Longitudinal blood cell transcriptomic profiling and *in vitro* temporal proteomics provides novel insights into metabolic reprogramming and host-immune responses against Crimean-Congo Hemorrhagic Fever Virus

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Running Head: Cellular response to CCHFV

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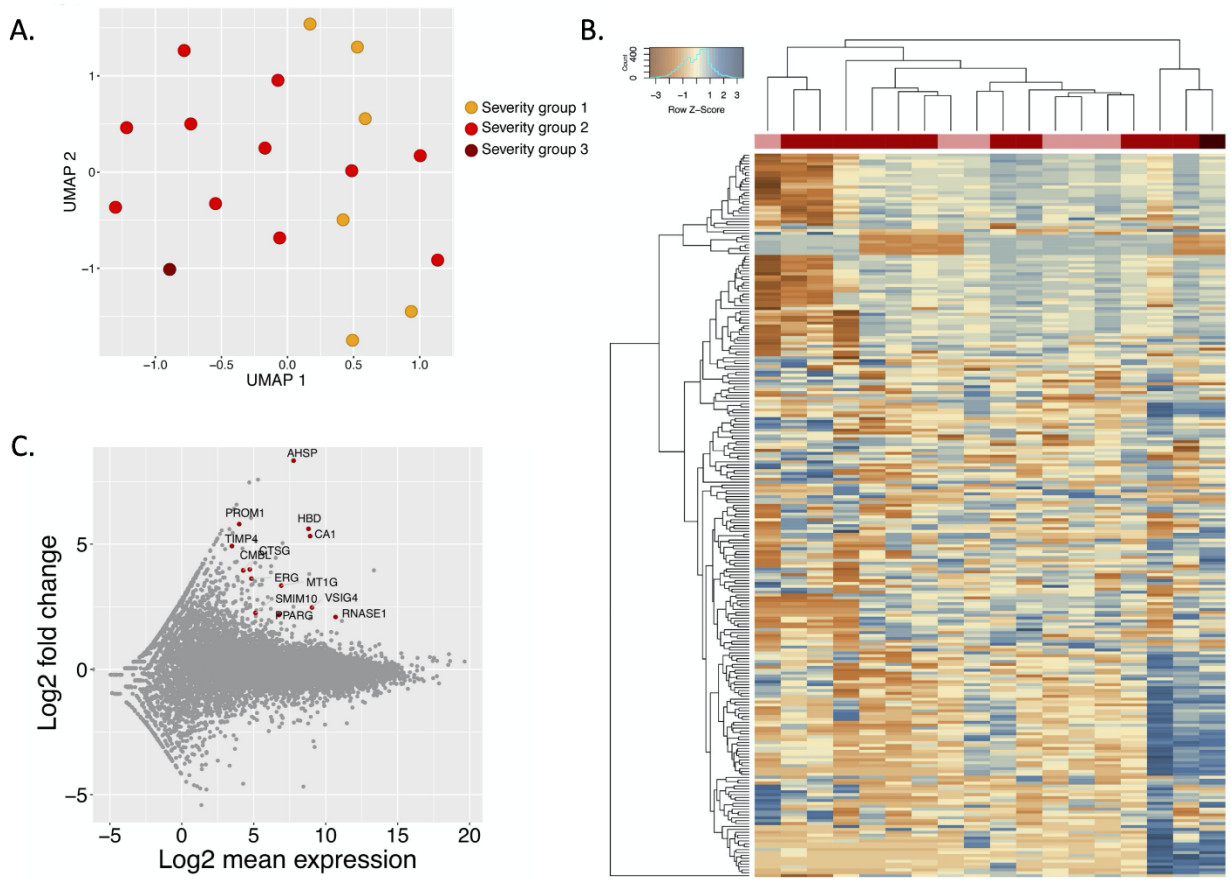
Supplementary Table S1. The CCHF patient characteristics.

