SCIENTIFIC FACT SHEET

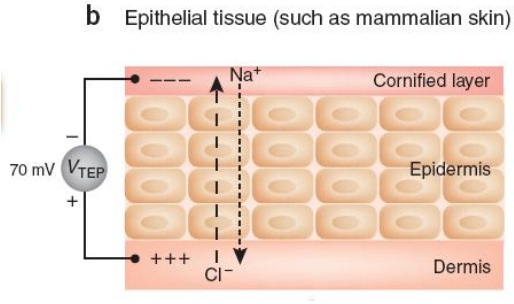
BioElectric Signals Control Wound Healing

King Fisher Healthcare
Technology for Life

A Skin Battery exists in normal human skin

Measurable voltage potentials have been found in the intact skin of mammals, including humans, known as transepithelial potential or TEP. These skin battery voltages occur because ions such as sodium (Na^+) are pumped across the membranes of the skin's cells [Foulds 1983, Vanhaesebroeck 2006].

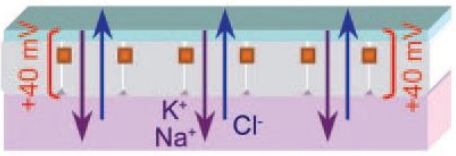
Schematic representation of the generation of a TEP in human skin. Selective, directional ion transport across the intact epithelium gives rise to a TEP that can be measured



A Current of Injury starts to flow when the skin is wounded

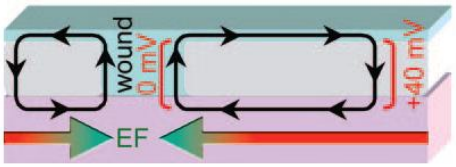
When human skin is cut or wounded, the normal transepithelial potential difference is short-circuited, inducing current to flow out of the lesion from underneath the wounded epithelium and giving rise to a steady electric field at the wound edge.

normal skin



Tight junctions between epithelial cells (red squares) create physical connections between cells, providing high electrical resistance and so maintaining the normal TEP in intact skin.

wound



In a wound, the epithelial seal is broken, the TEP drops to zero and ions (current) start to leak out. Further from the wound edge the normal TEP remains, and hence an electric field is created in the subepithelial tissues (horizontal arrow).

The term 'Current of Injury' has been introduced in 1960 by a US physician, Dr Becker. These injury potentials were discovered, however, as long ago as 1843 by the German physiologist Emil Du-Bois Reymond (the founder of modern electrophysiology), who used a galvanometer to measure microcurrent flowing out of a cut in his own finger [McCaig 2005].

Further clinical evidence was provided more recently when up to 35 µA/cm^2 were recorded from the accidentally amputated fingers of children [Illingworth 1980].

References

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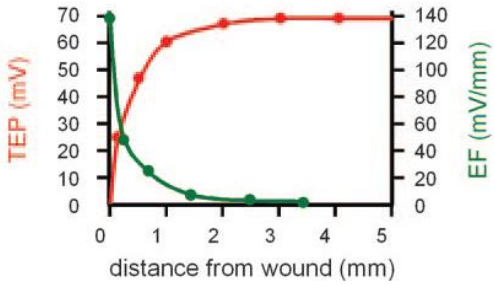
BioElectric Signals Control Wound Healing

BioElectric signals coordinate the wound healing process

Further research on this endogenous bioelectric current in wounds revealed some fascinating and clinically important aspects:

- the endogenous bio-electric current rapidly falls away within a few millimeters from the wound edge. In effect it is therefore limited to the wound surface area.
- the endogenous electric field persists until the migrating epithelium reseals the wound, and establishes the skin's normal high resistance, when the current drops to zero.

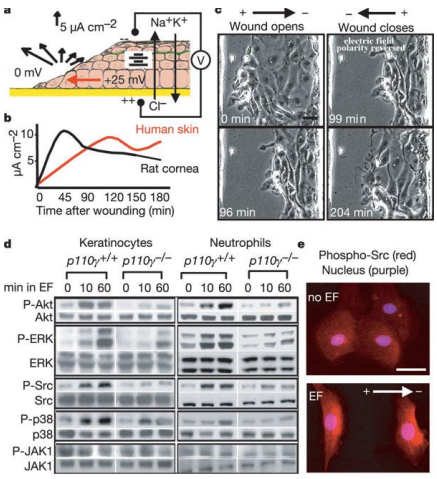


This in turn means all cellular activities in a wound take place within a gradient of voltage, and explains why bioelectric signals have such a diverse and wide-ranging effect on the many different cells and growth factors responsible for wound healing.

Some activities directly controlled by bioelectric signals are **cellular migration** (macrophages, fibroblasts, keratinocytes) , **fibroblast activation and proliferation** and **neo-angiogenesis** [Huttenlocher 2007].

- the endogenous current ceases when the wound becomes dry, but is maintained when moist dressings are used. This would explain in part why occlusive dressings work: they allow bioelectrical conduction to continue, and so support the regeneration process [Cheng 1995].

Specific genes and pathways exist through which bioelectric signals control wound healing



Another important chapter in the bioelectric wound healing story was completed recently when researchers discovered its molecular biology secret - which signaling pathways and genes are responsible for kick starting this amazing biological phenomenon.

In a recent Nature publication, Zhao et al identified genes that are essential for electrical-signal-induced wound healing and also showed which genes (PI(3)K γ and PTEN) control the migration of epithelial cells , fibroblasts and neutrophils under the influence of bioelectric signals [Zhao 2006].

Bioelectrical signals direct cell migration in wound healing

References

Huttenlocher A. Wound healing with electric potential *NEJM* 2007;356(3), 304-305.

Cheng K,Tarjan P, Oliveira-GandiaM, et al. An occlusive dressing can sustain natural electrical potential of wounds. *J Invest Dermatol* 1995;104(4):662-5.

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