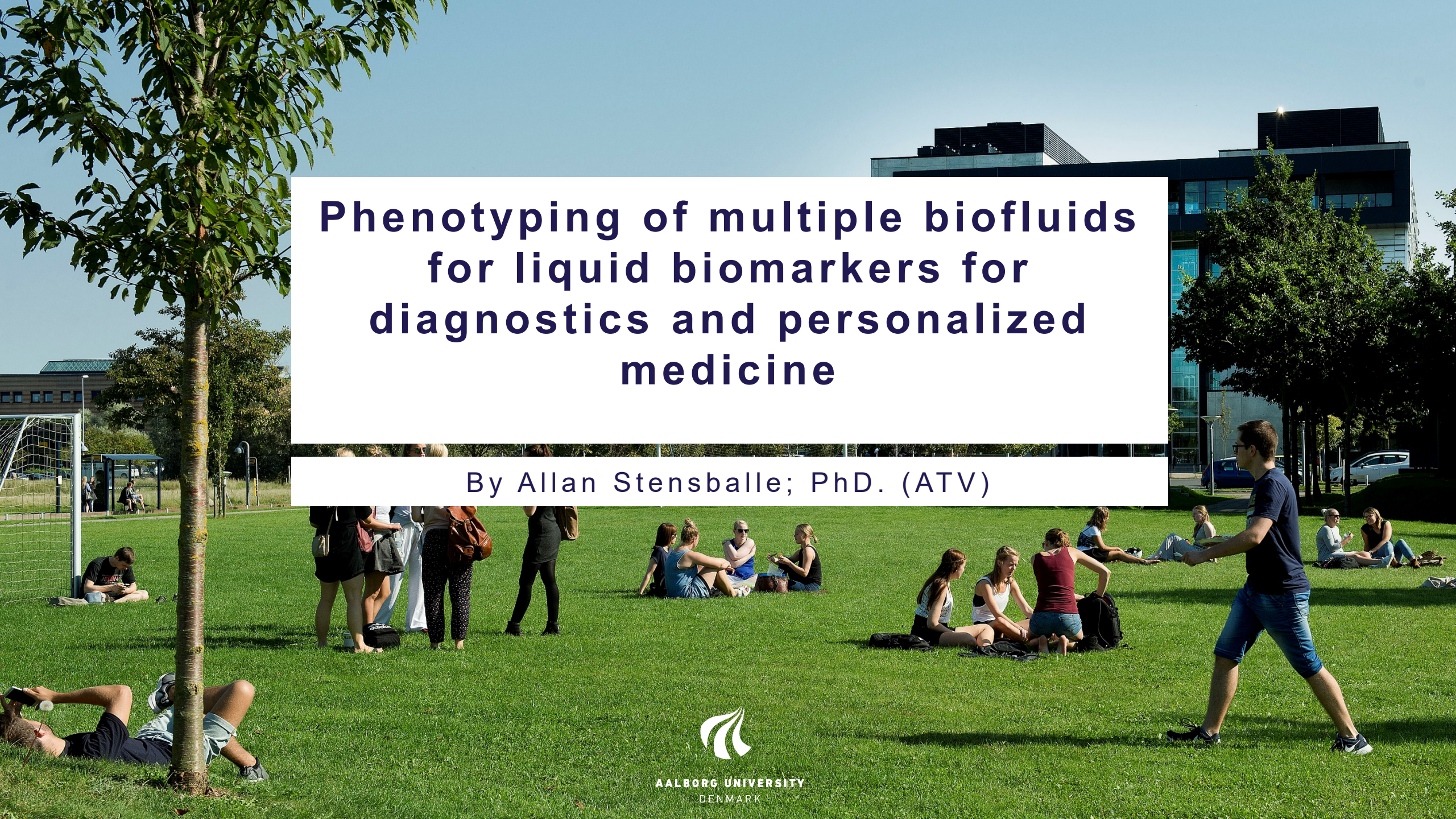

Phenotyping of multiple biofluids for liquid biomarkers for diagnostics and personalized medicine

By Allan Stensballe; PhD. (ATV)

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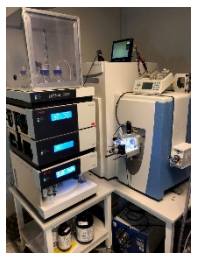
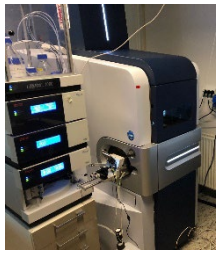
Translational Biomarker Omics Reserch Unit, AAU

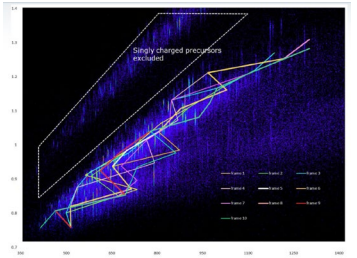


Thermo Sci
Qexactive HF-X
Pharma-option

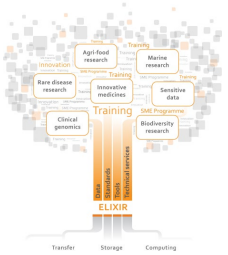


Bruker timsTOF
PRO
Multi-omics setup

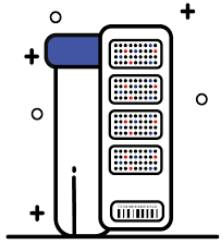
Bruker UltrafleXtreme
Imaging MS setup



4D Setup for biomolecule characterization down to low cell number

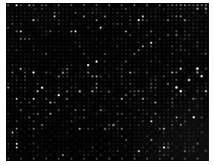


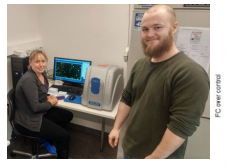
Extensive bioinformatics platform including multiple commercial solutions for quantitative proteomics and metabolomics

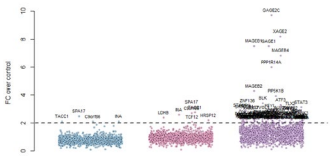


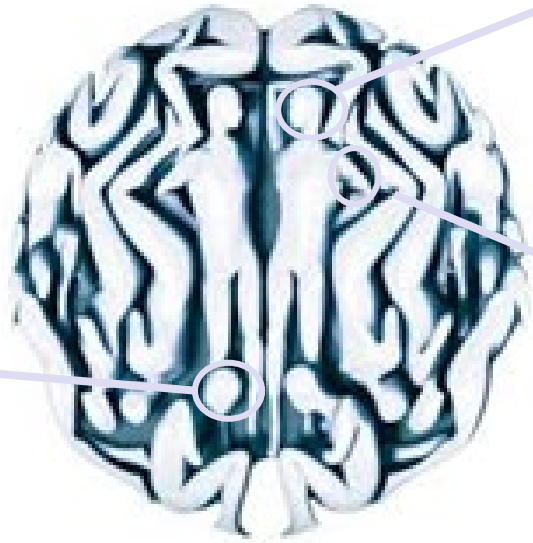
MS, Multiplex & Protein Array for cell signalling & autoantibody profiling

sengenics
The Functional Proteomics Company

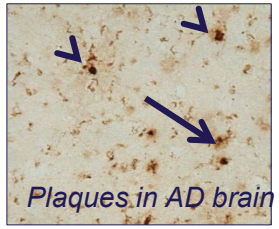


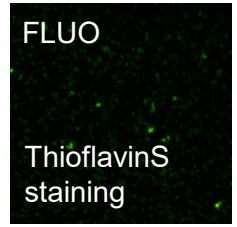


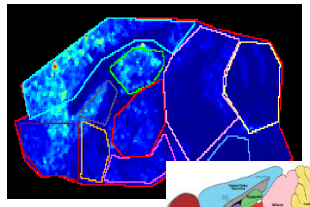


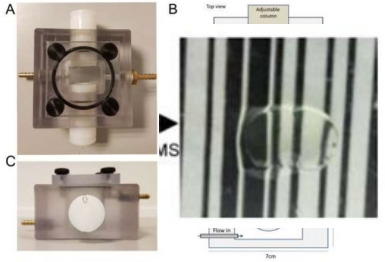


Imaging from cells to tissue









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Inflammation…

- A key focus area initiated 4 years ago..

