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Nitric oxide regulates intussusceptive-like angiogenesis in wound repair

Selvaraj Vimalraj and Suvro Chatterjee
MIT campus of Anna University, Chennai, India

Angiogenesis is the formation of new blood vessels that occurs by two distinct processes 1) sprouting angiogenesis (SA) and 2) intussusceptive angiogenesis (IA). Nitric oxide (NO) is known for its pro-angiogenic functions. However, NO implications in wound healing angiogenesis are not much understood. We propose that NO regulates SA to IA transition and vice versa in wound milieu. We have used a novel chick embryo extra-vasculature (CEV) burn wound and adult Zebrafish skin wound model to study the mechanisms. Wounds created in CEV were treated with NO donor (Spermine NONOate (SPNO)), NOS inhibitor (L-nitro-L-arginine-methyl ester (L-NAME)), NaNO_2 , NaNO_3 , and beetroot juice, a nitrite rich juice, respectively and followed the pattern of wound healing. The wound healings were tracked by morphological and histological techniques, and the molecular changes were tracked by using real time RT-PCR gene expression analysis. The result indicated that NO donor promotes wound healing by activating SA at early phase of healing while NOS inhibitor induces wound healing by IA. Later phase of healing attributed to NO donor dependant IA. However NOS inhibitor failed to promote healing in later phase of wound repair. Thus, we suggest that the NO regulation of angiogenesis in wound milieu would provide a new direction for treating wounds.

vimalr50@gmail.com