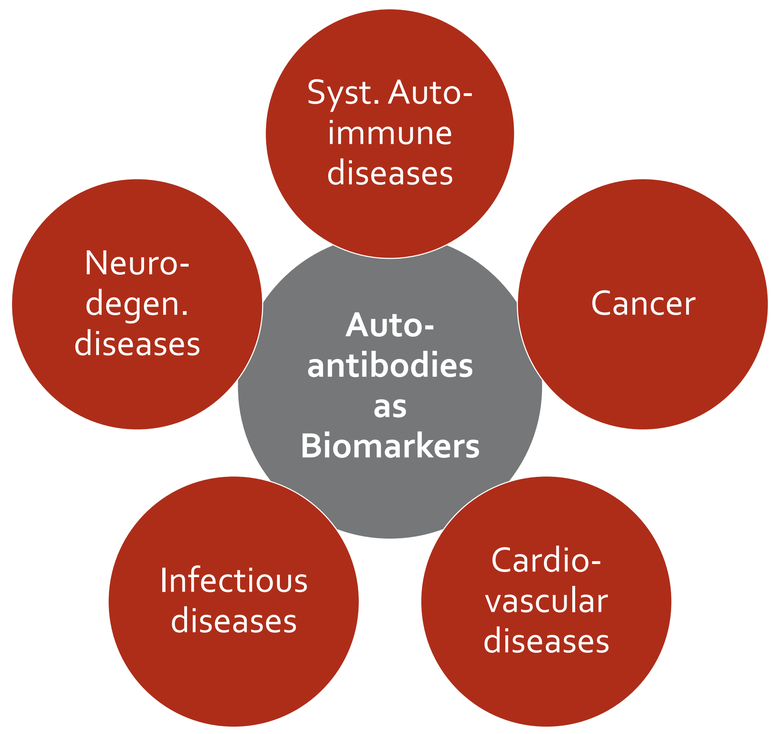
Biomarker Discovery for Systemic Lupus Erythematosus (SLE) using engine Human Protein Arrays

Background: SLE as Autoimmunity Example

- Causes are unknown
- Difficult early diagnosis due to unspecific symptoms
- Immune system attacks patients own tissues: joints, skin, brain, lungs, kidneys, and blood vessels
- Primarily immunosuppressive drugs as treatment
- Causes of death: organ failure, infection, or cardiovascular disease from accelerated atherosclerosis.

→ **Where to start biomarker discovery, if disease affects everything?**

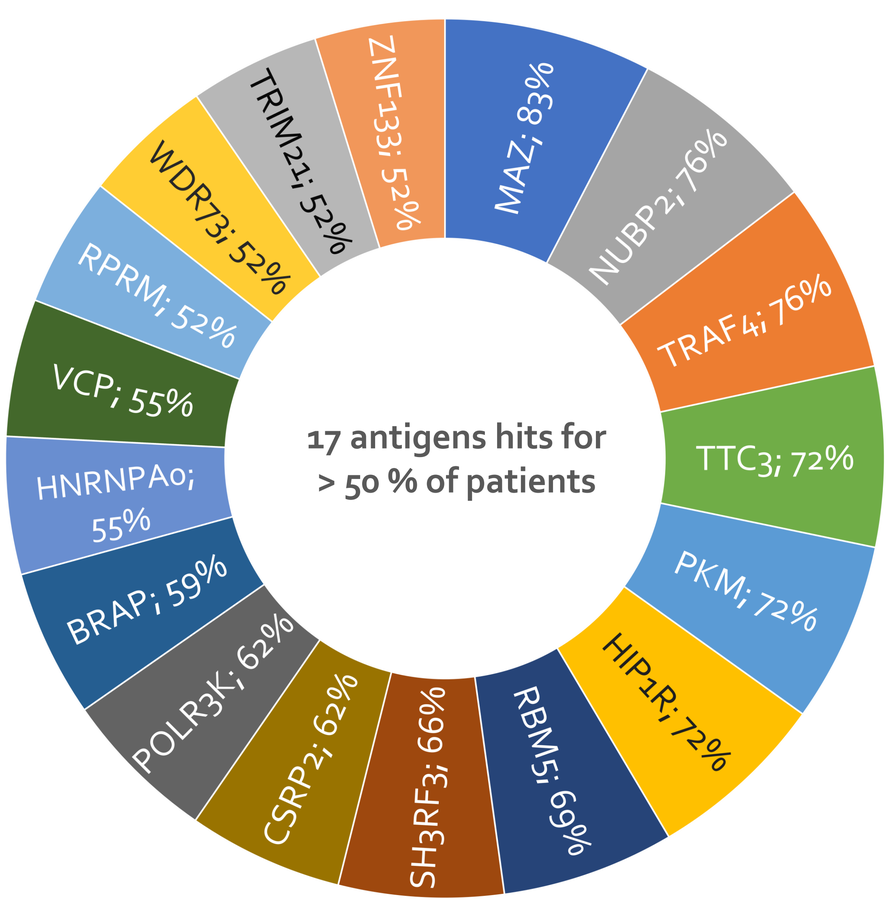


Methods: Protein Arrays as Top-Down Approach

- cDNA library, *E. coli* clones, PVDF based
- Investigate >10.000 human antigens in one experiment → high chance of discovery
- Antigens cover a broad range of human proteome → excellent for systemic diseases

Experimental Setup:

- 29 SLE patients & 2 self-reported healthy donors
- AP-conjugated anti-human-IgG secondary antibody
- fast & simple workflow - as simple as Western Blot
- positive hits: signal intensities for clone duplicates higher than background
- direct antigen identification without additional sequencing



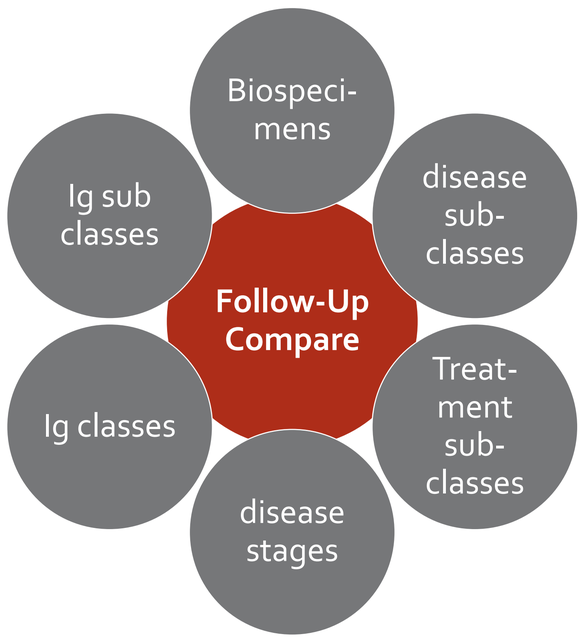
Results

- > 2.500 antibody-antigen-reactions in total, 16 - 183 interactions per patient
- 17 different antigen hits in > 50 % of SLE patients and in 0 % with self-declared healthy individuals.
  - 83 % of patients have IgGs against myc-associated zinc finger protein (**MAZ**) → patented biomarker for SLE (WO2012049225A2)
  - 52 % of patients have IgGs against **TRIM21** → published biomarker for SLE (PMID: 29385873)

→ 15 antigens remain as potential new biomarkers

Conclusion

Protein Arrays are an excellent tool for an unbiased start of biomarker discovery. To validate the results follow-up experiments are required to identify THE biomarker. So, more sera should be tested with a higher proportion of healthy donors in order to minimize the risk of false positives.



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