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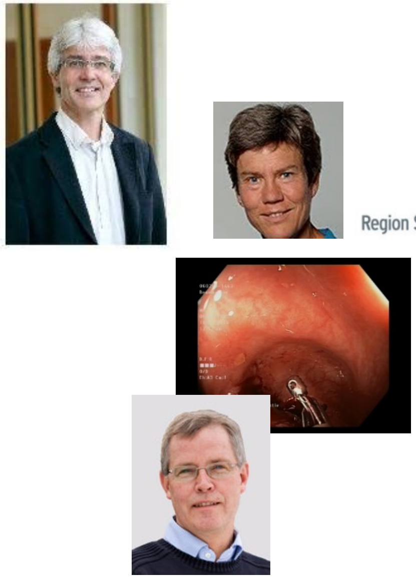
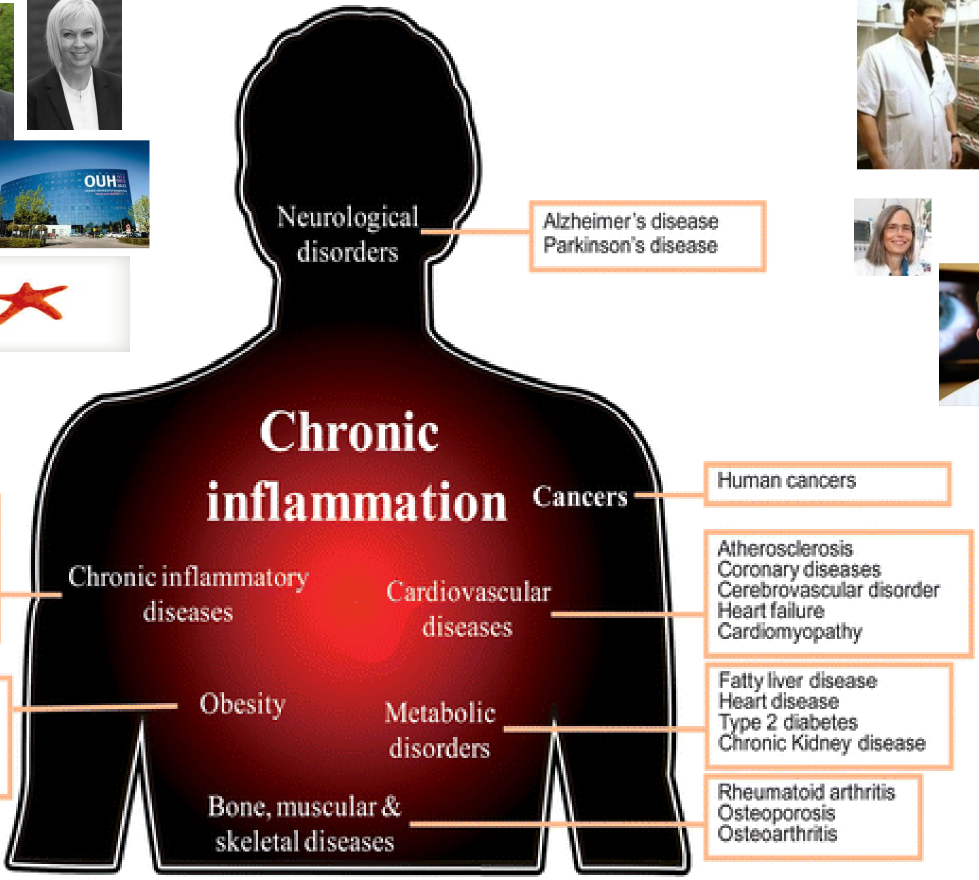
Lundbeck



Region Syddanmark

The Novo Nordisk Foundation Center for Basic Metabolic Research



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I gode hænder hos SYGEHUS VENDSSYSSEL

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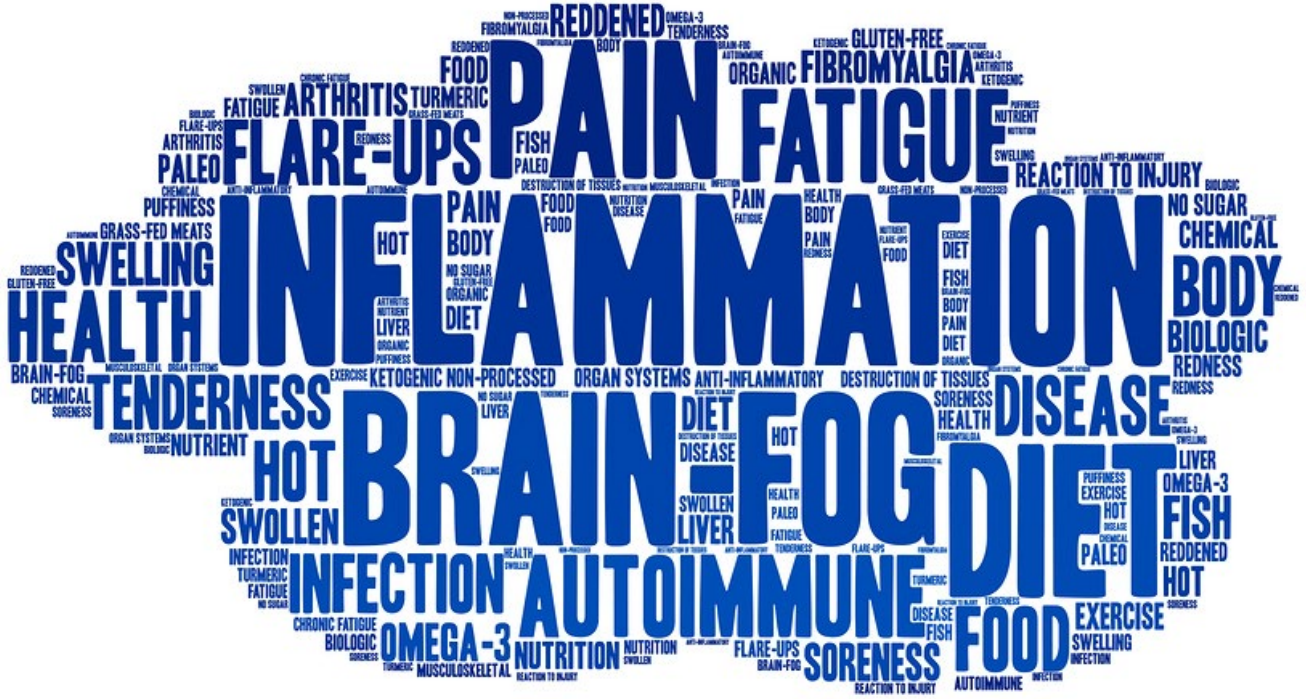
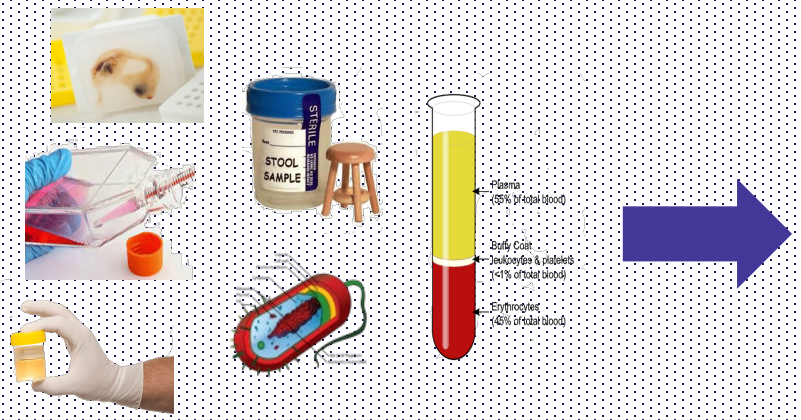
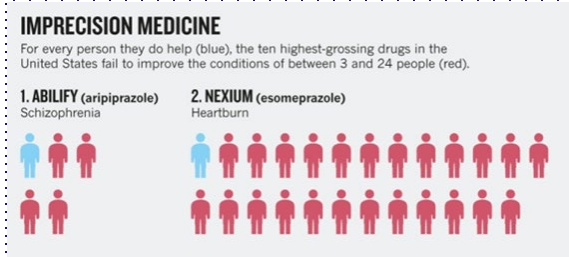
Phenotyping for enhanced diagnostics and personalized medicine