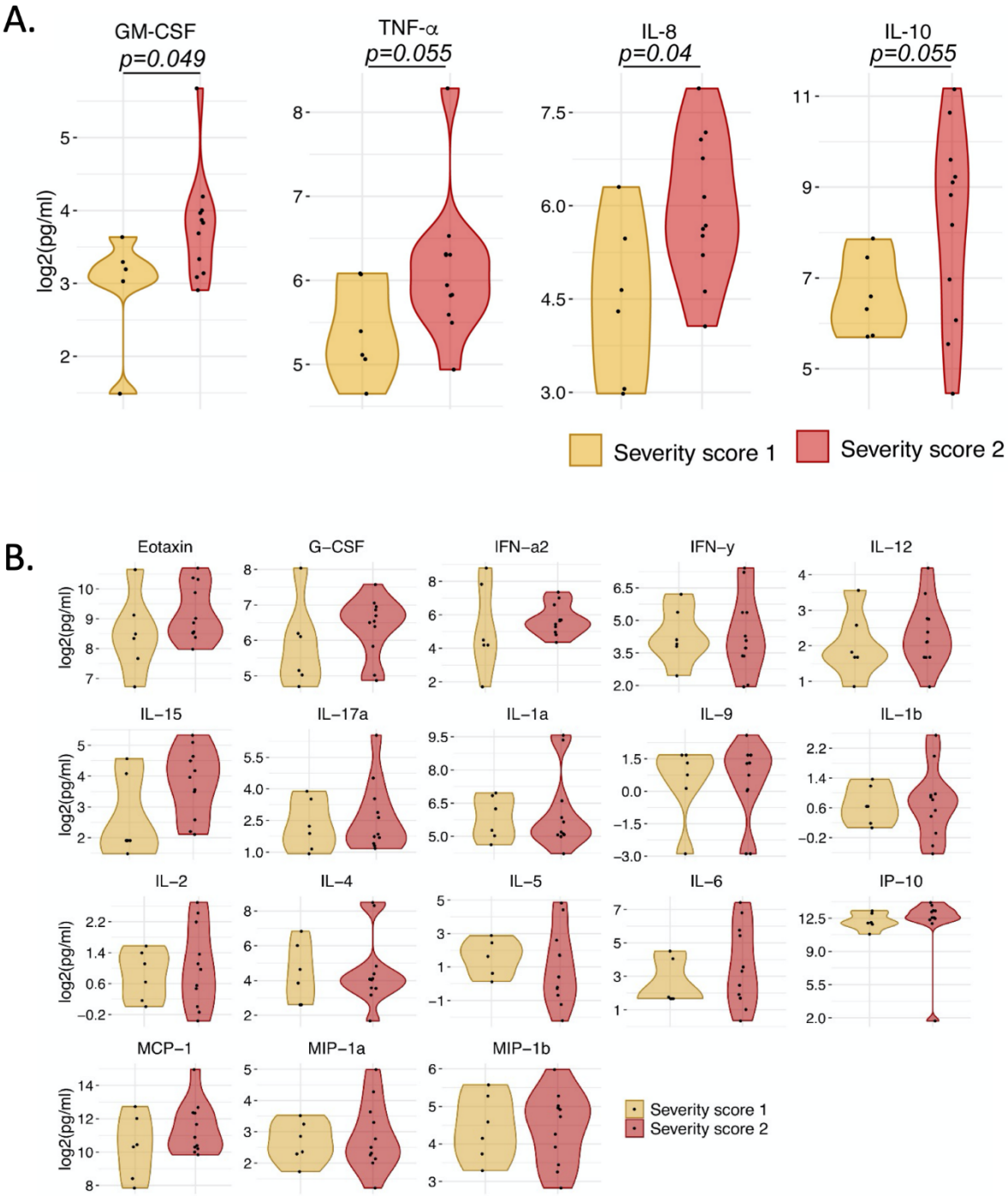
PID	Age	Gender	The date of symptoms onset	The date of hospitalization	Time to hospitalization (days)	The date of the first sampling	The date of the second sampling	SGS score	Severity group*	RT-PCR	Anti-CCHFV IgM	Outcome
P01	33	Female	30 May 2017	03 June 2017	4	03 June 2017	05 July 2018	5	1	positive	ND	Survived
P02	18	Male	06 June 2017	12 June 2017	6	12 June 2017	ND	7	2	positive	positive	Survived
P03	45	Male	12 June 2017	13 June 2017	1	14 June 2017	01 July 2018	0	1	positive	ND	Survived
P04	67	Male	13 June 2017	16 June 2017	3	17 June 2017	05 July 2018	8	2	positive	ND	Survived
P05	48	Male	12 June 2017	18 June 2017	6	19 June 2017	08 July 2018	7	2	positive	ND	Survived
P06	68	Male	13 June 2017	19 June 2017	6	20 June 2017	05 July 2018	5	1	positive	ND	Survived
P07	77	Male	19 June 2017	22 June 2017	3	23 June 2017	05 July 2018	6	2	positive	ND	Survived
P08	29	Female	20 June 2017	24 June 2017	4	25 June 2017	02 July 2018	6	2	positive	ND	Survived
P09	50	Female	20 June 2017	25 June 2017	5	26 June 2017	06 July 2018	4	1	positive	positive	Survived
P10	35	Female	07 July 2017	12 July 2017	5	12 July 2017	04 July 2018	3	1	negative	positive	Survived
P11	64	Female	15 July 2017	18 July 2017	3	19 July 2017	ND	10	2	positive	ND	Survived
P12	57	Male	16 July 2017	21 July 2017	5	22 July 2017	09 July 2018	9	2	positive	ND	Survived
P13	79	Male	22 July 2017	24 July 2017	2	24 July 2017	ND	11	3	positive	ND	Died
P14	36	Male	01 August 2017	06 August 2017	5	07 August 2017	04 July 2018	7	2	positive	ND	Survived
P15	62	Male	15 August 2017	20 August 2017	5	21 August 2017	06 July 2018	9	2	positive	ND	Survived
P16	48	Male	05 September 2017	07 September 2017	2	07 September 2017	ND	4	1	positive	ND	Survived
P17	55	Male	12 April 2018	17 April 2018	5	18 April 2018	ND	9	2	positive	ND	Survived
P18	44	Female	23 April 2018	27 April 2018	4	29 April 2018	ND	9	2	positive	ND	Survived

