Acute Viral and Bacterial Infection Differentiation: Comparison of Novel Analytical Methods of Myxovirus Resistance Protein A (MxA) Quantitative Determination

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Introduction

The early distinction between viral and bacterial infections in patients is difficult based on clinical or routinely available biological findings only. Due to this fact, patients are often unnecessarily treated with antibiotics, which results in the emergence of antibiotics resistance. Myxovirus resistance protein A (MxA) is mentioned in number of studies as an important antiviral factor that inhibits the multiplication of RNA and DNA viruses. It is an intracellular protein produced by cells of the immune system after stimulation by type I and III interferons in response to a viral infection. Rhedin et al. used MxA to differentiate between bacterial and viral infection in children with lower respiratory tract infection. The highest MxA values were achieved in samples positive for influenza and respiratory syncytial virus. A study by Toivonen et al. demonstrated that some types of viral respiratory disease agents (respiratory syncytial virus, influenza A and B viruses, parainfluenza virus, etc.) induced significantly higher levels of MxA than others (rhinovirus, coronaviruses).

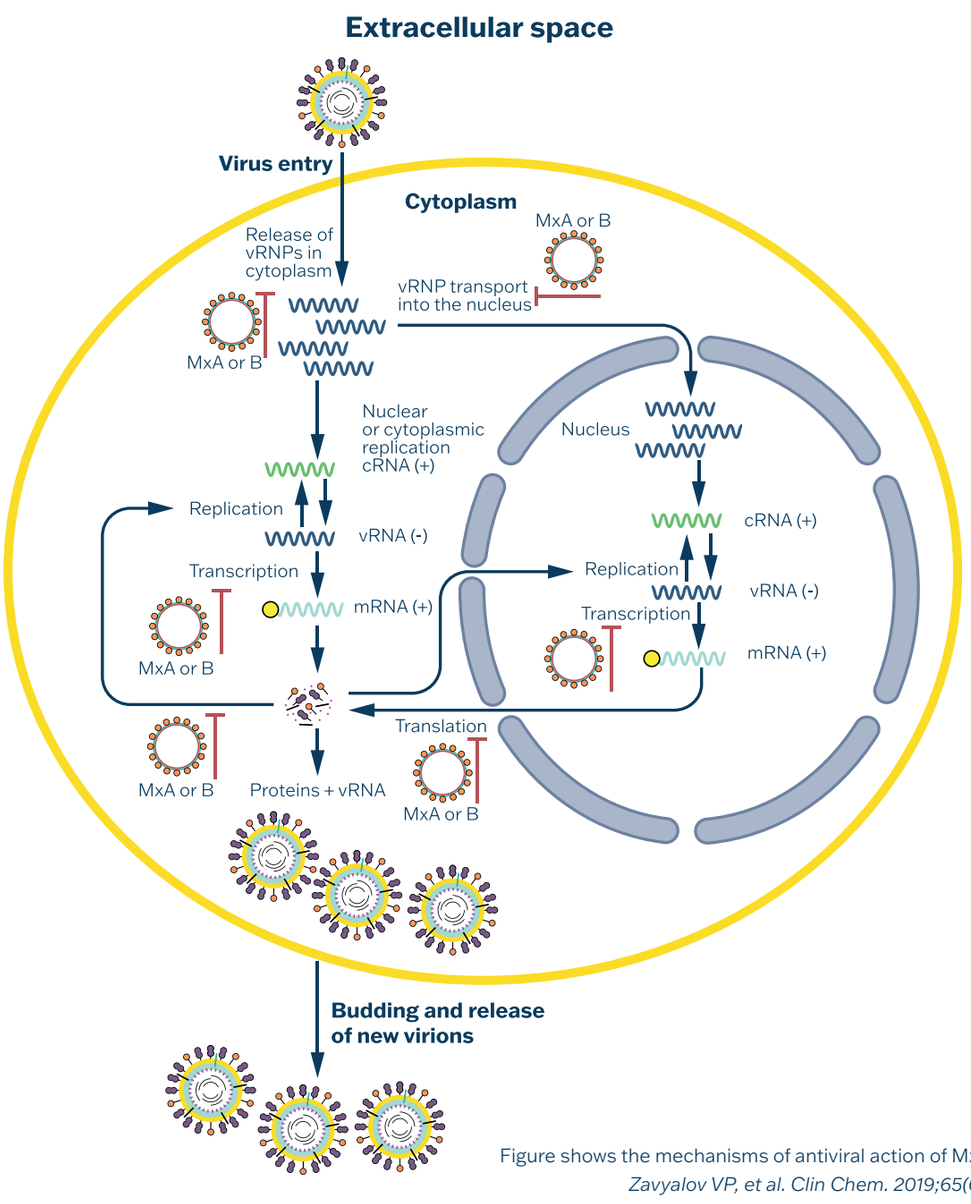


Figure shows the mechanisms of antiviral action of Mx proteins.
Zavyalov VP, et al. Clin Chem. 2019;65(6):739-750

Materials and methods

Sample collection

Whole blood samples were collected from healthy individuals, patients with > 50 mg/L CRP levels and patients with confirmed acute COVID-19 (each group n = 10). EDTA tubes for the sample collection were used.

Methods

MxA concentration in whole blood lysates was determined by three different analytical methods:

CLIA MxA KleeYa®, TestLine

CLIA MxA allows detection of MxA antigen in whole blood sample by the automated analyzer KleeYa. Whole blood samples are lysed using lysis buffer in the ratio of 1:10 for 30 minutes before analysis, outside the analyzer. Bead-based technology with sensitive flash chemiluminescence detection provides light intensity as measurement results that can be quantified according to a defined calibration and threshold for viral infection at concentration level 200 ng/mL.

MxA Protein Human ELISA, BioVendor

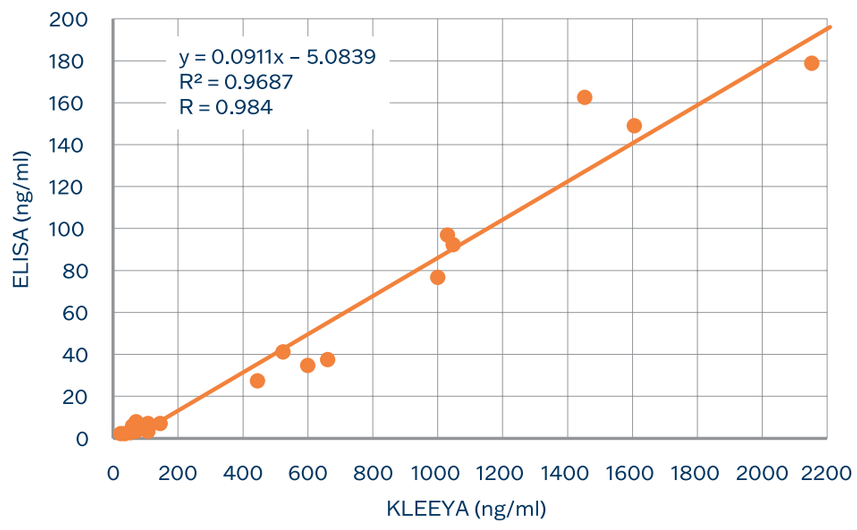
MxA Protein Human ELISA provides quantitative measurement of MxA protein in whole blood lysate. Cut-off value for viral infection is estimated to concentration MxA 20 ng/mL.