- More than 80 diverse autoimmune diseases affect 6.4% percent of women vs. 2.7 % of men
- Researchers don’t know exactly what causes many autoimmune diseases.
- Genetics, diet, infections, and exposure to chemicals might be involved.
- Many subtypes remain excessively difficult to validate and no single test can diagnose most autoimmune diseases.
- Low grade inflammation is central in most pathologies.



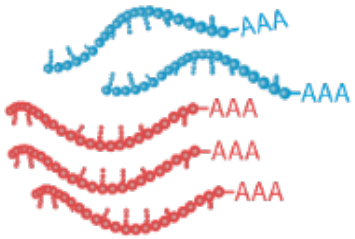
Personalized and precision medicine are key a focus in the future



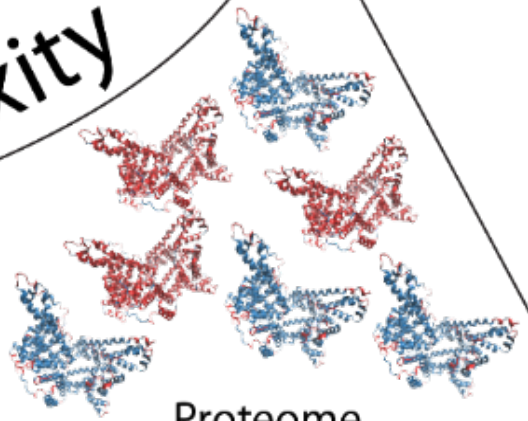


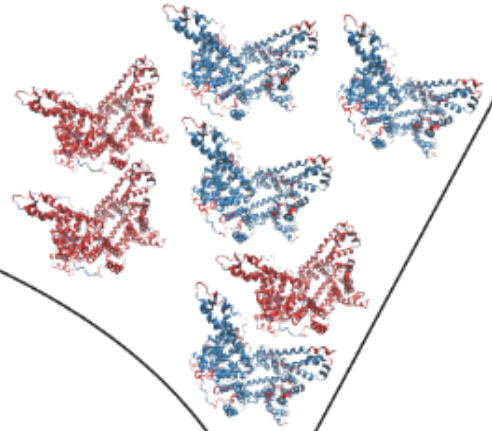
Proteome Complexity

Genome
~20,000 genes



Transcriptome
~100,000 transcripts





Proteome
>1,000,000 proteoforms

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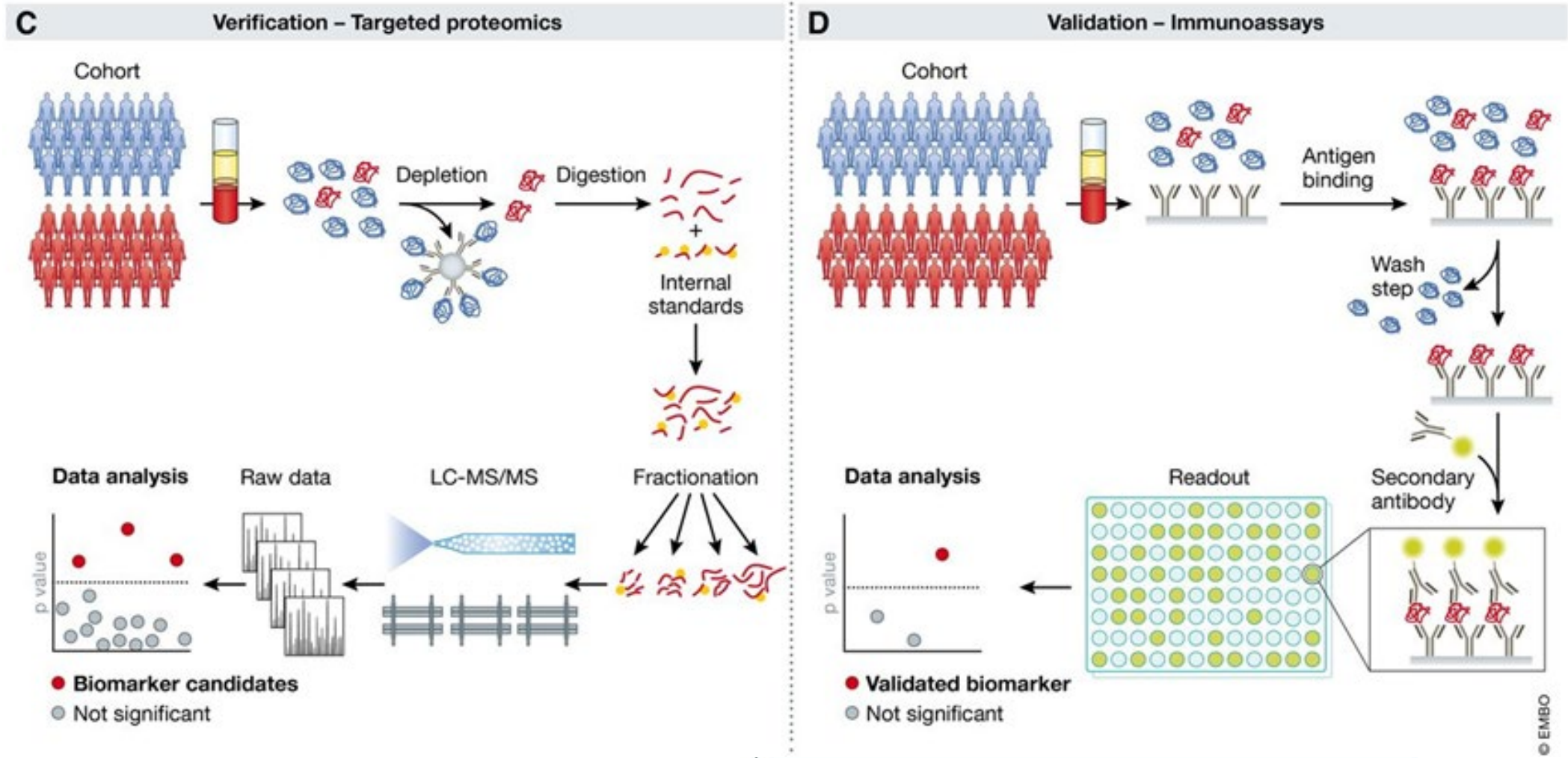
Bennike, T. World J. Gastroenterol. ***20,*** *3231 (2014).*

Proteomics - Key technology in Clinical research



Challenges in Clinical Mass spectrometry

Missing values

Improve sequencing speed

Improve duty cycle and sensitivity

LMM PRO-MS North Jutland node

High-end for clinical Proteomics & metabolomics..