* 1: Low (0-5); 2: Intermediate (6-10); 3: High (11-16)

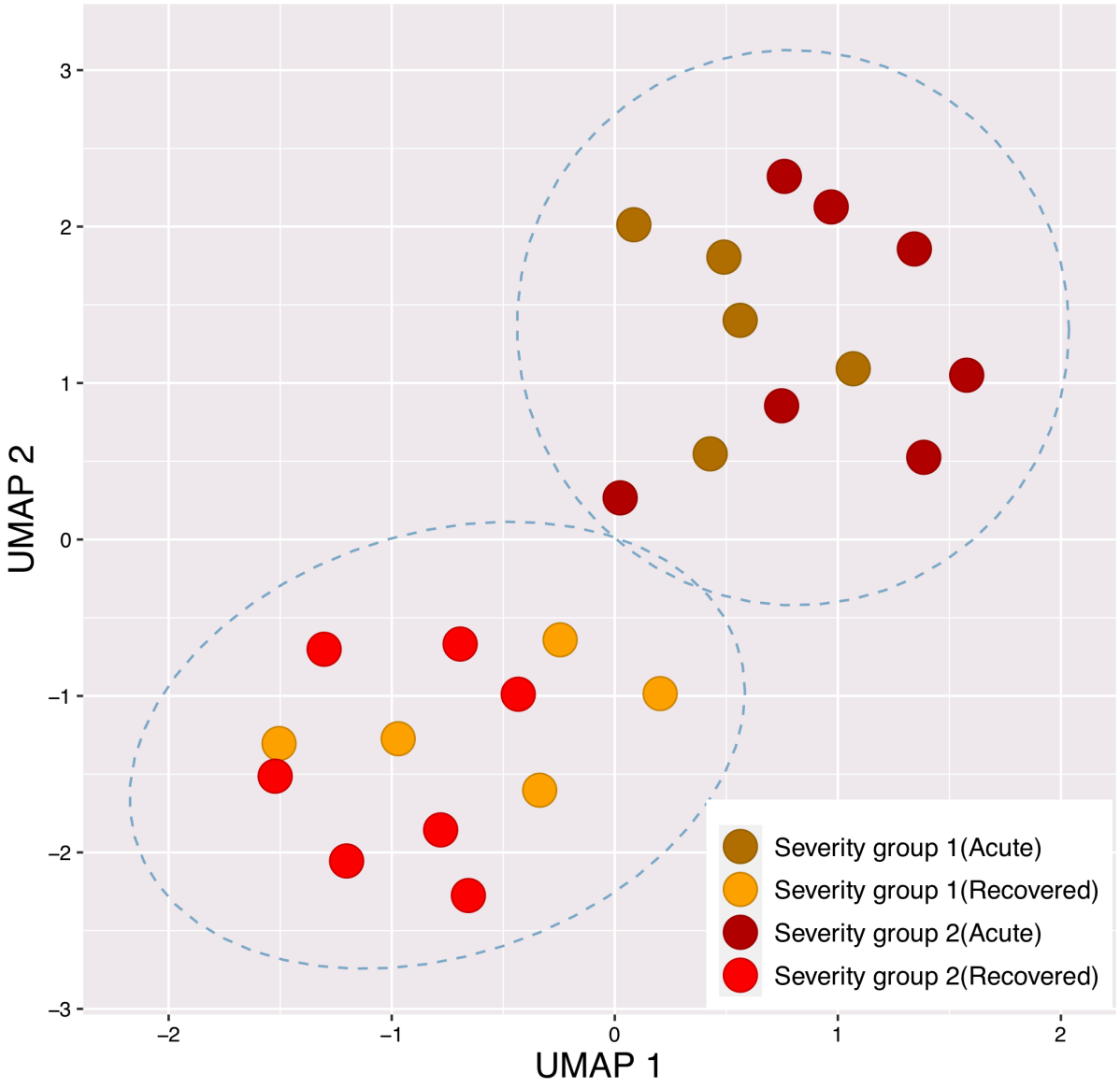
ND: not determined; SGS: severity grading system; RT-PCR: real time- polymerase chain reaction; CCHFV: Crimean-Congo haemorrhagic fever virus;



