Analysis of Blood Myxovirus Resistance Protein A For Diagnosis of Upper Respiratory Viral Infections

Sunjoo Kim

Department of Laboratory Medicine, Gyeongsang National University College of Medicine, Jinju, Korea

Abstract

Background: Upper respiratory tract infections are very common illness, and viruses are the most common cause. Myxovirus resistance protein A (MxA) is induced by type 1 interferons during viral infections and inhibits viral replication. We investigated the usefulness of blood MxA analysis for diagnosis of respiratory viral infections for the first time in Korea.

Methods: We evaluated the clinical performance of AFIAS MxA (Boditech Med, Inc., Korea) using EDTA, heparinized, and capillary blood collected from patients (n=66) with upper respiratory tract infections. Healthy people (n=48) without symptoms of respiratory infections were recruited as a control group. The Allplex™ Respiratory Panel 1, 2, 3 and Allplex™ SARS-CoV-2 Assay multiplex real-time RT-PCR (Seegene, Korea) were used to confirm viral infections using the nasopharyngeal swabs.

Results: The AFIAS models 1, 3, 6, and 10 showed excellent sensitivity (98%-100%) and specificity (92%-94%) for the EDTA blood regardless of virus type (SARS-CoV-2, n=19; Influenza A, n=11; Influenza B; n=39; Human Rhinovirus, n=4). The area under the ROC (receiver operating characteristics) curve ranged 98.7%-99.6%. Heparinized- and capillary blood showed an equivalent sensitivity and specificity.

Conclusion: AFIAS MxA was useful to screen respiratory viral infections. As MxA levels in capillary blood showed a comparable result with those of EDTA blood, it could be considered as a point-of-care test in outpatient clinics.

Introduction

- ❑COVID-19
- ❑Influenza
- ❑Human rhinovirus

Currently the most concerning RTIs

Very common

Over-prescribed Abx

Difficult to diagnose viral RTIs

Rapid and **accurate** screening test → Viral RTIs – No need Abx

Objective: To evaluate the usefulness of blood MxA analysis for diagnosis of upper respiratory viral infections for the first time in Korea.

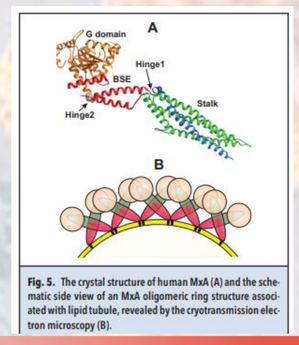

Fig. 5. The crystal structure of human MxA (A) and the schematic side view of an MxA oligomeric ring structure associated with lipid tubule, revealed by the cryotransmission electron microscopy (B).

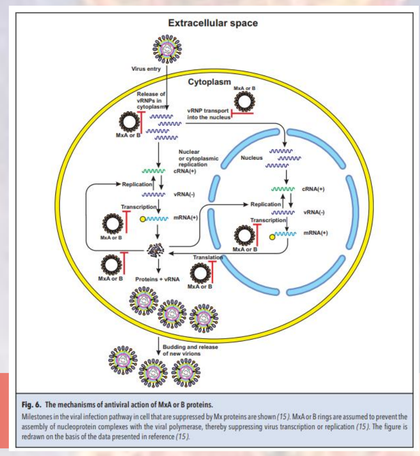

Fig. 6. The mechanisms of antiviral action of MxA or B proteins.
Milestones in the viral infection pathway in cell that are suppressed by Mx proteins are shown (*15*). MxA or B rings are assumed to prevent the assembly of nucleoprotein complexes with the viral polymerase, thereby suppressing virus transcription or replication (*15*). The figure is redrawn on the basis of the data presented in reference (*15*).

