Abstract

Physiological Electric Fields: A Central Determinant of Cell Behaviour

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Physiological electric fields (EF) have long been known to have direct effects on many aspects of cell behaviour underpinning physiological and pathological processes such as development, cell and tissue differentiation, cell migration, angiogenesis, and wound healing. EF are generated for instance in a healing wound by collapse of the transepithelial potential difference created by ion-transporting pumps which maintain ionic concentration differences across epithelial barriers. At a cellular level, we have shown that EF modify the activity of ligand receptor interactions eg in EGF receptor mediated migration of epithelial cells or in VEGF receptor-mediated orientation and directionality of endothelial cells. We have previously shown that these effects are regulated at the cytoskeletal level through intracellular signalling pathways such as phosphatidylinositol-3-OH kinase-gamma and PTEN. How an EF induces these effects is unclear. The direction of the electrotactic response varies with cell type (cathode vs anode) and even with the same cell type depending on conditions (eg lens epithelial cells). EF are thought to mediate their effects on cells via hydrodynamic viscous drag of cell-associated and cell membrane negatively charged proteins but may also have effects on the "charged water shell" surrounding cells. Possible mechanisms will be discussed in this presentation.

Layman's version

Electric field (EF)s are present in many physiological and pathological (disease) conditions such as in development of the embryo, in growing tumours and at the site of healing wounds. Flow of endogenous currents, for instance in a healing wound, is the result of a "short circuit" event that occurs at the wound site due to the collapse of the electrical potential difference (Pd) across cells lining the tissue (like skin). Electrical Pds across tissue surfaces occur because of cellular processes that pump ions in one direction against a gradient. The ionic differences on either side of the tissue create a charge (voltage) gradient across the tissue. In this sense, tissues such as the skin behave like a battery. When the Pd across the tissue is lost, an EF is generated with an outward flow of charge in a defined vector (the cathode is in the centre of the wound). We have mimicked EF conditions in vitro and in vivo and have shown that EF have many effects on cell behaviour, not solely at the tissue level but also at the single cell level. EF directly modify proteins on the surface of the cell and induce changes in the signals which are generated inside the cell leading to behavioural effects such as directed migration and polarisation of the cell. How EF achieve these effects are unclear but a general view is that EF cause changes in the level of hydrodynamic ("viscous") drag of proteins in the cell membrane and in their associated water molecules. However, EF theoretically might also have effects on the structure of the "water shell" around cells, which might modify cell surface protein conformation and function even transiently. To date, however, this notion remains hypothetical.