

Characterization of MX1 and ISG15 gene mutations and their functional implications in SARS-CoV-2 infected patients

Mashaba DM¹, Mothapo KM¹, Selabe SG^{1,2}, Gededzha MP¹

¹Department of Virology, School of Medicine, Sefako Makgatho Health Sciences University

²National Health Laboratory Service, Pretoria, South Africa

Introduction

The potential re-emergence of COVID-19 due to rapid development of SARS-CoV-2 mutations remains a significant thread. Interferon Stimulated Genes including MX1 and ISG15 have been demonstrated to play major roles in most RNA viral infections and shown to be upregulated after the onset of SARS-CoV-2 thus, highlighting their impact on disease susceptibility. Therefore, this study aimed to investigate genetic variations of interferon signaling genes (MX1 and ISG15) in the nasopharynx of SARS-CoV-2 infected patients.

Method

MX1 and ISG15 genes were amplified and sequenced using Sanger sequencing. Sequences were assembled using ChromasPro and aligned and translated using BioEdit. Phylogenetic construction was performed with MEGA 11. Post-translational modification analysis was performed using NetOGlyc 4.0, NetNGly 1.0 and Netphos 3.1 to predict O-linked glycosylation, N-linked glycosylation and phosphorylation sites, respectively.

Results

This study analyzed 119 residual nasopharyngeal swab samples collected from patients between 2020 and 2024. A total of 7 mutations were identified in MX1, while ISG15 exhibited 3 mutations. An estimated 9% of SARS-CoV-2 positive patients had an A26220 insertion in the MX1 gene resulting in a frameshift predicted to affect protein function.

These sequences uniquely showed a glycosylation site at position 26365, whereas the majority (91.2%) lacked predicted glycosylation sites and had variation in phosphorylation pattern. More variability was observed in MX1 compared to ISG15, which remained highly conserved in the phylogenetic tree with consistent glycosylation and no variation in phosphorylation sites.

Conclusion

These findings demonstrate that MX1 has more genetic and functional variability than ISG15, with specific mutations potentially influencing protein structure and antiviral activity. In contrast, the conserved nature of ISG15 suggests a stable role in host antiviral defense. Collectively, this study highlights the potential of MX1 as a biomarker for disease susceptibility and supports the relevance of both genes as targets for therapeutic intervention in COVID-19.