HCF 1

**Mechanisms of apoptosis suppression in influenza A virus infected cells - the viral NS1 protein activates the PI3K to prevent premature cell death**

°*Christina Ehrhardt (1), Thorsten Wolff (2), Stephan Pleschka (3), Oliver Planz (4), Mirco Schmolke (1), Stephan Ludwig (1)

(1) Institute of Molecular Virology, Muenster, Germany; (2) RKI, Berlin, Germany; (3) Inst. of Virology, Giessen, Germany; (4) FLI, Tuebingen, Germany

Recently we have shown that influenza A virus infection leads to activation of the PI3K/Akt pathway due to the expression of the viral non-structural protein 1 (NS1) (Ehrhardt et al. (2006) Cell Microbiol. 8, 1336-1348). Later it was demonstrated by us and others that activation occurs upon direct interaction of the A/NS1 to the regulatory subunits of PI3K, p85 alpha and beta (Ehrhardt et al, (2007) J. Virol. 8: 3058-67). However, it remained enigmatic for which virus-supportive event A/NS1 mediated activation of PI3K may be required. We present a novel mode of action of the A/NS1 to suppress apoptosis induction. A/NS1 binding and activation of PI3K results in the induction of the PI3K effector Akt and subsequently in inhibition of caspase 9 and GSK-3 beta limitation of the virus induced cell death program. This indicates that A/NS1 not only blocks but also activates signaling pathways to ensure efficient virus replication. Novel data indicate that the B/NS1 protein completely lacks the capacity to induce PI3K signaling. Thus, PI3K activation is another unique function of A/NS1 that is different from the action of its influenza B virus counterpart (Ehrhardt et al. (2007) J. Virol., 81: 12097-12100).

Corresponding author:
**Ehrhardt, Christina**
ehrhardc@uni-muenster.de
Phone: ++49 251 8352217
Fax: ++49 251 8357793