Electrical Cues Regulate Important Cell Behaviors

Min Zhao
Corresponding Author: min.zhao@ucdavis.edu
University of California at Davis, Departms. Dermatology and Ophthalmology, Davis, CA 95618, USA

Introduction
Biochemical factors control cell behaviors. In addition, important roles have been recognized for biophysical factors in regulating multiple cellular behaviors. We have been investigating the effects of both endogenous physiological electric fields (EFs) and exogenously applied electric fields on cell growth, division, migration and other cellular behaviors. The remarkable guidance effects of the electric cues on cell division, cell migration, and cell growth provide promising and exciting new approaches to engineering and regenerate tissues. With stem cells, progenitor cells and differentiated cells as building blocks, electrical cues together with other mechanisms will bring us closer to regenerate perfect tissues to repair wounds and damaged organs. I will present our results on nerve growth, neuronal migration, cell migration and vessel growth. Those are critical elements in healing and regeneration.

Materials and Methods
Four types of culture systems are used: 1. Nerve cells from the central nervous system; 2. Epithelial cells from the corneas and skin; 3. Angiogenesis models of explants; 4. In vitro and in vivo wound healing models. We use our well-established system to applied electric fields to either mimic endogenous electric fields or exogenously apply electric fields to guide nerve growth, neuronal migration, division and migration of epithelial cells, new blood vessel formation and wound healing.1-3.

Results
1. Mammalian hippocampal neurons extent neurites and migrate towards the cathode in an applied EF. EFs guide the growth cone, resulting directional growth of the neuritis, and neuronal migration towards the cathode.4 Peripheral nerve fibres at the corneal wounds appear to be guided by the endogenous electric fields. We manipulated pharmacologically the wound-generated EF. Enhancing the EF induced earlier and more directional nerve sprouting towards the wound edge5.
2. Applied EFs direct division and migration of corneal epithelial cells towards the cathode, the same direction of the endogenous wound EFs6.
3. Applied EFs direct endothelial cells to migrate to the anode and vessel-like structure from aortic explants to grow to the anode7.
4. In wound healing assays using monolayer cultures, organ culture and in vivo corneal wounds, applied EFs may override other co-existing cues to direct cell migration in epithelial wound healing3.

I proposed a biased intracellular signaling mechanism that may underlie the directional response of cells to electrical cues (Fig. 1).

Discussion and Conclusions
Electrical cues offer a powerful mechanism to engineer important cell behaviors for regenerative biology and medicine.

References

Acknowledgments
MZ is supported by the Wellcome Trust (58551, 068012), NIH (R01EY019101), and California Institute of Regenerative Medicine (RB1-01417) and UC Davis Dermatology Development fund.

Disclosures: none.