Methods

Viral RTI confirm — **MxA**

Sample collection

Fresh samples collected by nasopharyngeal swab

EDTA, heparin, capillary blood

Sample transport — **VTM**

AFIAS 1, 3, 6, 10

Analysis — **Seegene Allplex RT-PCR**

Analysis of MxA

Interpretation — **SARS-CoV-2, Flu A, Flu B, HRV**

Sensitivity, Specificity, AUC-ROC, cutoff

Subjects: Sx with RTI, n=66 vs. normal control, n=44

Results

Table 1. Clinical performance, area under the ROC curve, and optimal cutoff of the AFIAS MxA using EDTA blood for diagnosis of respiratory viral infections

AFIAS MxA	RT-PCR		Sensitivity	Specificity	AUC-ROC	Optimal Cutoff (ng/ml)
	Positive	Negative	%(95%CI)	%(95%CI)	%	
AFIAS1						
Positive	65	3	98(92-100)	94(83-99)	98.7	47.57
Negative	1	45				
AFIAS3						
Positive	66	4	100(95-100)	92(80-98)	99.7	58.69
Negative	0	44				
AFIAS6						
Positive	66	4	100(92-100)	92(80-98)	99.6	48.28
Negative	0	44				
AFIAS10						
Positive	66	4	100(95-100)	92(80-98)	99.6	35.04
Negative	0	44				

Table 2. Sensitivity and specificity of the AFIAS1 MxA for EDTA- and capillary blood

Sample type	RT-PCR		Sensitivity	Specificity	AUC-ROC	Optimal Cutoff (ng/ml)
	Positive	Negative	%(95%CI)	%(95%CI)	%	
EDTA blood						
Positive	65	3	98(92-100)	94(83-99)	98.7	47.57
Negative	1	45				
Capillary blood						
Positive	65	4	98(92-100)	92(80-98)	99.3	65.54
Negative	1	44				

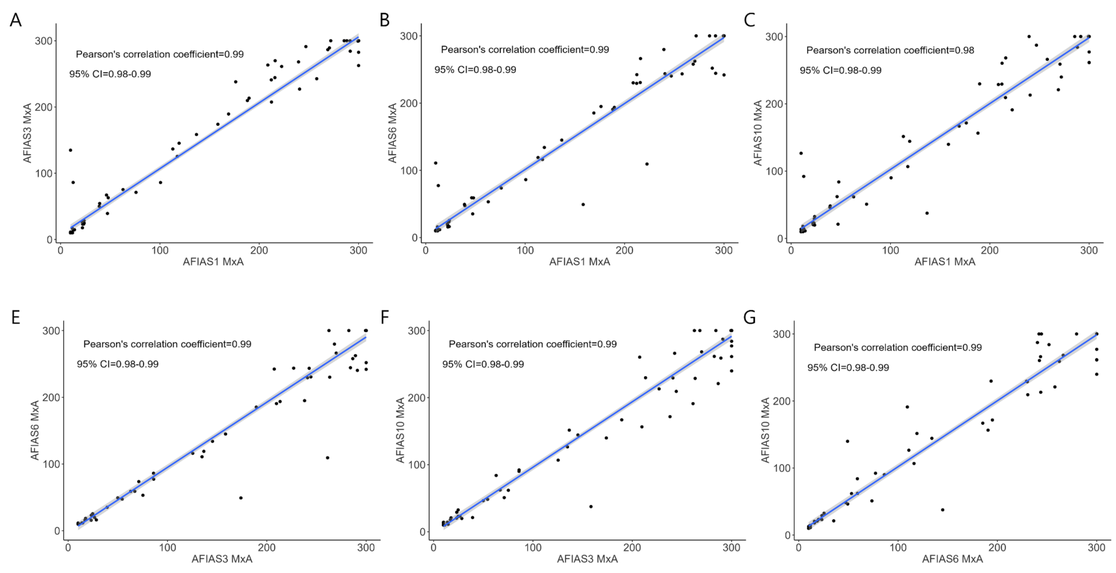

Fig. 1. Correlation analysis of four different AFIAS models, 1, 3, 6, and 10 for MxA for the EDTA blood.

Conclusions

- ✓The sensitivity (98-100%) and specificity (92-94%) of all AFIAS models were exceedingly high for EDTA blood. Optimal cutoff is slightly higher than the recommended (30 ng/ml) by the manufacturer.
- ✓The sensitivity and specificity of EDTA and capillary blood were excellent, indicating POC MxA could be applied in the outpatient clinic.
- ✓Regardless of the AFIAS model (1, 3, 6, 10), the MxA measurements were all highly correlated to each other (all correlation coefficients ≥ 0.98).
- ✓ Excellent sensitivity (100%) and specificity (92%) were confirmed regardless of virus type (SARS-CoV-2, n=19; FluA, n=11; FluB, n=39; HRV, n=4).
- ✓ In conclusion, blood MxA analysis proved to be useful to screen viral RTIs.