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Abstract

The Role of Gap Junctions in Disease and Potential Treatment Approaches

Dale W Laird
The University of Western Ontario, Canada

Abstract:

Our research program is engaged in examining the over two dozen distinct human diseases linked to genes that encode the proteins (connexins) used in gap junctional intercellular communication. Mutations in 50% of the 21 connexin gene family members result in conditions ranging from developmental abnormalities that include hearing loss to life-shortening organ failure. We use a multidimensional approach involving organotypic cultures, genetically-modified mice, connexinlinked disease patient cells and human inducible pluripotent stem cells to interrogate the scope of mechanisms that lead to disease in some tissues while other organs are spared. In principal, connexins are linked to disease or injury repair through three different mechanistic paradigms. First, connexin-mediated intercellular communication is often up-regulated or downregulated in response to cellular cues that in turn drive connexin gene expression, connexin assembly or connexin turnover. This scenario has been most widely studied in cancer prevention, onset and progression. Secondly connexin-linked disease/injury paradigm is based on the concept that connexin expressions acts as a brake in wound healing and that a transient down regulation would act to jump start the healing process. An equally intriguing corollary to this notion is that a spike in GJIC could stimulate chronic wound healing. Thirdly, a strong driver of disease was the finding that connexin gene mutations lead to development of abnormalities and chronic disease conditions. Once it is better understood how connexin gene mutations cause diseases and deformities that often intensify in aging, it is anticipated that these findings could be translated to preclinical studies and possible treatments of gap junction-linked diseases.

Biography:

Dale W Laird is a Professor and Canada Research Chair in Gap Junctions and Disease. He has over 30 years of experience working with connexins and more recently pannexins and has published over 150 papers on their role in health and disease. He has received many awards for his research and is currently funded by the Canadian Institutes of Health Research.

Publication of speakers:

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2. Abitbol, Julia & Beach, Rianne & Barr, Kevin & Esseltine, Jessica & Allman, Brian & Laird, Dale. (2020). Cisplatin-induced ototoxicity in organotypic cochlear cultures occurs independent of gap junctional intercellular communication. Cell Death & Disease. 11. 342. 10.1038/s41419-020-2551-8.
3. Beach, Rianne & Abitbol, Julia & Allman, Brian & Esseltine, Jessica & Shao, Qing & Laird, Dale. (2020). GJB2 Mutations Linked to Hearing Loss Exhibit Differential Trafficking and Functional Defects as Revealed in Cochlear-Relevant Cells. Frontiers in Cell and Developmental Biology. 8. 215. 10.3389/fcell.2020.00215.

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