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Impairment of diabetic wound healing: Key genetic players

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Type-2 Diabetes Mellitus (T2DM) is a multifactorial disease characterized by hyperglycaemia and a series of micro- and macro-vascular secondary complications including wound healing impairment. Acute inflammation is necessary for wound healing as it brings about proper wound debridement. During the inflammatory phase of wound healing, innate immune system activation is crucial to combat invading microbes. Toll like receptors (TLRs) are the important members of innate immune system and are shown to be an important regulator of wound repair and regeneration in mouse model. We observed differential expression of extracellular TLRs in human diabetic wounds. Epigenetic silencing mediated by methylation analysis of CpGs of promoter regions of TLR2 and TLR4 revealed that this mechanism is contributing towards the down-regulation of TLR2 and TLR4. Some endosomal TLRs like TLR7 and TLR9 have been shown to promote tissue necrosis and sensory neuropathy. The levels of these endosomal TLRs were found to be significantly elevated in diabetic wounds along with their signalling molecules like S100A8 and IL8. Recruitment of anti-inflammatory CD11b⁺CD33⁺ myeloid cells during initial phase of wound healing is necessary for proper healing. Comparative analysis of the counts of these CD11b⁺ CD33⁺ myeloid cells using flow cytometry in healthy controls, T2DM cases and Diabetic foot ulcer (DFU) cases revealed the reduced level of these cells to be involved in the impairment of wound healing. In conclusion, our study indicated that the combined genetic and epigenetic deregulation of immuno-inflammatory phase due to persistent hyperglycaemia lead to development of chronic ulcers in T2DM subjects.

Biography

Kiran Singh has completed her PhD from Cytogenetics Laboratory, Department of Zoology; Banaras Hindu University in 2005. She is currently working as an Assistant Professor in Department of Molecular and Human Genetics, Banaras Hindu University. Her area of interest includes molecular human reproductive genetics, clinical cytogenetics & genetics and epigenetics of diabetic wound healing impairment. She has published 48 papers in various national and international journals and has been serving as Reviewer and Editorial Board Member of various reputed journals.

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