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# 3rd International Influenza Meeting

FluResearchNet. September 2nd – 4th

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# P124

## Novel antiviral drug ingavirin$^{R}$ restores the cellular antiviral response in influenza A virus infection and enhances viral clearance in ferrets

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All licensed antiviral drugs against influenza A virus infection target structural proteins of the virus, allowing development of drug resistance by means of compensatory mutations. Another strategy to fight viral infections is the reinforcement of the antiviral cellular pathways, which are down-regulated by viral pathogenicity factors. Those pathways include activation of PKR, the translocation of IRF3 and IRF7 into the nucleus and the induction of MxA.

We here investigated the possible mechanism of action of a novel antiviral drug Ingavirin$^{R}$ (Imidazolyl Ethanamide Pentandioic Acid), which is applied for upper respiratorial tract viral infections in Russia. We found, that infection of A549 lung epithelial cells with the wild type influenza A virus in the presence of the Ingavirin induces PKR activation, translocation of IRF3 and IRF7 and increases levels of MxA. Thus, wild type infection in the presence of the drug is associated with the induction of danger signal associated pathways, which are usually inhibited by the influenza virus NS1 protein.

We then tested the antiviral effect of the drug in ferrets. Ingavirin$^{R}$ was given once per day in a dose of 13 mg/kg and therapy was started 36 hours after infection with influenza A(H1N1)pdm09 virus. Ingavirin$^{R}$ accelerated viral clearance from nasal washes starting at day 4. No toxic side effects were observed.

We conclude that the drug may restore evolutionary evolved antiviral response pathways usually induced by pathogen associated patterns but inhibited by non-structural proteins of viruses.

**Key words:** antiviral drug, PKR, IRF-3, MxA, ferrets