ID der Kurzfassung : **52**

The balance between intrinsic cellular innate, host innate and host adaptive immune responses matters for the outcome of influenza virus respiratory infection

Inhalt

After lung infection, influenza A viruses (IAVs) have to overcome at least three highly efficient immune defense barriers: the intrinsic cellular innate response, the host innate immune response and the host adaptive immune response. To circumvent these immune defense barriers and propagate successfully, influenza A virus proteins enter into a symbiosis with cellular proteins, altering host intrinsic pathways and gene transcription. The multifunctional adaptor protein FHL2 is a cellular protein with fine-tuning adjustment properties. It acts as a regulator of signaling cascades but also as a cofactor of transcription and controls several anti-inflammatory immune responses. Regarding IAV infection, FHL2 plays a dual role. By infecting FHL2 wildtype and knockout cells and mice, we showed that FHL2 restricted viral replication at early phases of infection but supported it at later phases. On the one side, FHL2 supported the IRF-3-dependent transcription of the Ifnb1 gene, accelerating thereby the intrinsic cellular innate response. On the other side, it restricted the migration of antigen-presenting CD11c+CD103+CD11b- dendritic cells from infected lungs into adjacent lymph nodes, decreasing thereby the recruitment of specific anti-viral CD3+CD8+IFNγ+ T lymphocytes into sites of inflammation. This effect of FHL2 was abrogated when RAG1KO mice lacking mature T lymphocytes were used.
Thus, a 1.5-fold stronger boost of the third defense barrier to influenza A virus infection in FHL2KO over wildtype mice was able to compete out the beneficial effect the influenza viruses originally had in FHL2KO mice due to the 10-fold weaker first barrier of cell intrinsic innate immune response.

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