

International Conference on Medical Physics

August 03-05, 2015 Birmingham, UK



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Biophysical signaling in carcinogenesis: Implications for therapeutics

The strong focus on genetics in carcinogenesis research has somewhat obscured the important role of the microenvironment in regulating gene expression and controlling mutations. The membranes of all cells and mitochondria contain multiple ion channels that create a voltage gradient across the cell membrane, and combined with gap junctional currents create endogenous bioelectrical fields. These fields have long range effects on physiological functioning. Extensive research into multiple aspects of this bioelectric signaling system indicates that they play an important role in development, cell cycle progression, differentiation, migration and apoptosis; and interact with epigenetic mechanisms to influence gene expression. Depolarization (a prerequisite for the epithelial mesenchymal transition initiating tumor formation) has also been experimentally demonstrated to initiate mutagenic cell behavior in the absence of any primary tumor or genetic mutation. The current 'targeted' treatment modalities aim to bioengineer specific parts of signaling systems (e.g. kinases), but even in the most successful cases, inevitably perturb other, unintended components, having unintended consequences. Preliminary work on limb regeneration in frogs (the Levin lab) has demonstrated that an appropriate bioelectric signal can activate an entire subroutine to initiate limb regeneration, without micromanaging individual components. Implications for cancer therapeutics will be discussed.

Biography

Sarah S. Knox, received her PhD and MS degrees from Stockholm University (S.U.), Sweden; and began her career as a Principal Investigator at the Karolinska Institute in Stockholm.

After spending many years at the National Institutes of Health, Dr. Knox came to WVU where her research interests have focused on a systems biology approach to carcinogenesis, integrating gene x environment interactions and biophysical signaling. She has published widely, reviews for a broad range of medical and scientific journals, and been the recipient of multiple honors and awards.

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