FALL 2019

Biochemistry and Molecular Biology Brown Bag Series

Ryan Rakoczy

Ph.D. Student

"Acute Oxygen-Sensing by the Carotid Body: The Thermal Microdomain Model"

Tuesday, December 3, 2019

11:00 AM

141 Medical Sciences Building

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http://www.med.wright.edu/bmb

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"Acute Oxygen-Sensing by the Carotid Body: The Thermal Microdomain Model"

The carotid bodies (CB) are peripheral chemoreceptors that detect changes in arterial oxygenation and, via afferent inputs to the brainstem, correct the pattern of breathing to regain blood gas homeostasis. Detection of a hypoxic stimulus causes closure of a yet-to-be identified potassium channel and subsequent cellular depolarization; however, the precise mechanism used by the oxygen-sensitive CB Type I cell to detect hypoxia has resisted a satisfying theory of explanation (Rakoczy & Wyatt, 2018). Of late, an oxygen-sensing micro-domain has been described by several groups whereby a large CB Type I cell nucleus confines a dense mitochondrial population to a fine cytosolic ribbon directly under the cellular membrane. Recently, it has also been demonstrated in several cell types that mitochondrial thermogenesis, during peak oxidative phosphorylation, can be measured at 50°C using a new thermo-fluorophore. Interestingly, CB Type I cells express several heat sensitive ion channels. Through an interplay between mitochondrial thermogenesis and heat-sensitive ion channels, it is hypothesized that the lack of oxygen experienced by a cell during hypoxia slows oxidative phosphorylation, thus lowering mitochondrial thermogenesis. This heat reduction may then be sensed by heat-sensitive channels that close in response, causing subsequent cellular depolarization and downstream correction of breathing. As the mitochondria serve as the oxygen sensor producing a thermal signal that interacts with heat-sensitive ion channels, this theory may underpin the mechanism by which the CB Type I cell detects low oxygen levels. Prospective experiments will measure CB Type I cell mitochondrial thermogenesis under varying oxygen tensions, identify the channels co-localizing to the oxygen-sensing micro-domain, and determine if these channels conductance properties vary with temperature.