The Robert M. Berne Cardiovascular Research Center Presents

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Translating redox biology to medicine: Novel properties of hemoglobin in NO and CO signaling and therapeutics

Inhaled nitric oxide (NO) exerts distal "endocrine" signaling effects via intravascular oxidation and conversion to the anion nitrite. Nitrite has a 45-minute half-life, compared to 2 mili-seconds for authentic NO, and thus functions as a circulating storage pool for NO bioactivity that contributes to physiological vasodilation, blood pressure regulation, and the cellular resilience to low oxygen and ischemia. Recent studies suggest that a number of cellular enzymes regulate nitrite reduction to NO at different oxygen tensions, with organ system specificity. The role of heme-globin superfamily proteins, such as hemoglobin, myoglobin, neuroglobin, cytoglobin and the plant hemoglobins, and the molybdenum containing enzymes, such as xanthine oxidase, aldehyde oxidase and sulfide oxidase, are the subject of active current study, and recent advances in this area of investigation will be briefly reviewed. Human physiological studies and mouse studies in the myoglobin knock-out model suggest a physiological function for hemoglobin and myoglobin in hypoxic nitrite-NO signaling. Studies of neuroglobin and plant hemoglobins have identified a role for heme coordination in the redox-regulated control of nitrite reduction to NO (six-to-five coordinate regulation of nitrite binding and reduction). Mutagenesis studies have helped characterize these functions and have identified unexpected properties that can be harnessed therapeutically in the design of hemoglobin based oxygen carriers and antidotes for CO poisoning. Recent therapeutic developments using recombinant mutant neuroglobin are reviewed.

Objectives:

To understand how nitric oxide and nitrite signal in the vasculature and how hemoglobin modulates this signaling.

To define the functions of globin superfamily members in nitric oxide signaling and biology, including hemoglobin, myoglobin, cytoglobin, neuroglobin, globin X and androglobin.

To explore new therapies based on nitrite and globin signaling.

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11:00 AM-12:00 PM
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Hosted By: Swapnil Sonkusare, PhD
Refreshments Served