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Novel small molecules as broad-spectrum therapeutics for high consequence viral and bacterial pathogens

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Ebola virus (EBOV) and Marburg virus (MARV), the causative agents of Ebola and Marburg hemorrhagic fever respectively, are classified in the family *Filoviridae*. These viruses are important human pathogens with case-fatality rates ranging from 70% to 90% for EBOV up to 90% for MARV. These agents are classified as Category A Priority Pathogens by the NIAID/NIH, and there is presently no licensed vaccine or treatment against filoviral infection. According to the latest figures from the WHO, since March 2014 West Africa's first-ever Ebola outbreak in humans is the most deadly and geographically widespread outbreak on record, and it threatens to spread. Rickettsioses represent some of the most devastating human infections. These tick-borne diseases are caused by obligately intracellular bacteria of the genus *Rickettsia*. It has been forecasted that temperature increases due to global climate change will lead to the more widespread incidence of rickettsioses. In addition, a high infectivity and severe illness after inhalation make rickettsiae potential bioterrorism threats. Although rickettsial infections can be controlled by appropriate broad-spectrum antibiotic therapy if diagnosed early, up to 20% of misdiagnosed or untreated and 5% of treated Rocky Mountain spotted fever (RMSF) cases result in a fatal outcome. In fact, a fatality rate as high as 32% has been reported in hospitalized patients of Mediterranean spotted fever. Strains of *R. prowazekii* resistant to tetracycline and chloramphenicol have been developed in laboratories. Therefore, novel host mechanism-based treatments are urgently needed. Currently, we discovered that cAMP signaling axes play critical roles in filoviral infection and rickettsial pathogenesis. This exciting avenue of research, coupled with recent success in developing small molecules that specifically inhibit exchange proteins directly activated by cAMP (EPAC), has implications to develop broad-spectrum therapeutics that have activity against both viral and bacterial pathogens.

Biography

Dr. Bin Gong is an Associate Professor of Pathology, the University of Texas Medical Branch at Galveston, TX. Dr. Gong's laboratory is active in the determination of novel pathogenic mechanisms focusing on the interface between the endothelium and highly virulent intracellular pathogens, in particular the highly invasive bacterial genus *Rickettsia* and the viral family *Filoviridae*. Dr. Gong is being the P.I. of active R01 project R01AI121012 and the co P.I. of active R01 projects R01AI111464.

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