Multiplex analysis of serum cytokine profiles in patients with multiple sclerosis and systemic lupus erythematosus

Evgeny Ermakov[1], Mark Melamud[1], Anastasia Boiko[2], Daria Parshukova[2], Alex Sizikov[3], Svetlana Ivanova[2], Georgy Nevinsky[1], and Valentina Buneva[1]

[1] Institute of Chemical Biology and Fundamental Medicine, SB RAS, Novosibirsk, Russia
[2] Mental Health Research Institute, Tomsk National Research Medical Center, Tomsk, Russia
[3] Institute of Clinical Immunology, SB RAS, Novosibirsk, Russia

Motivation and Aim

- Cytokines are peptide regulators of the immune system cells.
- A cytokine profile is a set of a wide range of cytokines in one person at a certain point in time.
- Dysregulation of cytokine networks is known to be associated with various autoimmune diseases including multiple sclerosis (MS) and systemic lupus erythematosus (SLE).
- However, the detailed changes in serum cytokine profiles in MS and SLE are poorly understood.
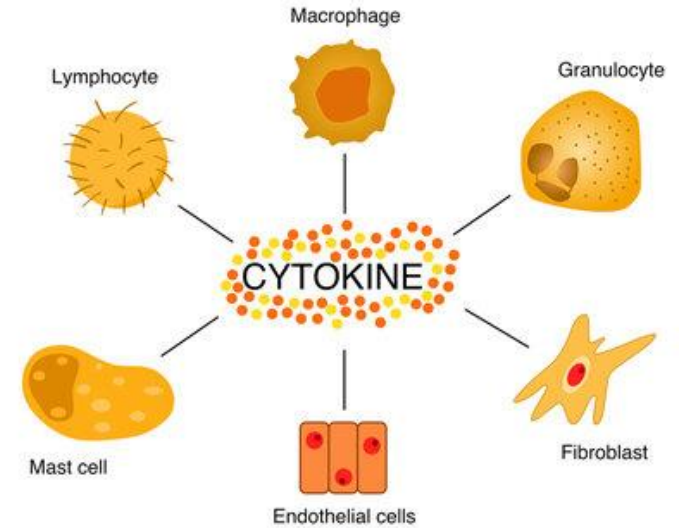
The aim of this work was to investigate changes in the serum cytokine profiles in MS and SLE patients in comparison with healthy donors in one series of experiments.

Methods

- The analysis was carried out by the multiplex method on a MAGPIX analyzer (Luminex, USA) using the MILLIPLEX MAP Human Cytokine/Chemokine Magnetic Bead Panel - Premixed 41 Plex - Immunology Multiplex Assay kit (Merck Millipore, USA).

- The concentration of the following 41 cytokines was measured: EGF, FGF2, Eotaxin 1, TGF-a, G-CSF, Flt-3L, GM-CSF, Fractalkine, IFNa2, IFNy, GRO, IL-10, MCP-3, IL-12P40, MDC, IL-12P70, PDGF-AA, PDGF-AB/BB, IL-13, IL-15, sCD40L, IL-17A, IL-1RA, IL-1a, IL-1b, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IP-10, MCP-1, MIP-1a, MIP-1b, RANTES, TNFa, TNFb, VEGF.

- Statistical analysis (Kruskal-Wallis ANOVA, Dunn's test, Spearman correlation analysis, Bonferroni correction for multiple hypothesis testing) was carried out in STATISTICA 10 and ORIGIN 2021 programs.

- Analysis of changes in cytokine profiles was performed by principal component analysis and partial discriminant least squares analysis using the CytokineExplore online resource (http://al-saleh.cc/exabx.com/apps/cytokineexplore/).

- Volcano plots that reflect the dependence of the Log_2 fold changes of the median values on the $-\text{Log}_{10}$ p-value were plotted.

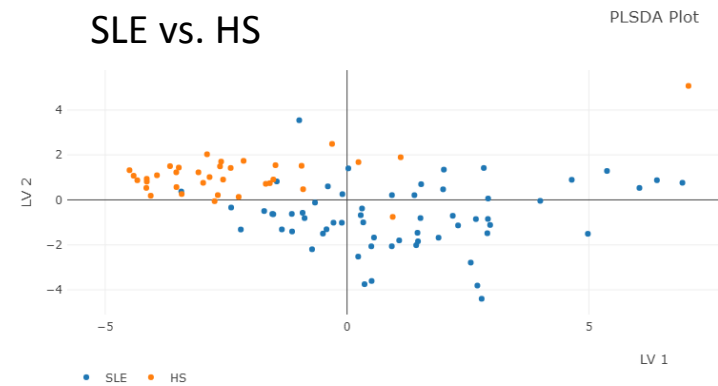| Population	n, peoples
Healthy Subjects (HS)	36
SLE patients	60
MS patients	55

All patients received anti-inflammatory therapy.

