IL-6, IL-8, COX-2, CCL-20, etc, was observed in the presence of NS1. Real-time PCR and ELISA were used to further confirm the microarray results. Luciferase activity assay indicated that the NF-κB binding sites were essential for the regulation of IL-6 and IL-8 by NS1 protein. Further studies demonstrated that NS1 protein can suppress NF-κB activity in a dose-dependent manner. Western blot assay suggested that NS1 did not alter the expression level of NF-κB, but prevented the translocation of NF-κB from cytosol to nucleus. This inhibitory property of the NS1 protein was dependent on its ability to bind IKKα and IKKβ, which confirmed by the GST pull down, co-immunoprecipitation and confocal assay.

Results: We for the first time demonstrated that NS1 can prevent activation of NF-κB through binding to IKK& and IKK$.

Conclusion: NF-κB, an important transcription factor, plays an essential role in the regulation of immune and inflammatory responses. Therefore, NS1-mediated inhibition of the NF-κB pathway may thus play a key role in regulating the host innate and adaptive immune responses during virus infection.

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28.003

H5N1 NS1 change the cell cytoskeleton and interferes with host cell motility through the GTPase

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Background: NS1 protein of highly pathogenic avian influenza virus H5N1 contributes significantly to disease *pathogenesis* by modulating virus replication. It can inhibit innate immunity by preventing type I IFN release and inhibit adaptive immunity by attenuating human DC maturation. The ability of the protein NS1 to induce cytoskeleton changes and alter the cell motility in infected host cells is a key event in these processes. And all these may associate with the Rho subfamily of small GTP-binding proteins which mediates many fundamental cellular functions. The commonly studied members (Rho, Rac, and Cdc42) regulate actin reorganization, affecting diverse cellular responses, including adhesion, cytokinesis, and motility.

Methods: In our experiment, we use the three-dimensional cell culture system and the scanning electron microscope to detect the cell surface change after transfection of NS1 in A549 cell.

Results: We found forced expression the NS1 in A549 cell could curve the stress fibers, decrease lamellipodia and inhibit cell migration. And we found a new interaction about the NS1 and Rap1$, a member of the Ras family of small G proteins, which has been recognized as an important regulator of cell proliferation, differentiation, and adhesion, may impact the Rac1 activity and interfere the cell morphology and motility.

Conclusion: Taken together, our results suggest that the avain influenza A virus NS1 protein is a multifunctional virulence factor which can also inhibit the cell motility and change the cell morphology through interfere the GTPase' activity. Demonstrate the importance of the NS1 protein in regulating the host cell response triggered by virus infection.

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28.004

Novel influenza A H1N1 infection among healthcare workers

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Background: Knowledge of epidemiological, clinical characteristics and outcomes in healthcare workers (HCW) exposed to novel Flu A H1N1 could be useful in order to improve protection measures.

Methods: A longitudinal study was carried out at CEMIC among 1,465 HCW from June-July, 2009. Those with influenza like illness (ILI) were swabbed for detection of novel Flu A H1N1 virus by RT-PCR. Fisher's exact test or Wilcoxon were employed. Logistic regression (LR) model to identify variables associated with H1N1 virus were analyzed.

*Results:*HCW with ILI n = 85	H1N1 positive		H1N1 negative		p
	n = 43	(%)	n = 42	(%)	
Female	26	(60)	24	(57)	0.83
Age, mean (±SD)	33.4	(9)	34.1	(9)	0.72
Nurse or physician	33	(77)	31	(74)	0.81
Comorbidities	6	(14)	7	(17)	0.77
Contact with suspected/confirmed case	30	(70)	35	(83)	0.20
Use of adequate protection measures	28	(65)	26	(62)	0.82
Flu vaccination †	32	(76)	32	(78)	1.0
Fever	37	(86)	34	(81)	0.57
Asthenia	31	(72)	02	(48)	0.03
Cough	34	(79)	18	(43)	0.008
Diarrhea	4	(9)	12	(29)	0.03
Complications	5	(12)	4	(9.5)	1.0
Pneumonia	2	(5)	1	(2)	—
Oseltamivir					
Prophylactic	2	(5)	13	(31)	0.002
Therapy	41	(95)	36	(86)	0.16
Days of oseltamivir, median (IQR)	5	(5-5)	5	(3-5)	0.002
Adverse events with oseltamivir	12	(28)	8	(19) 0.44	
Days off, median (IQR) †	7	(5-7)	4	(2-6.5)	0.0004
Hospital admission	1	(2.33)	0	1.0	
Death	0	0	—		

† In 94/96 HCW.

LR with H1N1 as dependent variable showed: cough (OR 6.93; 95%CI 2.24, 21.4); prophylactic oseltamivir (OR 0.08; 95% CI 0.01, 0.43); and diarrhea (OR 0.17; 95% IC 0.04, 0.74).