LC-MS system (PRO-MS2)
- ThermoSci QE HF-X Pharma option
- *Deep proteomics and analysis of biologics*
- *Targeted MS by PRM*

LC-MS system (PRO-MS1)
- Bruker timsTOF PRO
- *Optimized for high-end proteomics and high-sensitivity metabolomics with IMS*

MALDI MS
- Bruker Ultraflex Extreme
- Bruker Autoflex
- Protein & peptide profiling and MS Imaging

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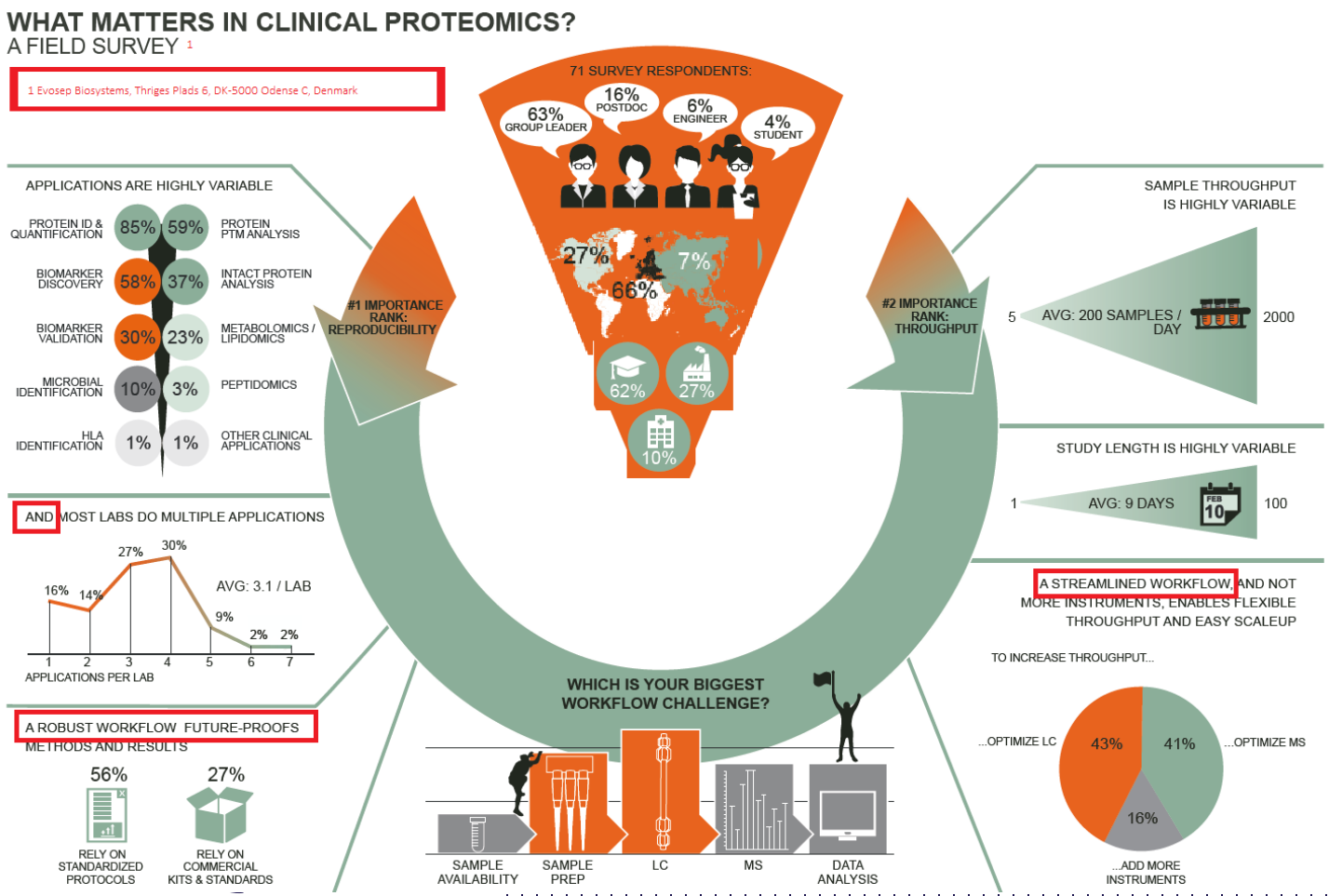
CURRENT EFFORTS TO IMPROVE BIOFLUID ANALYSIS

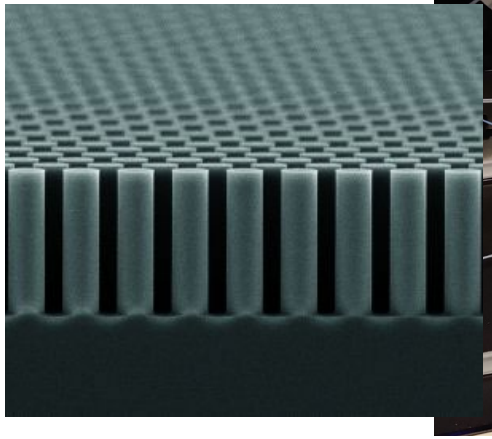
- Improve sample preparation prior to MS
- Improve LC robustness, performance and scalability
- Improve MS duty cycle and speed

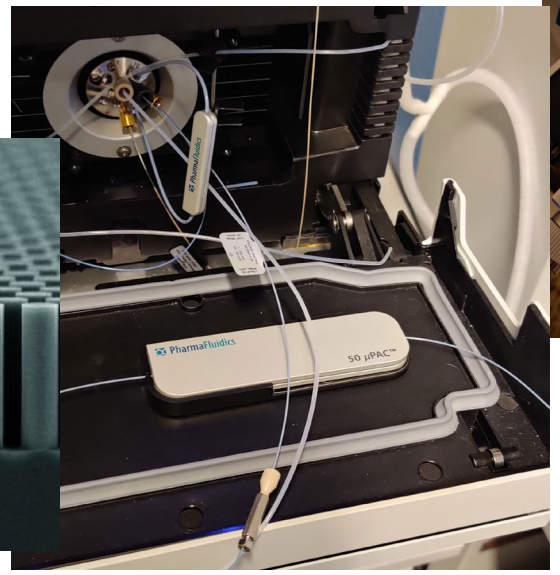


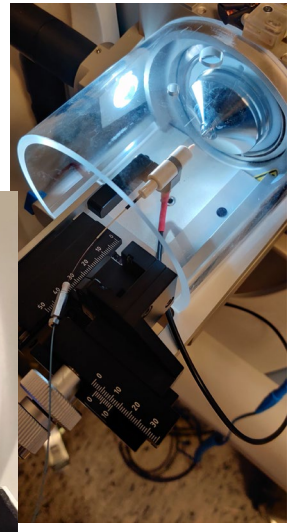
Chromatographic solutions optimized for clinical LC

- **Several key advancements seek to increase robustness and chromatographic performance**

Examples:
Ionoptiks Auroa
Pharmafluidics uPAC
EVOSEP ONE.







