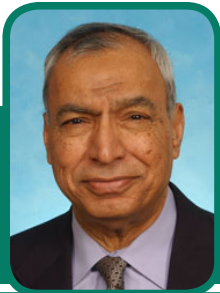# INTERNATIONAL HEART CONFERENCE

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S Jamal Mustafa

West Virginia University, USA

Coronary flow regulation by adenosine it's signaling

Adenosine acts through its receptors (A1, A2A, A2B, and A3) via G-proteins and causes an increase in coronary flow (CF) mostly through A2A AR. However, the role of other ARs in the modulation of CF is not well understood. Using KOs, we investigated the role for each AR in the regulation of CF. Using the isolated heart from A3 KO mice; we reported an increase in A2A-mediated CF. Similarly, we found an increase in CF in A1 KO mice with A2A agonist (CGS-21680). Also, in A2A KO mice, response to CGS was abolished. On the other hand, A2A KO mice showed a decrease in CF to NECA (non-selective agonist). BAY60-6583 (A2B selective agonist) was without an effect on CF in A2B KO mice; however, it increased CF significantly in A2A KO. CGS also caused a significant increase in CF in A2B KO mice. Also, exogenous adenosine-induced increase in CF in WT, A2A KO, and A2B KO mice were significantly reduced with catalase. BAY-induced increase in CF in WT was significantly inhibited with glibenclamide. Overall, our data support stimulatory roles for A2A and A2B and inhibitory roles for A1 and A3 in the regulation of CF. These observations provide new evidence for the presence of all four ARs in CF regulation. We propose, that activation of A2A/B may release H_2O_2 which then activates KATP channels, leading to vasodilation. These studies may lead to better understanding of the role of ARs in coronary disease and may lead to better therapeutic approaches.

Biography

S Jamal Mustafal is the Professor of Pharmacology at West Virginia University School of Medicine and a Senior Advisor to the Pilot Core of the West Virginia Clinical Science and Translational Institute. He served as an Assistant Dean for Research and the Health Sciences Center from 2005-15. He has received Dean's Award for Excellence in Research from School of Medicine in 2008 and became a Robert C. Byrd Professor in 2010. In addition, he received Chancellor's Award for Outstanding Achievement in Research and Scholarly Activities from HSC in 2013. He has published over 200 manuscripts. Prof. Jamal and the coworker's past work have led to the approval of an A2A selective AR agonist (Lexican®) for myocardial perfusion imaging. Currently, they are using AR and β adrenergic receptor KOs to better understand the relationship between these receptors in coronary flow regulation.

sjmustafa@hsc.wvu.edu