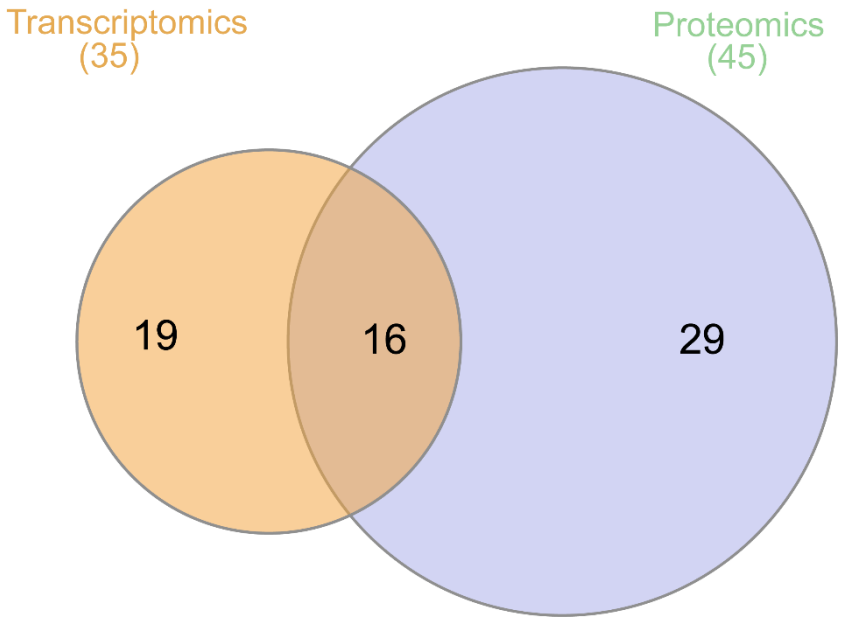
Supplementary Figure S1: S**everity group association with gene expression. (A)** Sample distribution during the acute phase of infection in different severity groups as reported. (B) The heterogenous gene-expression profile was further refined by hierarchical clustering analysis of the top 500 high variable genes **(C)** MA plot of differentially regulated genes during the acute phase between samples of severity group 1 and severity group 2 or 3.



Supplementary Figure S2. (A) Violin plot of significantly changed proteins as determined from ELISA assays. **(B)** The levels of all of the rest 18 soluble marker.