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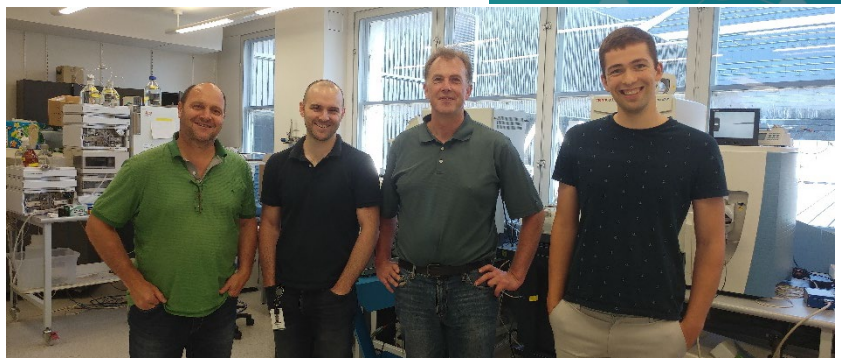
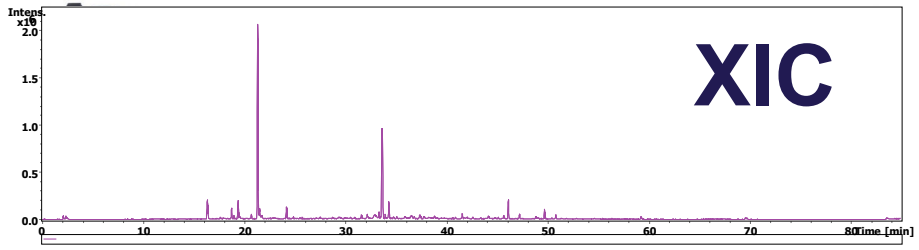
ionopticks

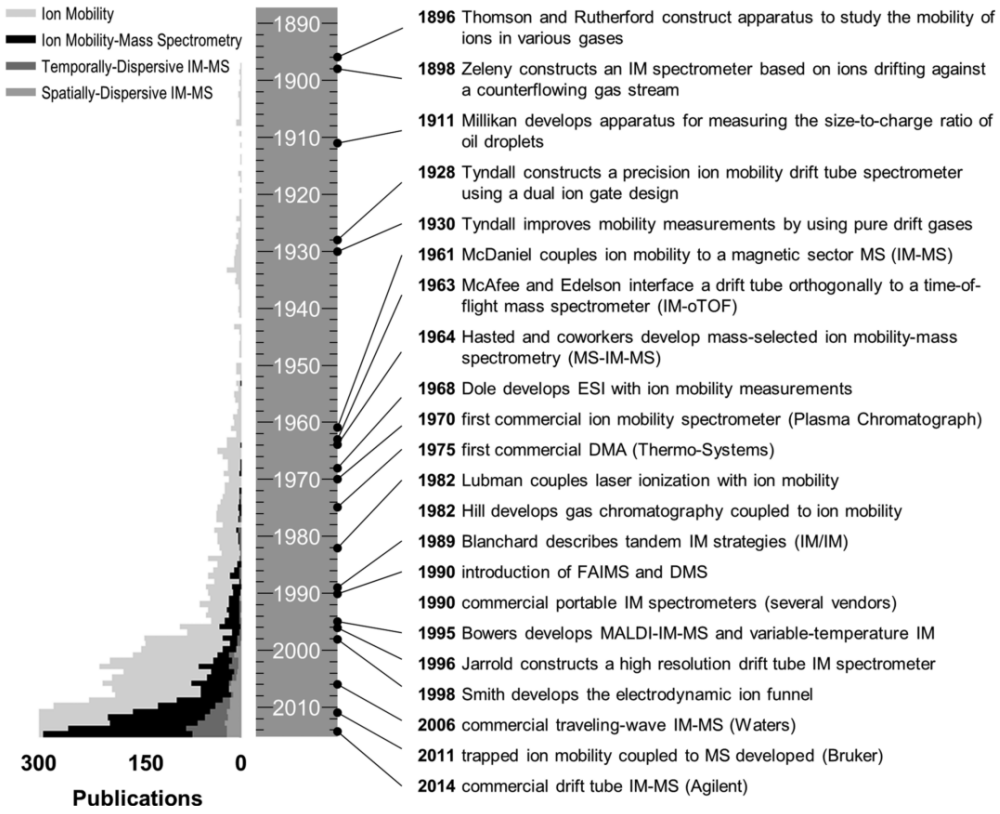


Aurora UHPLC Column with **nanoZero**™ fitting



XIC

FASTER AND MORE COMPREHENSIVE MS – ION MOBILITY MS



1896 Thomson and Rutherford construct apparatus to study the mobility of ions in various gases

1898 Zeleny constructs an IM spectrometer based on ions drifting against a counterflowing gas stream

1911 Millikan develops apparatus for measuring the size-to-charge ratio of oil droplets

1928 Tyndall constructs a precision ion mobility drift tube spectrometer using a dual ion gate design

1930 Tyndall improves mobility measurements by using pure drift gases

1961 McDaniel couples ion mobility to a magnetic sector MS (IM-MS)

1963 McAfee and Edelson interface a drift tube orthogonally to a time-of-flight mass spectrometer (IM-oTOF)

1964 Hasted and coworkers develop mass-selected ion mobility-mass spectrometry (MS-IM-MS)

1968 Dole develops ESI with ion mobility measurements

1970 first commercial ion mobility spectrometer (Plasma Chromatograph)

1975 first commercial DMA (Thermo-Systems)

1982 Lubman couples laser ionization with ion mobility

1982 Hill develops gas chromatography coupled to ion mobility

1989 Blanchard describes tandem IM strategies (IM/IM)

1990 introduction of FAIMS and DMS

1990 commercial portable IM spectrometers (several vendors)

1995 Bowers develops MALDI-IM-MS and variable-temperature IM

1996 Jarrold constructs a high resolution drift tube IM spectrometer

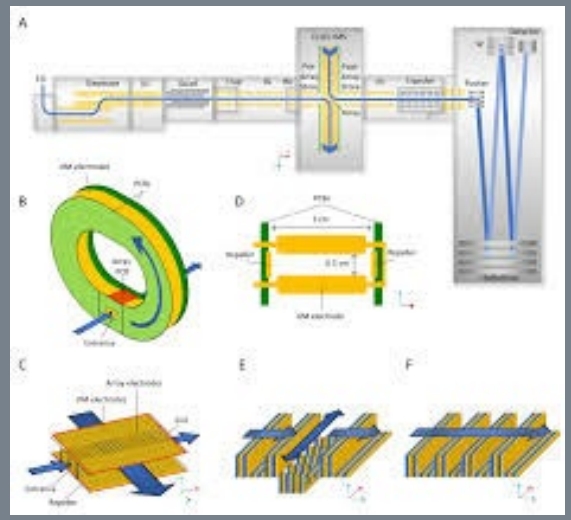
1998 Smith develops the electrodynamic ion funnel

2006 commercial traveling-wave IM-MS (Waters)

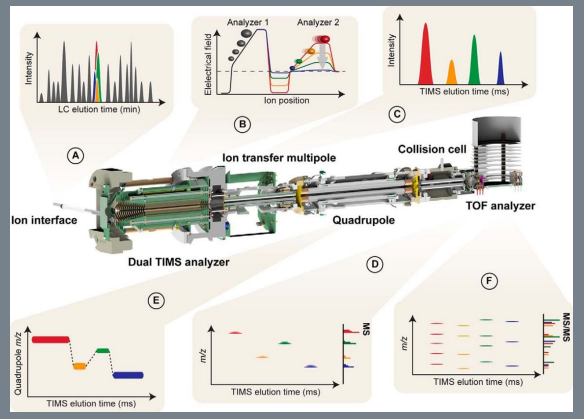
2011 trapped ion mobility coupled to MS developed (Bruker)

2014 commercial drift tube IM-MS (Agilent)