3

Results: The combined multicytokine profiles are different
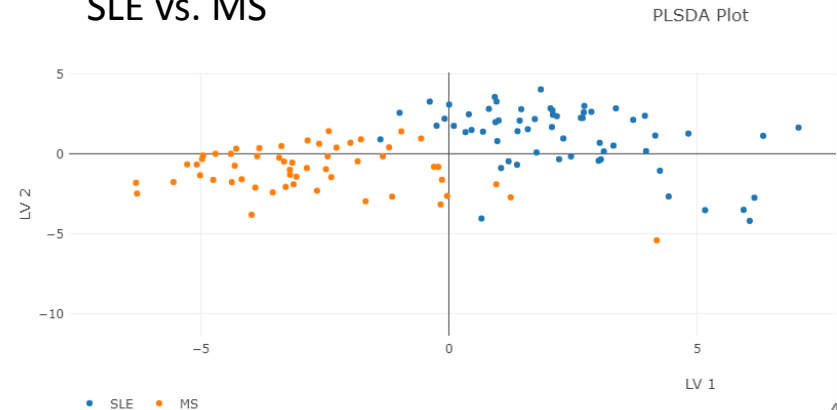

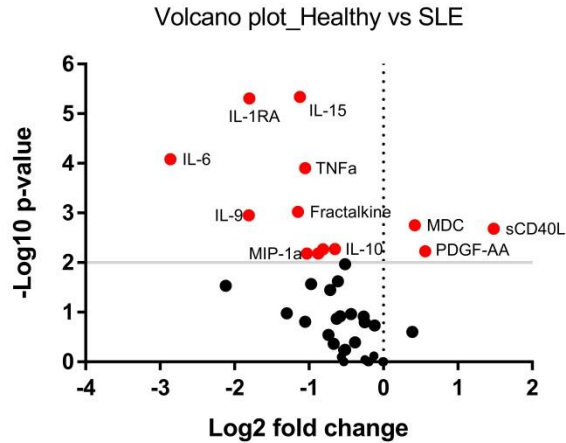MS vs. HS
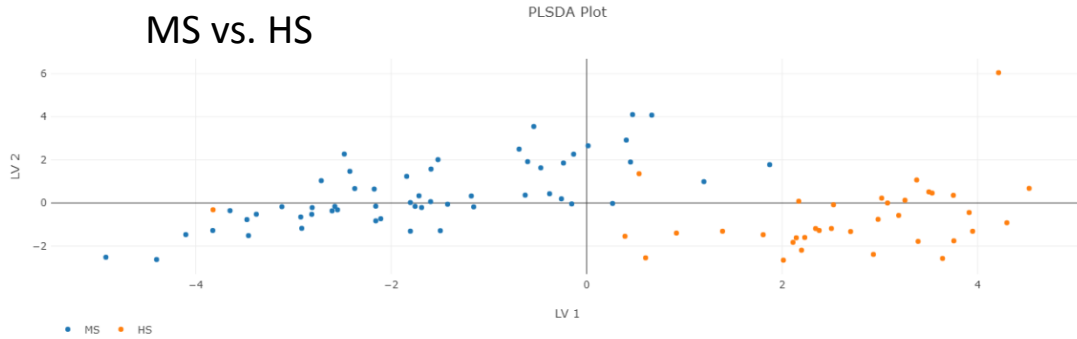
SLE vs. HS

SLE vs. MS

Principal component analysis and discriminant least squares analysis showed that the combined multicytokine profiles of the studied groups differed significantly.
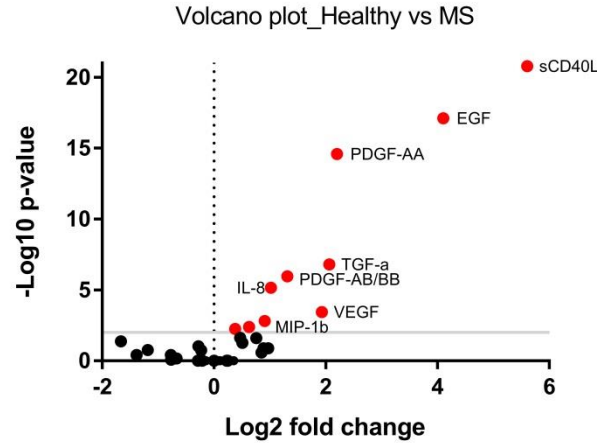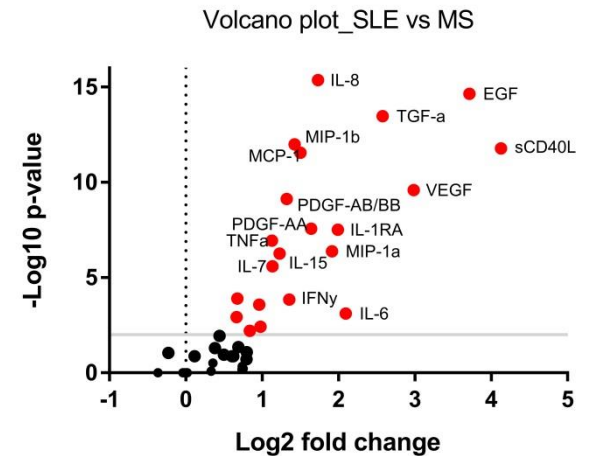
Results: Changes in cytokine levels in SLE or MS patients and healthy controls

Volcano plot_Healthy vs SLE

Volcano plot_Healthy vs MS

Volcano plot_SLE vs MS

Significantly changed 13 of the 41 analyzed cytokines

Significantly changed 10 of the 41 analyzed cytokines

Significantly changed 21 of the 41 analyzed cytokines

Conclusion

The cytokine profiles in SLE and MS patients differ significantly both in comparison with healthy individuals and between these diseases. These data will help to better understand the differences in cytokine network dysregulation in MS and SLE.

Thank you for your attention