Skin MDA5⁺ dermatomyositis is associated with stronger type I interferon signature with up-regulation of IFN- κ transcript

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Introduction

Dermatomyositis (DM) is a chronic auto-immune disorder affecting skin and muscle.

The transcriptomic signature of DM is characterized by a type I interferon (IFN) signature.

Among autoantibodies, anti-Melanoma differentiation associated gene 5 (MDA5) antibodies are associated with a unique presentation.

We assessed the global gene expression in the skin of 3 MDA5⁺ DM and compared it to 5 MDA5⁻ DM and 5 healthy individuals.

Results

Methodology

Patients: 8 DM patients were enrolled according the ENMC criteria. No patient received immunosuppressive drugs before sample collection.

Skin samples and RNA extraction: 20 10- μ m-thick frozen sections were taken and total RNA was extracted using the "RNeasy Mini Kit Plus".

Microarray experiments: 2ng of total RNA was amplified, labeled, and fragmented using Gene Chip WT Pico and hybridized onto Human Transcriptome 2.0 (ThermoFisher Scientific).

Immunohistochemistry: MxA expression was assessed on FFPE skin tissue samples. An indirect immunoperoxidase method on 5 μ m-thick tissue sections was performed using anti-human-MxA/Mx1 as primary antibody

Conclusion

DM skin is associated with a specific transcriptomic signature including an activation and infiltration of immune cells and a type I IFN response signature.

The type I IFN signature is more strongly expressed in the skin of MDA5⁺ versus MDA5⁻ DMs. Potential role of keratinocytes and IFN- κ over IFN- α in the skin pathophysiology of MDA5⁺ DM.