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Cardiac toxicity associated with chronic ozone inhalationmay be linked to caveolin mediated p38MAPK signaling

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Abstract

Although epidemiology studies have associated exposure to particulate matter (PM) with acute mortality and morbidity, only recently have they found associations between ozone and mortality. It has been challenging to disentangle the toxic effects of ozone from those of PM in these studies because the 2 pollutants are often closely correlated temporally and geographically. In studies using rats from controlled ozone (O3) exposure environment we showed moderate and chronic cardiac dysfunction after 4 and 8 weeks of O3 inhalation respectively. This stage dependent O3 – mediated progressive decline in cardiac function was associated with increasing levels of inflammatory mediators. Our findings were cited and the results validated in a recent USEPA sponsored human study where exposure to O3 was shown to modulate the cardiovascular system by increasing the levels inflammatory mediators. Later studies from our laboratory suggest a balance between caveolin-1 and caveolin-3 may play a role in O3 associated cardiac toxicity. Since interaction of caveolins with p38MAPK is involved in regulating death and survival signaling in the cardiac muscle, our recent findings in O3 - exposed rats suggest a stage dependent involvement of caveolin mediated p38MAPK associated death and survival signaling and that more than one pathways may be involved in the pathology of O3- mediated cardiac toxicity.

Biography

Rajat Sethi received his Ph.D from the Department of Medicine, University of Manitoba, Canada. Sethi is currently the Chair of Department of Pharmaceutical and Biomedical Sciences at the California Health Sciences University, Clovis, California. Prior to this he served as the Assistant Dean for Research and Evidence Based Practice at the Texas A&M Health Science Center. He has more than 100 publications in the field of cardiac toxicology, holds 18 patents, has authored 7 books, and serves in the editorial board for many journals. Sethi has received grants from federal and local agencies and from various foundations and has been an invited speaker in many national and international meetings and he is the recipient of numerous awards and honors for his contribution to research and education.