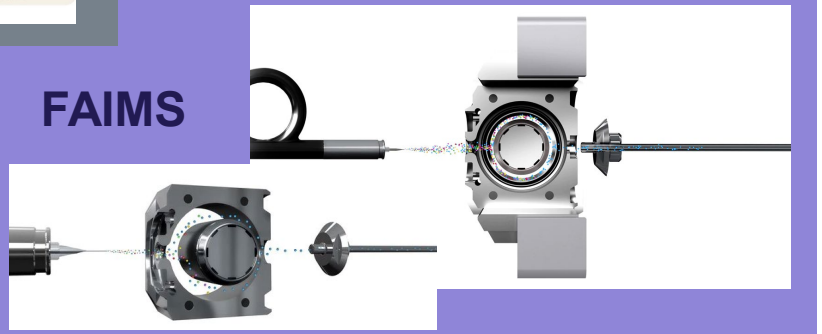
Cyclic IMS



tims PASEF



FAIMS



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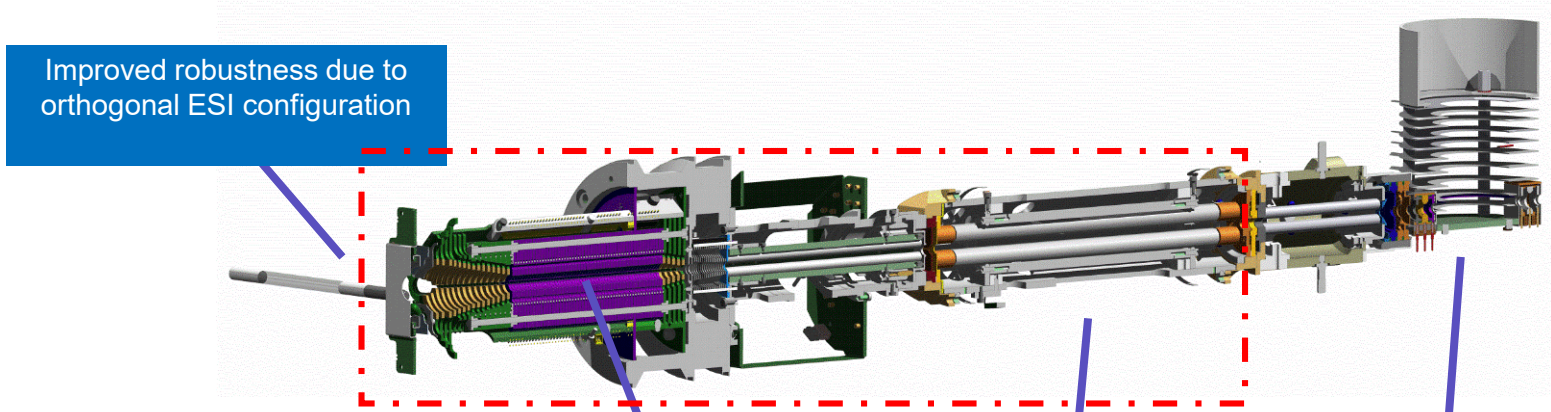
TIMS Scan Rate in LC-MS/MS Timescale

Only on UHR-TOFs with fast switching quadrupole mass filter



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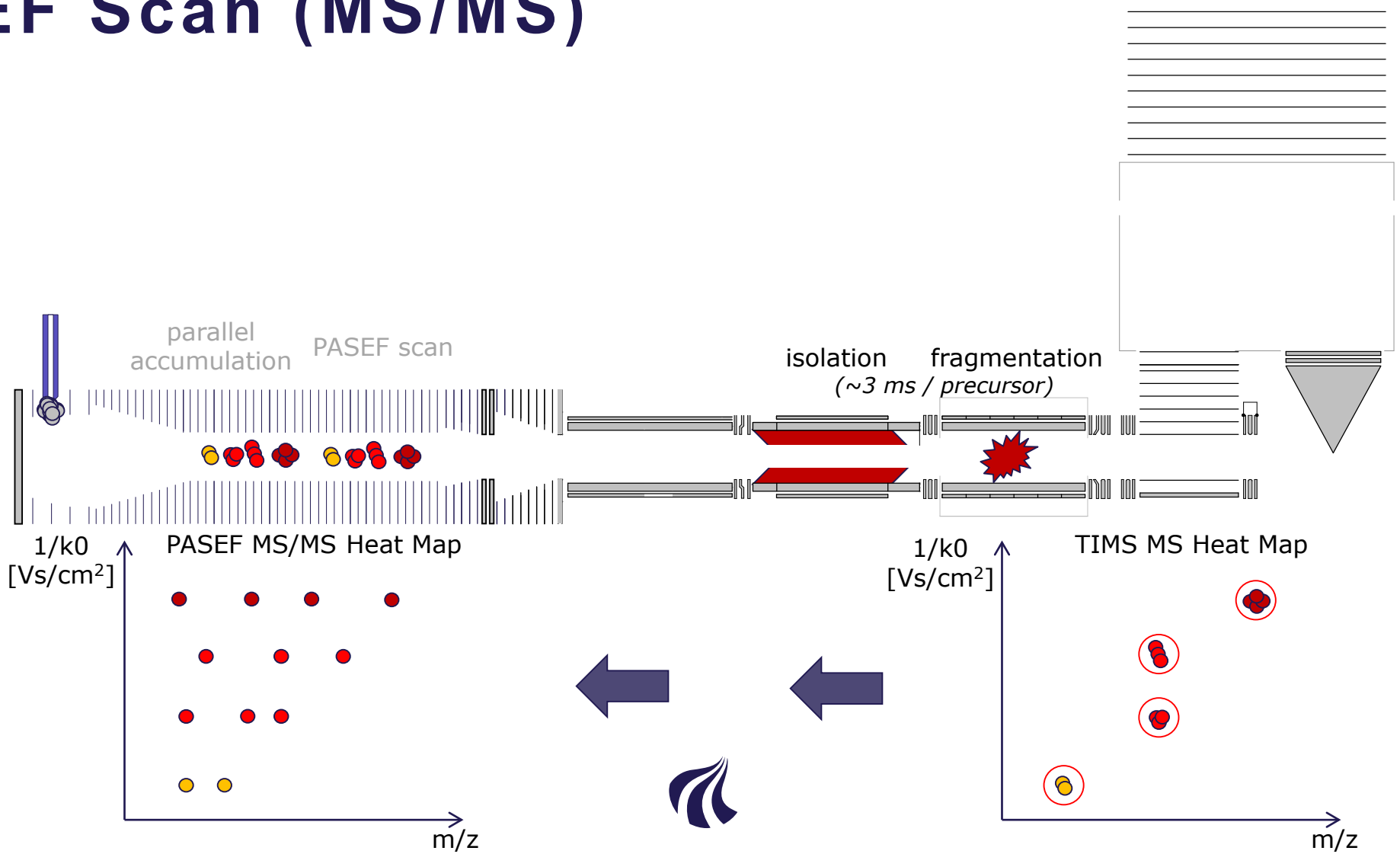
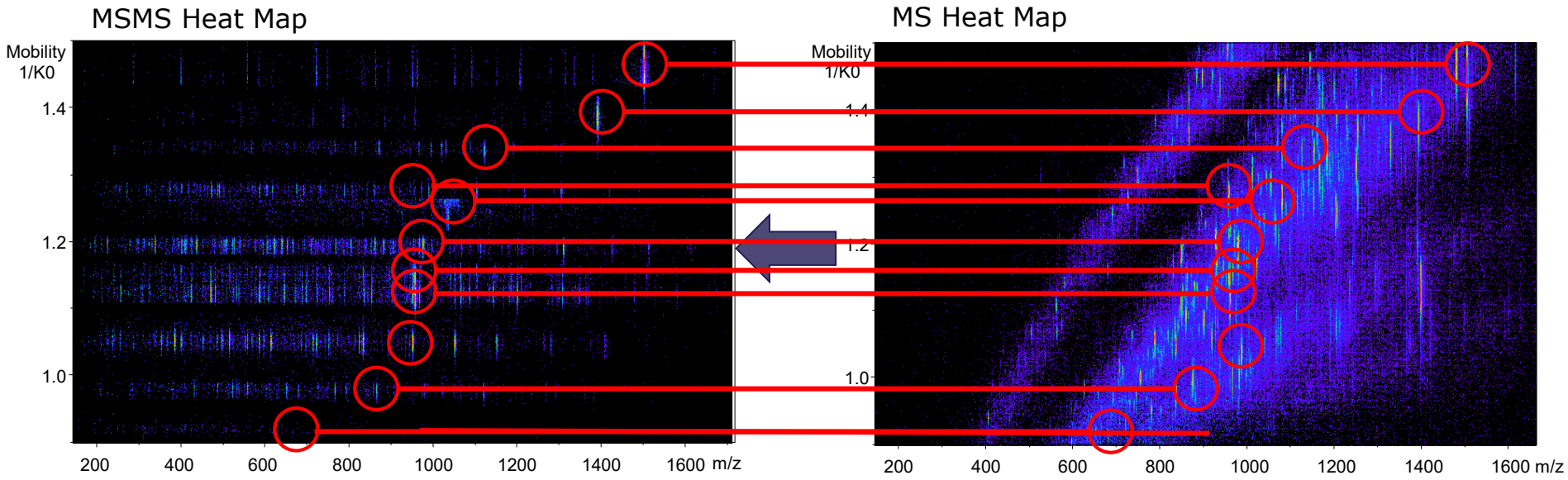
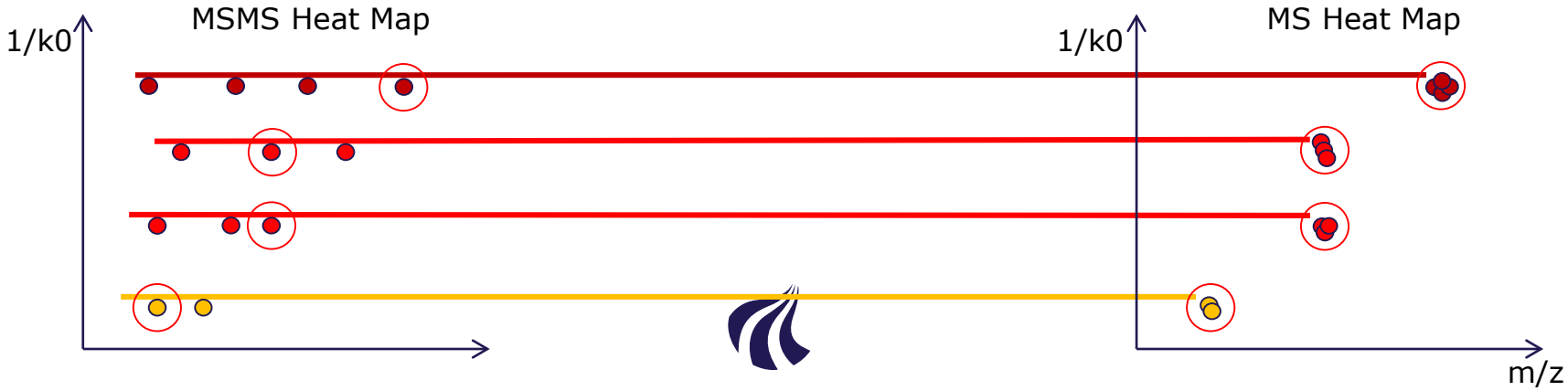
PASEF Scan (MS/MS)



