Diabetic foot ulcers and surgical wound healing: Where is the immunological difference? Löffler M^{1,2}, Schmohl M³, Schneiderhan-Marra N³, Joos T³, Königsrainer A¹, Beckert S¹ Dept. of General, Visceral & Transplant Surgery, University of Tuebingen/ Germany, Dept. of Immunology, University of Tuebingen & Natural & Medical Sciences Institute (NMI) at the University of Tuebingen, Reutlingen/ Germany

Introduction: Chronic inflammatory activity in diabetic foot ulcers (DFU) is considered an important reason for non-healing. However, also in the physiological course of healing, inflammation is a crucial initial step that has to be overcome. Therefore, differences in cytokines and mediators observed in acute surgical wounds vs. non-infected diabetic foot ulcers may be indicative for their respective immunological state. Methods: Consecutive DFU without clinical signs of infection (n=11) and patients with subcutaneous postoperative wounds (n=13) were enrolled at the Department of Surgery, University of Tuebingen, Germany. Wound fluid was obtained by superficial wound swabbing and subsequent centrifugation or from intra-operatively inserted suction drains at the first post-operative day. Cytokines and mediators were assessed by bead-based sandwich immunoassays. In case detection limits were reached, the respective values were assigned. Exploratory statistical assessment was performed by one way ANOVA correcting for multiple testing by the Bonferroni method. A p<0.05 was considered statistically significant. Results: Wound fluid samples were analysed for IL-1B, IL1-ra, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-13, IL-17, IP-10, IFNγ, TNFα, MCP-1, CCL-17 and TSLP. Wound fluid of non-infected DFU showed significant differences to surgical wound fluid with respect to IL-1B, IL-8 and IL-1ra. Differences between the two groups with regard to the other above referenced analytes were not statistically significant. Conclusions: The anti-inflammatory mediator IL-1 receptor antagonist was found significantly elevated in non-infected DFU compared to surgical wounds. Concurrently, pro-inflammatory cytokines IL-1B and IL-8 were significantly elevated in non-infected DFU compared to surgical wounds. This might suggest an immunological imbalance in diabetic foot ulcers with possible relevance for an effective immune response and progression towards healing.