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Research Interests

Our research strategy is based on the idea that ion channels play a vital role in retinal disorders. We use the patch-clamp technique to study ion channels in various types of retinal cells. A major focus of our research is on retinal pericytes, which are positioned on the outer wall of the capillaries and are selectively lost early in the course of diabetic retinopathy.

A working hypothesis is that pericyte function is altered in pathophysiological disorders, such as diabetes. We hope to determine how molecules in the retinal microenvironment alter ion channel activity and, thereby, disturb the function of pericytes. In the long-term, understanding the mechanisms by which retinal cells respond to pathophysiological conditions may enable us to devise new therapeutic strategies for disorders affecting the retina.

Based on the premise that ion channels are likely to play a role in mediating the responses of microvascular cells to vasoactive signals, we developed a technique to isolate from the adult rodent retina viable pericyte-containing microvessels in which we can monitor pericyte currents via patch-pipettes, measure pericyte calcium levels with fura-2 and visualize pericyte contractions and lumen constrictions by time-lapse photography. Thus, we can study retinal microvessels from the level of ion channels (and electrogenic ion transporters and exchangers) to pericyte function. This experimental preparation has proven to be a gold mine for discoveries because we can now make observations that previously were not feasible for the pericyte-containing microvasculature of any tissue.



By studying pericyte-containing microvessels isolated from diabetic animals, we have generated new ideas concerning the mechanisms by which diabetes causes retinal dysfunction. For example, our experiments indicate that an enhanced formation of potentially lethal P2X7 pores is a newly discovered mechanism by which diabetes may cause microvascular cell death in the retina. Another newly observed pathophysiological effect of diabetes on the retinal microvasculature is a PKC-dependent disruption of cell-to-cell electrotonic transmission (IOVS 2001). We hypothesize that this disruption of intercellular communication adversely affects the ability of a capillary network to efficiently and effectively direct nutrients and oxygen to vulnerable neurons. A goal for the future is to experimentally test our proposed scenerio that a diabetes-induced disruption of the multicellular organization of the retinal microvasculature compromises neuronal function and ultimately may cause neurodegeneration.

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