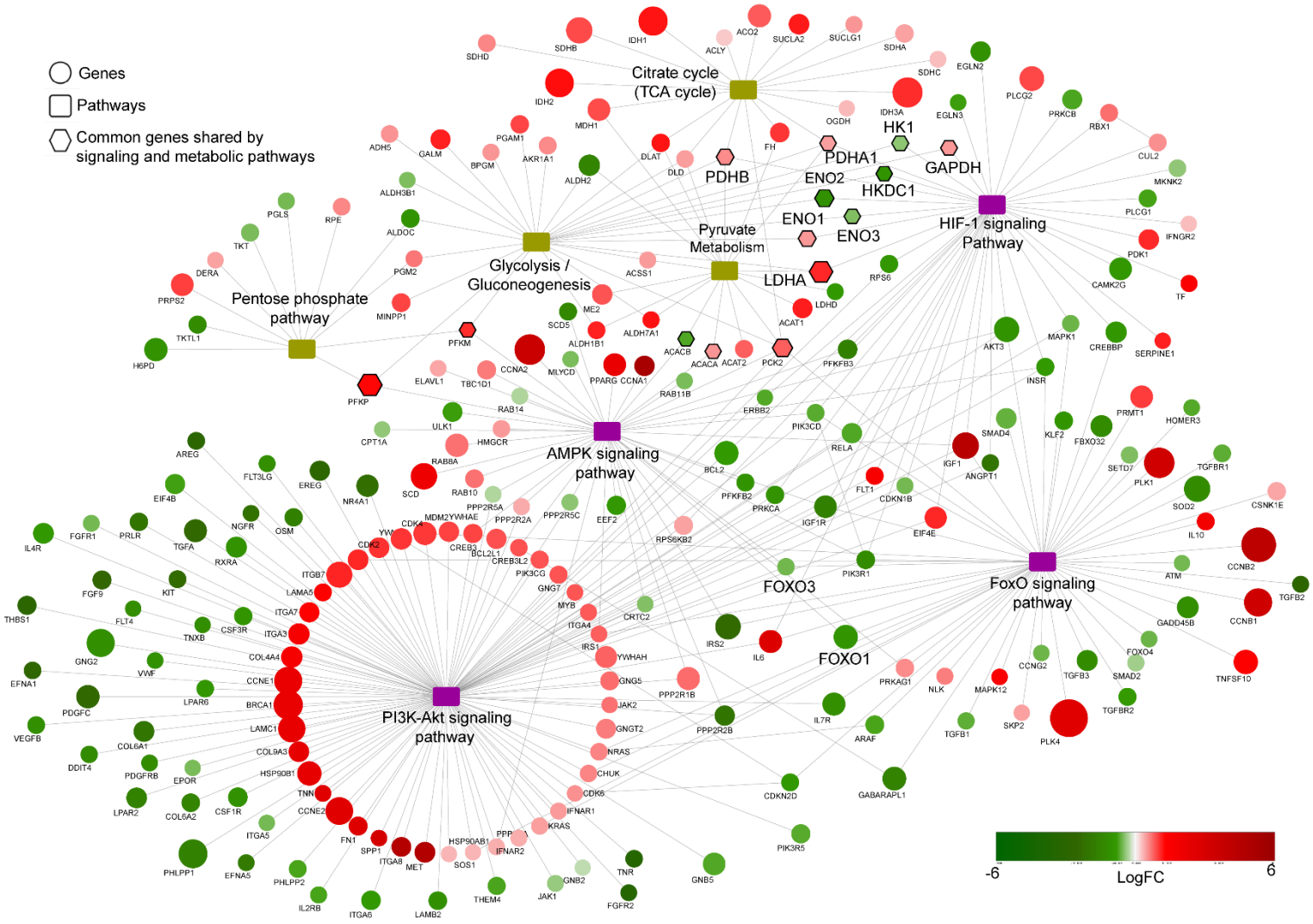


Supplementary Figure S3: UMAP clustering of the caute phase and recovered phase samples.



N-Glycan biosynthesis
Citrate cycle (TCA cycle)
Amino sugar and nucleotide sugar metabolism
FoxO signaling pathway
HIF-1 signaling pathway
One carbon pool by folate
Terpenoid backbone biosynthesis
Propanoate metabolism
AMPK signaling pathway
Fc gamma R-mediated phagocytosis
Pyrimidine metabolism
Pyruvate metabolism
Thermogenesis
Glycine, serine, and threonine metabolism
Glycolysis / Gluconeogenesis
Purine metabolism

Supplementary Figure S4: Overlap of the pathways identified between patients based transcriptomics data and in vitro cellular data.



Supplementary figure S5. Potential pathways regulated by CCHFV during acute phase of infection

Supplemental Table Sx:

Name	**Fwd** **Sequence (5' to 3')**	**Rev** **Sequence (5' to 3')**
ISG15	CGCAGATCACCCAGAAGATCG	TTCGTCGCATTTGTCCACCA
IFIT1	TCTCAGAGGAGCCTGGCTAA	TGACATCTCAATTGCTCCAGA
MX1	CCAGCTGCTGCATCCCACCC	AGGGGCGCACCTTCTCCTCA
MX2	CAGAGGCAGCGGAATCGTAA	TGAAGCTCTAGCTCGGTGTTC
β-actin	AAAGCCTGCCGGTGACTAAC	AGGAAAAGCATCACCCGGAG