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Title: Expression of innate immune genes, proteins and microRNAs in lung tissue and leukocytes of pigs infected with influenza virus

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Abstract Body: This study aimed at providing a better understanding of the involvement of innate immune factors including microRNA (miRNA) in the local and systemic host response to influenza virus infection. Twenty pigs were challenged by influenza A virus subtype H1N2. Expression of miRNA, mRNA and proteins were quantified at different time points after challenge (24h, 72h, and 14days post infection (pi)). Gene expression was quantified using 48.48 Dynamic Arrays (Fluidigm Corporation, CA, USA) combining 48 samples with 48 primer sets for 2304 individual and simultaneous qPCR reactions. Several groups of genes were significantly regulated according to time point and infection status: Pattern recognition receptors (TLR2, TLR3, TLR7, RIG1, MDA5), IFN and IFN induced genes (IFNB, IFNG, IRF7, STAT1, ISG15 and OASL), cytokines (IL1B, IL1RN, IL6, IL7, IL10, IL12A, TNF, CCL2, CCL3 and CXCL10), and several acute phase proteins. Likewise, the following miRNAs were differentially expressed in one or more time groups compared to the control pigs: miR-15a, miR-21, miR-146, miR-206, miR-223 and miR-451. At day one pi lung tissue protein levels of IL-6, IL-12 and IFN- α were significantly increased compared to the control group, and haptoglobin and C-reactive protein were at significantly increased at day three pi. MiRNA are small non coding RNA molecules, that regulate gene expression in a wide range of organisms. Cellular miRNAs might be involved in influenza infection, both by targeting immune related host transcripts but also by targeting viral gene products. Our results suggest that in addition to a wide range of immune factors, miRNAs are involved in fine tuning of an efficient innate immune response to influenza infection.