00027 Surviving Burns: Connexin 43 Downregulation Prevents Burn Progression

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Aims: Burns are highly dynamic injuries characterized by an initial zone of necrosis that progresses to compromise surrounding tissue. Burn progression has profound clinical implications resulting in significant diagnostic and therapeutic challenges. Acute inflammation and cellular apoptosis are two of the main contributing factors in the burn progression. Higher morbidity and mortality, and poorer functional recovery are inevitable sequelae of burn progression. Connexin43 (Cx43), a building block of gap junctions, plays central modulating roles in both processes in traumatic injuries and chronic wounds. Cx43 antisense oligonucleotide is developed to downregulate Cx43 and accelerate burns healing.

Methodology: Immunofluorescence studies were carried out on human and rat burn tissues to establish the spatial and temporal correlation between Cx43, apoptosis and neutrophils during the burn progression. Cx43-downregulating therapeutics were tested in rat burn model to mitigate burn progression and improve healing and scaring.

Result: Our data shows a high level of Cx43 in human and rat burn wounds associated with activated neutrophils and apoptotic dermal cells. The Cx43-downregulation therapeutics is able to prevent burns progression. Drug depot using scaffold is also developed to improve drug delivery and further improve burns wound healing

Conclusion: Apoptosis caused by harmful signals through connexin channel plays a important role in burn progression. Connexin channel blockage using antisense DNA reverses burn progression. Long-acting drug delivery is improved with polyehyleneglycol scaffold (PEG) applied topically.