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Cathelicidins have direct antiviral activity against respiratory syncytial virus in vitro and protective function *in vivo*

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Respiratory syncytial virus (RSV) is a leading cause of respiratory tract infection in infants, causing significant morbidity and mortality. No vaccine or specific, effective treatment is currently available. A more complete understanding of the key components of effective host response to RSV and novel preventative and therapeutic interventions are urgently required. Cathelicidins are host defence peptides, expressed in the inflamed lung with key microbicides and modulatory roles in innate host defence against infection. Here we demonstrate that the human cathelicidin LL-37 mediates an antiviral effect on RSV via direct damage to the viral envelope, disrupting viral particles and decreasing virus binding to, and infection of, epithelial cells. Delivery of exogenous LL-37 is protective *in vivo* in a murine model of pulmonary RSV infection, demonstrating maximal efficacy when applied concomitantly with virus. Furthermore, endogenous murine cathelicidin, induced by infection, has a fundamental role in protection against disease following infection with RSV. Finally, higher nasal levels of LL-37 are associated with protection in a healthy human adult RSV infection model. These data lead us to propose that cathelicidins are a key, non-redundant component of host defence against airway infection with RSV; functioning as a first point of contact antiviral shield, and having additional later phase roles in minimizing the severity of disease outcome. Consequently, cathelicidins represent an inducible target for preventative strategies against RSV infection and may inform the design of novel therapeutic analogues for use in established infection

Biography

Donald J Davidson has completed his PhD at the MRC Human Genetics Unit and undertook Postdoctoral training in Innate Immunity research at the University of British Columbia, Vancouver as a Welcome Trust Fellow. In 2004, he has joined the University of Edinburgh/MRC Centre for Inflammation Research, where he established an independent research group as a Welcome Trust funded Fellow

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