LFT Bi-VirTest® with Bi-Reader®, Bioinova

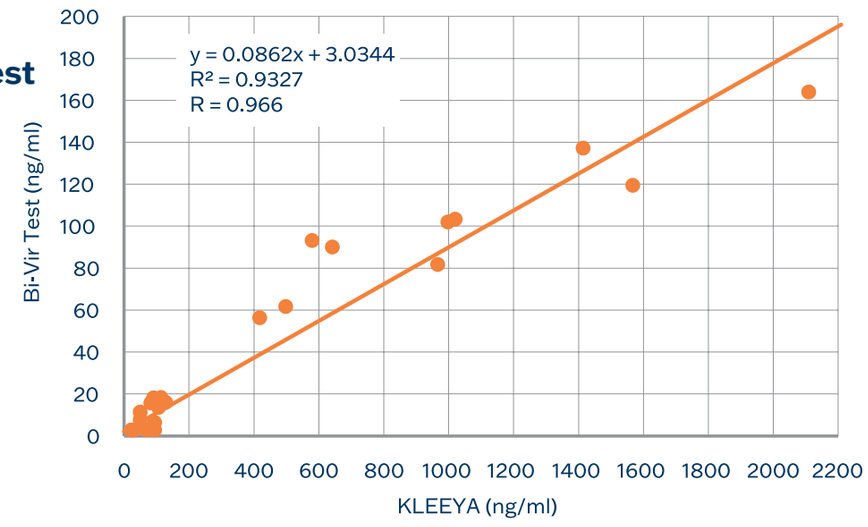
Bi-VirTest is intended to detect MxA in lysed whole blood sample. After the incubation period specified within the test reaction cassette is inserted into a calibrated Bi-Reader instrument for results quantification. Threshold for viral infection is set to concentration level 25 ng/mL.

Results

Correlation KleeYa and ELISA



Correlation KleeYa and Bi-Vir test



Correlation ELISA and Bi-Vir Test

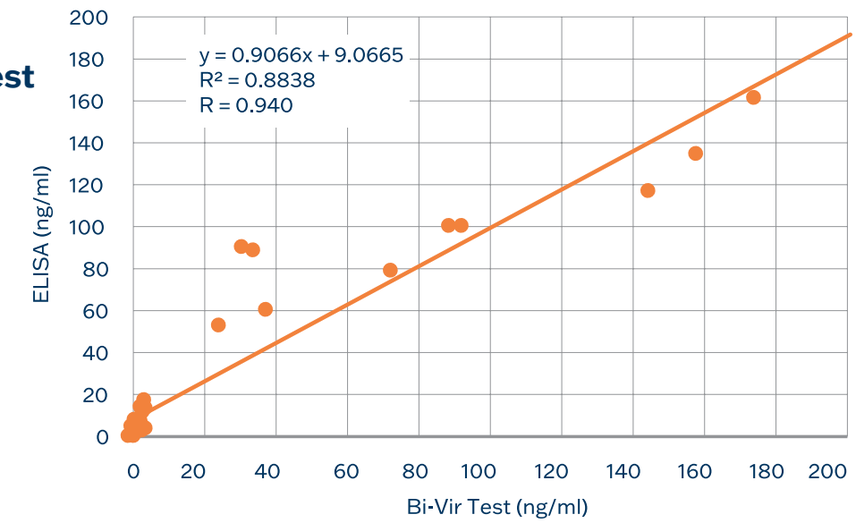


Figure shows correlation graphs for three different analytical methods (CLIA MxA KleeYa®, MxA Protein Human ELISA and Bi-VirTest®).

The measurement results depend on used analytical method. The average MxA concentrations in healthy individuals were determined at 2.0 ng/mL, 1.9 ng/mL, and 64.7 ng/mL in ELISA, LFT, and CLIA, respectively. In the CRP-elevated group, the average MxA levels were 4.2 ng/mL (ELISA), 9.7 ng/mL (LFT), and 88.4 ng/ml (CLIA). Significantly higher average MxA concentrations were found in the patient group with COVID-19: 86.2 ng/mL (ELISA), 99.4 ng/mL (LFT) and 1028.8 ng/mL (CLIA). The performance of CLIA and ELISA/LFT displayed excellent correlation with regression coefficients of r = 0.98 and r = 0.97, respectively. Very good correlation was observed also between ELISA and LFT (r = 0.94). Differences in order of magnitude in read concentrations between ELISA/LFT and CLIA result from previously exercised calibration setup using cell lysate with native MxA for the former methods in contrast to recombinant protein-based calibration utilized for the latter technique.

Conclusions

- The MxA measurement has a high potential for early diagnosis of acute viral infections
- The new sensitive CLIA method correlates well with ELISA and the new LFT Bi-VirTest®
- Introduced analytical methods are suitable for clinical laboratory requirements

References

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