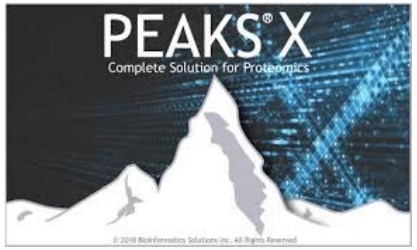
PASEF MS - >120Hz MSMS





Processing SW for identification, label free and labeled quantification

Peaks studio



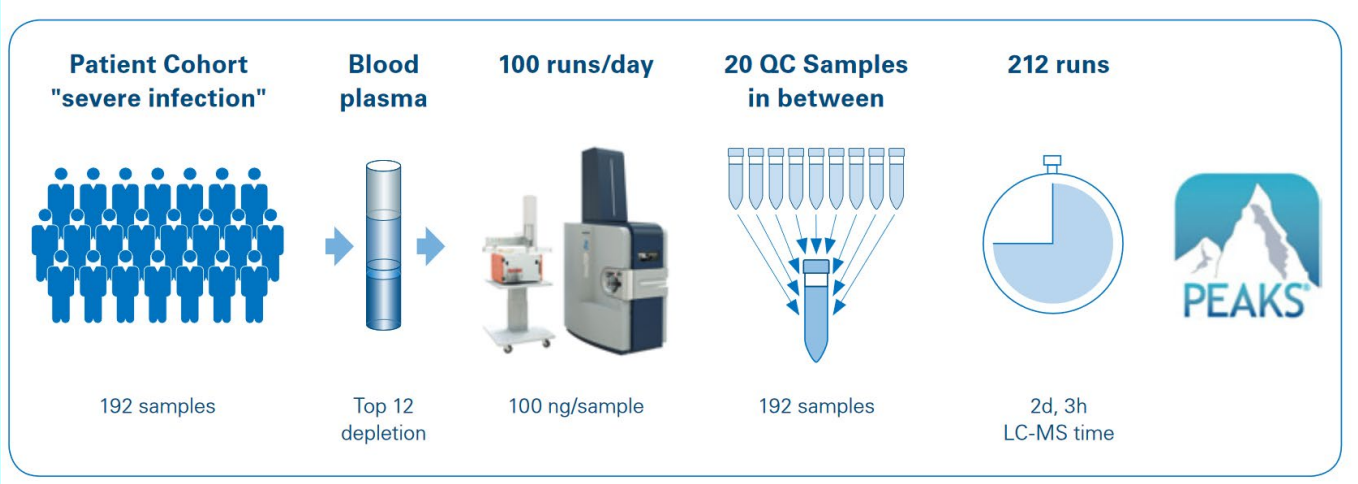
MaxQuant

Biognosys

BIOGNOSYS
NEXT GENERATION PROTEOMICS

New opportunities

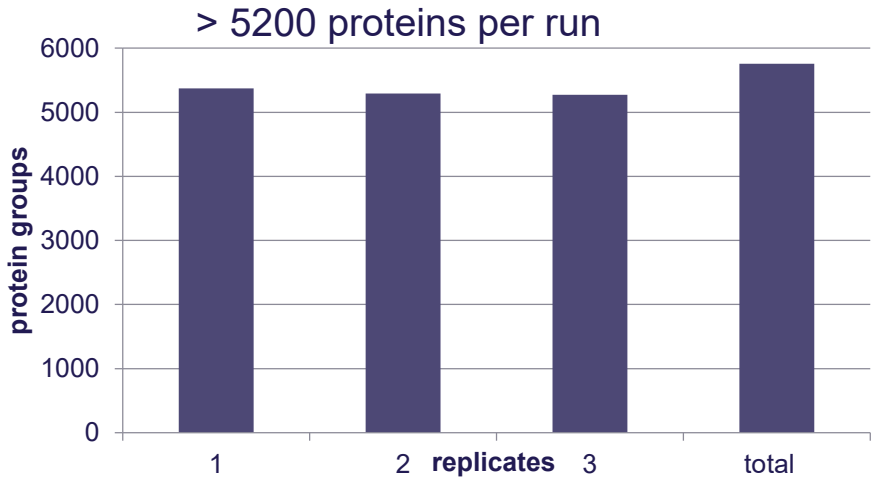
- 4D feature finding by including CCS value
- diaPASEF

