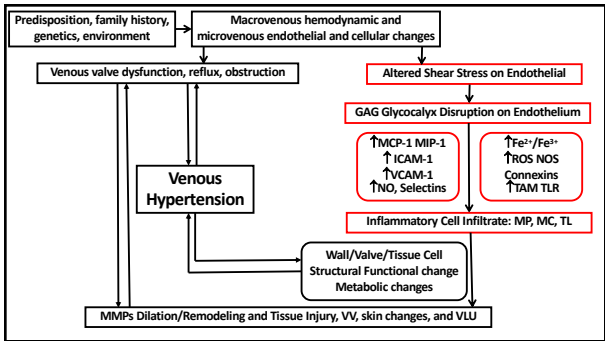
### Inflammatory Pathways of CVD

Joseph D. Raffetto, MD  
Associate Professor of Surgery  
VA Boston HCS, West Roxbury, MA, Harvard Medical School, Boston, MA; Brigham and Women's Hospital, Massachusetts  
Veith 2024



### Disclosures

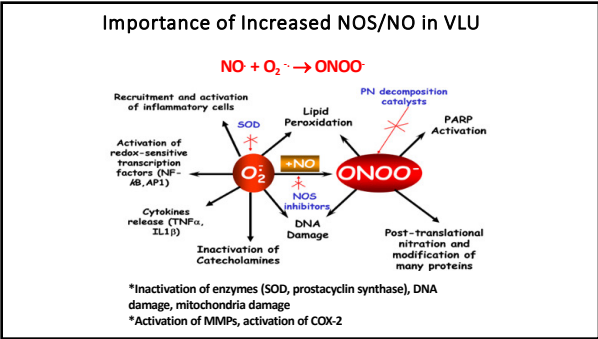
Nothing to Disclose  
No Other Conflicts of Interest

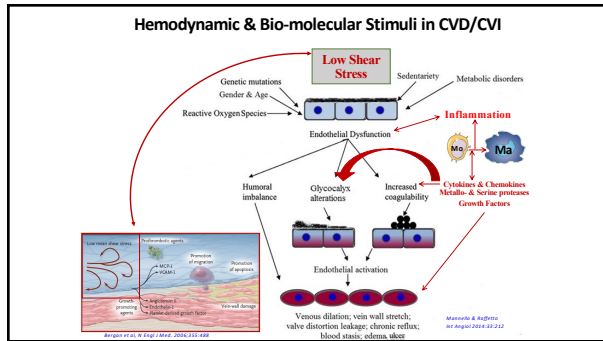


### Oxidation and Nitration

- Reactive oxygen species (ROS)
- Reactive nitrogen species (RNS)
- Proteins → protein carbonylation
- Lipids → lipid peroxidation
- DNA → oxidation/nitration ONOO, SSB, PAR/PARP

Doddar S et al Oxid Med Cell Longev 2018;5286785.





Chronic venous disease – Part I: Inflammatory biomarkers in wound healing

Daniela Ligi<sup>1</sup>, Giovanni Mosti<sup>2</sup>, Lidia Croce<sup>3</sup>, Joseph D. Raffetto<sup>4,5</sup>, Ferdinando Mannello<sup>6,7</sup>

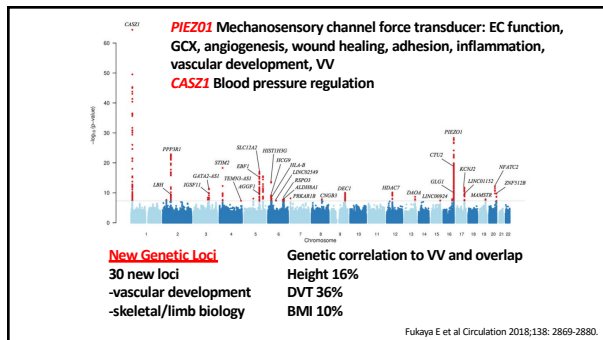
**Chronic Venous Insufficiency: Transforming Growth Factor-β Isoforms and Soluble Endoglin Concentration in Different States of Wound Healing**

Daniela Ligi<sup>1</sup>, Lidia Croce<sup>1</sup>, Giovanni Mosti<sup>2</sup>, Joseph D. Raffetto<sup>3,4</sup> and Ferdinando Mannello<sup>1,5,6</sup>

Chronic venous disease – Part II: Proteolytic biomarkers in wound healing

Daniela Ligi<sup>1</sup>, Giovanni Mosti<sup>2</sup>, Lidia Croce<sup>3</sup>, Joseph D. Raffetto<sup>4,5</sup>, Ferdinando Mannello<sup>6,7</sup>

Ligi D et al *Biochim Biophys Acta* 2016;1862:1964-74.  
Ligi D et al *Int J Mol Sci* 2017;18:2206.  
Ligi D et al *Biochim Biophys Acta* 2016;1862:1900-8.



**Endothelium *Piezo1* deletion alleviates experimental varicose veins by attenuating perivenous inflammation**

Jiani Zhao<sup>1</sup>, Yacheng Xiong<sup>1</sup>, Yu Liu<sup>1</sup>, Jin Ling<sup>1</sup>, Shuai Liu<sup>1</sup>, Wei Wang<sup>1,2</sup>

- Assess piezo type mechanosensitive ion channel component 1 (PIEZO1) and castor zinc finger 1 (CASZ1)
- Varicose veins and normal control
  - PIEZO1 mRNA elevated in VV not CASZ1
- Mouse endothelial *Piezo1* deletion model vs. control
  - CTRL high abundance of *Piezo1* in veins
  - l-liac vein ligation model Yoda1 → increased inflammation in veins
  - Mouse *PIEZO1* deletion inflammatory knockdown

Zhao, J., et al *Mol Cell Biochem* 2024 DOI: 10.1007/s11010-024-05115-9

### Other Pathways

- Metabolomics VV and VLU
  - VV: Expression of cell adhesion molecules and inflammatory pathways, regulation of cellular proliferation, cell signaling, proteinases, apoptosis and hypoxia pathways
  - VLU: Energy consumption and healing pathways, hypoxia and immune response pathways
  - Tryptophan (TRP)-l-kynurenine (KYN) pathway higher levels for VLU healing

Onida S et al *J Proteome Res* 2019;18:3809-3820.  
Anwar MA et al *Sci Rep* 2017;7:2369.  
Kim J et al *Adv Wound Care* 2024;13:494-507.