Presenting Author Name
Júlia Cerato

Presenting Author Category
PhD Student

Research Category
Basic Science

Abstract Title
Targeting B-Raf kinase protects airway epithelial cells from RSV infection and modulates interferon responses

Background
Respiratory syncytial virus (RSV) is the leading cause of hospitalization due to acute bronchiolitis in children under 2 years old. It is responsible for 200,000 deaths annually worldwide. There are no effective antiviral therapies or clinically approved RSV vaccines for children. Dabrafenib is an FDA-approved anticancer drug that inhibits B-Raf kinase. Dabrafenib impairs SARS-CoV-2 and Zika virus replication and ameliorates tissue injury in different inflammatory disease models.

Objective
Thus, we hypothesized that dabrafenib could be repurposed to treat RSV infection.

Methods
A549 and HBEC3-KT cell viability was measured using MTT assay. A549, HBEC3-KT and HNECs cells were infected with RSV-GFP (0.5 MOI) and treated with dabrafenib at different timepoints. Infection rate, IC50, and fluorescence intensity were quantified by immunofluorescence. Lytic cell death was assessed by measuring LDH release. IFNs secretion was measured using ELISA. RT-qPCR was used to measure ISGs and RSV mRNA expression. The effect of dabrafenib on virus infectivity was determined by plaque assay.

Results
Dabrafenib evokes a dose-dependent inhibition (IC50 40.17μM) of RSV infection in A549 cells. Moreover, the drug also decreases infection after different treatments: prophylactic, simultaneous, and therapeutic. In addition, cell death was reduced by 23.4% after dabrafenib treatment and no effect on cell viability was observed. Virus infectivity and the release of infectious progeny virions were decreased by dabrafenib. B-Raf kinase blockade with dabrafenib also diminished RSV infection in immortalized and primary airway epithelial cells (HBEC3-KT and HNECs). The treatment decreased viral mRNA expression by 72% in HNECs. Furthermore, IFIT1 and ISG15 mRNA expression, as well as IFN-β and INF-λ release, were significantly reduced after dabrafenib treatment in both A549 and HBEC3-KT cells, which is consistent with the observed reduction in viral loads.

Conclusion
Dabrafenib treatment significantly impairs RSV replication in vitro, demonstrating its potential as an antiviral drug against RSV infection.

Authors

Name	Role	Profession
Júlia Cerato	Presenting Author	Graduate
Maria Serda	Co Author	
Testimony Olumade	Co Author	Graduate
Wenming Duan	Co Author	
Theo Moraes	Co Author	
Deanna M. Santer	Co Author	Assistant Professor
Kevin Coombs	Co Author	Full Professor
Barbara Porto	Co Author	Assistant Professor