

CONNEXIN 43 MIMETIC PEPTIDE GAP27 ACCELERATES NORMAL CUTANEOUS WOUND HEALING BUT HAS NO EFFECT ON KERATINOCYTES FROM DIABETIC ORIGIN

Simone Pollok¹, Ann-Catherine Pfeiffer¹, Pia Houdek¹, Uwe Hauswirth¹, Ralf Lobmann², Ingrid Moll¹, Johanna Brandner¹

¹*Department of Dermatology and Venerology, University Hospital Hamburg-Eppendorf, Hamburg, Germany,* ²*Department of Endocrinology, Diabetology and Geriatrics, Clinical Centre Stuttgart, Stuttgart, Germany*

Connexins form Gap Junctions (GJ), communicating channels between adjacent cells. Connexin 43 (Cx43) is ubiquitously expressed in human epidermis and is down-regulated during early wound healing at the wound margins and in regenerating epidermis. The fact that Cx43 is still present at the margins of chronic wounds implicates that the downregulation is important for effective wound closure. Phosphorylation of Cx43 on serine368 (S368) has been shown to decrease gap junctional intercellular communication (GJIC).

To further elucidate the role of Cx43 in wound healing we investigated the effects of a Cx43 mimetic peptide (Gap27) which results in a disruption of GJIC.

Treatment of porcine ex-vivo wound healing models with Gap27 resulted in decreased GJIC, accelerated wound healing and a higher number of proliferative keratinocytes compared to the controls. Confluent keratinocyte and fibroblast cultures treated with Gap27 prior to a scratch wound assay showed significantly enhanced migration resulting in a faster wound closure. Additionally, proliferation was increased. Interestingly, the amount of S368 Cx43 was increased in the presence of Gap27 indicating phosphorylation to be involved in disruption of GJIC. Surprisingly, Gap27 treatment had no effect on migration/proliferation of human keratinocytes from diabetic origin.

These data show the importance of Cx43 in wound healing and suggest that the application of Gap27 might be beneficial for normal wound healing but not for diabetic wounds.