Discovery and Subsequent Diagnostic Verification of Autoantibodies Against the Major Vault Protein (MVP) in Systemic Lupus Erythematosus

P. Budde1, Johannes Schulte-Pelkum1, Daniel Wirtz1, Hans-Dieter Zuchl1, Heike Göhler1, Stefan Vordenbümmel1, Peter Schulz-Knappe1 and Matthias Schneider2,

1Protagcn AG, Dortmund, Germany, 2Rheumatology, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany

Introduction

- SLE is a clinically and genetically heterogeneous disease with a high demand for biomarkers to discriminate subgroups of patients with different risk profiles, disease activity, organ-specific involvements, and drug response profile.
- The broad spectrum of autoantibody specificities in SLE may mirror several pathogenic mechanisms and pathways promoting loss of B cell tolerance.
- Here we describe the identification of autoantibodies against the major vault protein (MVP) in SLE and its subsequent development into an ELISA-based assay.
- MVP is an interesting autoantibody target, because it plays a pivotal role in virus-induced host response and induces upregulation of IFN type I expression (1).

Methods

Anti-MVP antibodies were discovered by high-content autoantibody profiling using the bead-based Luminex xMAP platform SeroTag® and validated in >700 SLE samples. To assess the added benefit of this novel SLE marker, we combined MVP with classical SLE autoantibodies into a multi-marker assay. The NavigAID SLE array contains 86 antigens and expands the clinician’s ammamentarium to stratify SLE into five serological distinct subgroups (2). To enable the development of smaller ELISA-based multi-marker panels, we have developed anti-MVP into a prototypic bead-based ELISA format.

Results

Prevalence of anti-MVP antibodies in SLE

Anti-MVP antibodies occurred with frequencies of 15-30% in three different SLE cohorts.

Specificity of anti-MVP antibodies

Anti-MVP antibodies and anti-ribosomal P have comparable sensitivity (23% vs 25%) and specificity (97%) for SLE (Fig. 3).

Exploratory testing of multi-marker panels including anti-MVP in combination with anti-dsDNA, anti-ribosomal P and anti-SmD yielded a 6% increase in sensitivity at 98% without loss of specificity.

Anti-MVP defines a distinct subset of SLE patients

VisRank data visualization was applied to analyze whether anti-MVP in combination with established markers can separate the groups. The RadViz plot in Fig. 5 shows that anti-MVP is detected in a subset of SLE patients with little overlap to other markers.

Development of anti-MVP prototype ELISA

A bead-based ELISA was developed for measuring anti-MVP antibodies. The performance of the anti-MVP ELISA was assessed in a small sample set. The Pearson’s correlation coefficient of ELISA values with Luminex signal intensities was R=0.88 indicating successful platform transfer.

Conclusions

Anti-MVP autoantibodies represent a useful diagnostic marker in SLE and, in combination with anti-dsDNA, anti-Sm and anti-ribosomal P, optimizes the strategy for autoantibody testing. Furthermore, although more studies are needed, our findings suggest a previously undescribed linkage of type I INF and autoantibody targets in SLE.