

## Molecular mechanisms of hyperoxic lung injury: Implications for bronchopulmonary dysplasia (BPD) and ARDS

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Hyperoxia is routinely used in the treatment of pulmonary insufficiency and respiratory distress in preterm and term infants and in adults with acute respiratory disease (ARDS). However, in infants, hyperoxia contributes to the development of chronic lung disease (CLD), which is termed bronchopulmonary dysplasia (BPD). The molecular mechanisms of oxygen-mediated lung injury are not understood, but reactive oxygen species (ROS) are the most likely candidates. ROS are also responsible for many other lung diseases such as acute respiratory distress syndrome (ARDS), asthma, emphysema, chronic obstructive pulmonary disease (COPD), and lung cancer. Results from our laboratory demonstrate a novel role for cytochrome P450 (CYP)1A enzymes in the detoxification of ROS-mediated lipid peroxidation products, e.g., F<sub>2</sub>-isoprostanes. Our major observations are that mice lacking the genes for CYP1A1 or 1A2 are more susceptible to hyperoxic lung injury than wild type mice, with Cyp1a2-null mice being the most sensitive. On the other hand, mice lacking the gene for CYP1B1, are less susceptible to lung injury, suggesting a pro-oxidant role for CYP1B1. Mice pre-treated with the CYP1A inducer ( $\beta$ -naphthoflavone (BNF)), followed by exposure to hyperoxia leads to protection against lung injury. We also found formation of bulky oxidative lesions (oxidative DNA adducts) in tracheal aspirates of premature infants and adults who received supplemental oxygen, and this was associated with BPD and ARDS, thereby suggesting that these adducts could serve as novel biomarkers of these diseases. Future studies could lead to the development of rational strategies for the prevention/treatment of lung diseases associated with hyperoxia.

### Biography

Bhagavatula Moorthy had completed his Ph.D from the Indian Institute of Science in 1989, and underwent postdoctoral studies at the Medical College of Wisconsin and Baylor College of Medicine. He is currently Professor of Pediatrics and Director of Neonatology Research Laboratories at Baylor. He has published more than 70 papers in reputed journals and serving as an editorial board member of several journals. He also has received multiple grants from the National Institutes of Health and other agencies. He recently received the AstraZeneca Travel Lectureship award from the Society of Toxicology and will be a visiting Professor in 7 European Universities.

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