When a virus uses another entrance - Immune mechanisms involved in innate anti-lyssavirus immune response in nasal cavity of European bats

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Lyssaviruses are neurotropic viruses causing fatal encephalitis of central nerve system, rabies. In Europe, bats act as reservoir hosts for two specific types of lyssaviruses, European Bat Lyssavirus type 1 and 2 (EBLV-1 and -2). Although cases of rabies in bats caused by and transmission to humans of EBLV 1 or 2 are described, there are no reports about epidemics in bats. Moreover, lyssavirus specific antibody titers in European bat colonies were only rarely detected. This indicates that innate immune pathways might be responsible for the observed resistance without contribution of adaptive immune mechanisms in bats.
Therefore, we characterized the interferon (IFN) type I and III family of two European bat species *Eptesicus serotinus* and *Myotis myotis*. Both species do have a typical IFN structure with type I IFN β, δ, ε, κ, ω and τ and type III IFN λ. Until now there are no evidences for an active IFN α as only one pseudogene could be sequenced yet. Using established cell lines from nasal epithelium (MmNep), nervus olfactorius (MmNol),brain (MmBr) of *M. myotis* we analyzed in-vitro the IFN responses along the aerosol infection route by investigation of IFN-specific signaling pathways, induction of IFNs/interferon stimulated genes (ISGs) and anti-viral effects in correlation to the expression of viral receptors in each cell line.
Interestingly, we found a gradually decreased susceptibility along the aerosol route combined with an increased IFN response indicating that the observed resistance of bats is based on a specific co-evolutionary relation between lyssaviruses and their reservoir hosts.

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