SCOPE,
HYPOTHESIS AND
OBJECTIVES OF
THE STUDY
CHAPTER 3

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3.1 Scope of the study

Compared to other diabetic complications like retinopathy and nephropathy, the genetics of DFU remains poorly studied. Single nucleotide polymorphisms (SNPs) in inflammatory genes serve as valuable candidates for DFU since the pro-inflammatory cytokines IL-6 and TNF-α, the chemokine stromal cell-derived factor (SDF-1/CXCL12) and heat shock proteins (HSPA1B and HSPA1L) have been shown to coordinate the three phases of wound healing (Kristiansen et al., 2005). The IL-6 -174G/C (rs1800795), TNF-α -308G/A (rs1800629) and -238 G/A (rs361525), SDF-1 801 G/A (rs1801157), HSPA1B 1538 A/G (rs1061581) and HSPA1L 2437 C/T (rs2075800) are well characterized SNPs which have previously been linked to various diabetic complications (Libra et al., 2006); (Sikka et al., 2014); (Djuric et al., 2010); (Mir et al., 2009). However, the involvement of these SNPs in DFU remains poorly studied especially in the South Indian population which has a high prevalence of DFU. This thesis explores the possibility of the association of SNPs in these cytokine/chemokine/HSP with DFU which are responsible for wound healing (disease phenotype) and correlate it with the serum levels of these biomarkers along with clinical parameters including adiponectin, leptin and C-reactive protein (CRP) (intermediate phenotype).

3.2 Hypothesis of the study

Does SNPs in immune related genes (cytokines, chemokines and heat shock proteins) confer susceptibility to DFU?
3.3 Aims and Objectives

Towards this end the following aims and objectives were tested. Four main genes were chosen based on their vital role in wound healing process in DFU patients from South India.

- To study the involvement of *IL-6* promoter SNP (-174G/C) in determining serum IL-6 levels and susceptibility to DFU.
- To study the involvement of *TNF-α* promoter SNPs (-308G/A and -238G/A) in determining serum TNF-α levels and susceptibility to DFU.
- To study the involvement of *SDF-1* SNP (801G/A) in determining serum SDF-1 levels and susceptibility to DFU.
- To study the involvement of *HSP-70* SNPs (*HSPA1B* 1538 A/G and *HSPA1L* 2437 C/T) in determining susceptibility to DFU.