Approaches to Personalized Rheumatic Medicine using Mass Spectrometry

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No conflicts of interest

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Inflammatory Diseases

Pneumonitis

Arthritis

Vasculitis
Anti-Inflammatory Drugs

Nature Reviews | Rheumatology
RA immunology and treatment

Adapted from Personalized medicine: Time for one-person trials. Nicholas J. Schork, Nature 520, 609–611. doi:10.1038/520609a, and based on:

When an anti-arthritis drug does not work?

*is because the immune system is active elsewhere?*

*or is it because it simply is not present in the patient?*
Inflammatory Immunology

To central issues needs to be solved to bring arthritis treatment into the era of personalized medicine:

Immune Response Monitoring

Biological Drug Quantification
Expanding the Patient with Systems Biology

Samples or treatment

Omics Technology:
- Sequencing or Mass Spectrometry

Metabolites
Proteins
mRNA
DNA

Control

Modeling / biological understanding

Bioinformatics

Samples or treatment

Metabolites
Proteins
mRNA
DNA

Omics Technology:
- Sequencing or Mass Spectrometry

Control

Modeling / biological understanding

Bioinformatics
Immune Response Monitoring

Biological samples: blood cells or fluid, synovial tissue or fluid
Immune Response Monitoring

Mass spectrometry

Multi-array electrochemiluminescence

400-6000 serum protein quantifications

10-71 cytokine quantifications

(in-review) Michael Kruse Meyer, Msc, Marlene Andersen, Troels Vindbæk Stausbo, Kirstine Juul Elbæk, Grethe Neumann Andersen MD, Dr. Med, Allan Stensballe, PhD. Polymyalgia Rheumatica Treatment Serum Biomarkers versus Rheumatoid Arthritis.
Biological Drug Quantification

(Biological drgs are antibody based)

Spiked-in therapeutics serum, or patient serum

Anti-human-IgG

30% in total v/v ammonium sulfate then centrifugation

Solubilise TFE, reduce (TCEP), alkylate (IAA), then trypsinize

Acidify + heavy spike then do SRM, MRM, PRM

Patient serum → Complex binding IgG → Precipitate → MS-prep → Targeted MS

[Willrich et al. 2015]
Biological Drug Quantification

Pharmacokinetics of biological drugs from subcutaneous tissue to serum

(in-review) Precision Medicine Approach to Abatacept treatment in Rheumatoid Arthritis. Michael Kruse Meyer, Marlene Andersen, Troels Vindbaek Stausbo, Kirstine Juul Elbaek, Tue Bjerg Bennike PhD, Grethe Neumann Andersen MD, PhD, Allan Stensballe PhD
De-Novo Sequencing Biological Drugs

We’re sorry to inform you that the sequence is confidential.

SAMPLE CHARACTERIZATION AND PREPARATION

Discovery experiments

MALDI-TOF

LC-MS/MS

Peptide identifications
Spectral library
LIFT-Mode de-novo sequencing
Brute force unscheduled PRM
De-novo sequencing with PEAKS

Meyer MK, Andersen M, Stausbo TV, Bennike TB, Andersen GN, Stensballe A. Unpublished
Targeted Repository Anti-disease Proteomics (TRAP)

• arthritis-TRAP
  – 11 biological drugs
• cancer-TRAP
  – ~17 biological drugs
• IBD-TRAP
  – ~6 biological drugs

Collaboration needed