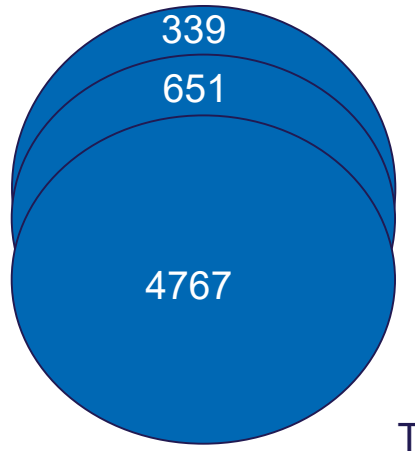


Thomas Kosinski 1, Raphael Heilig 2, Dalila Bensaddek 1, Nicolai Bache 3, Ole Bjeld Hørning 3, Roman Fischer 2, Heiner Koch 1; 1 Bruker Daltonik GmbH, Bremen, Germany; 2 Target Discovery Institute, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom.3 Evosep Biosystems, Odense, Denmark

Processing SW for identification, label free and labeled quantification

MaxQuant





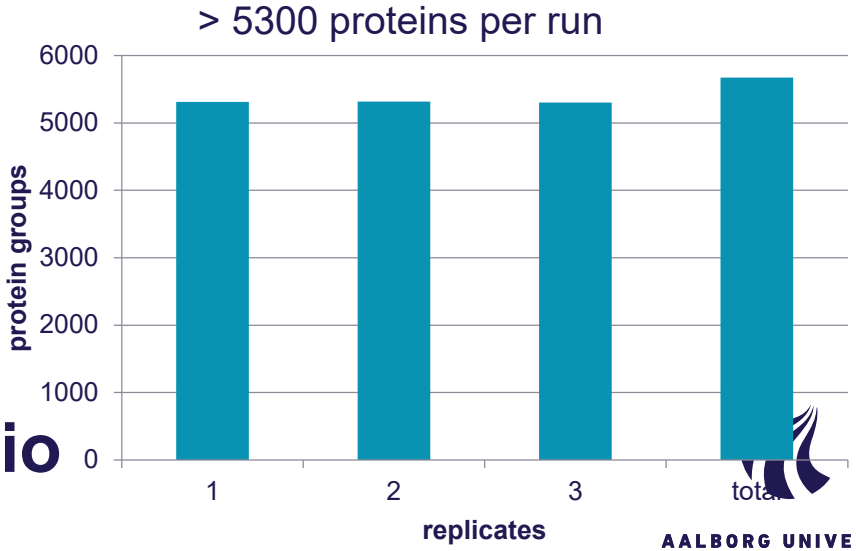
In 1 replicate

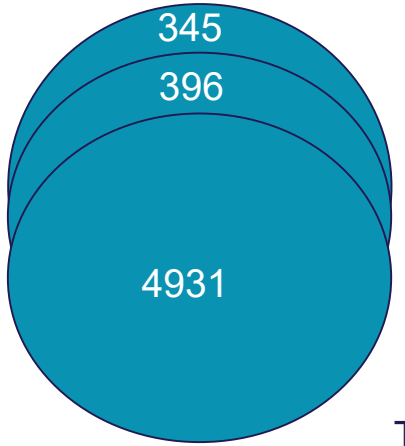
In 2 replicates

In all 3 replicates

Total: 5757 proteins

Peaks Studio





In 1 replicate

In 2 replicates

In all 3 replicates

Total: 5672 proteins

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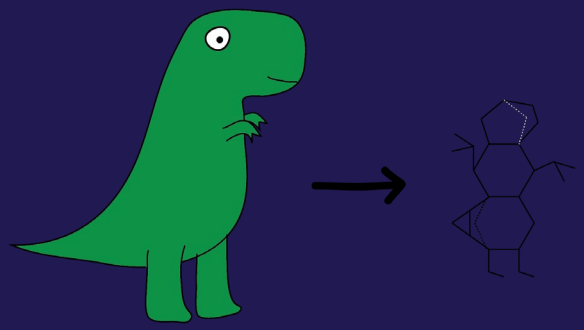
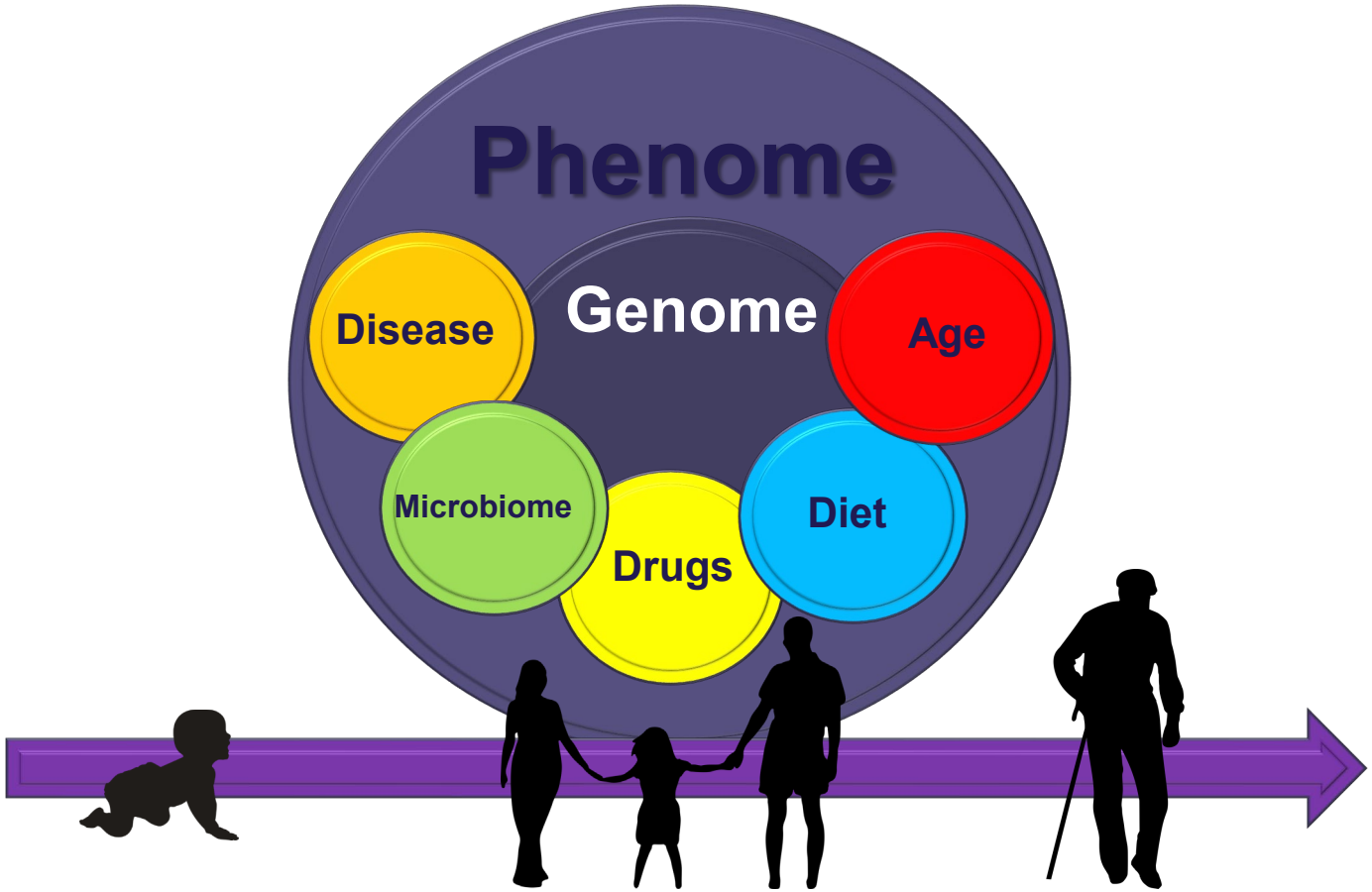
Improved and truely translational biomarkers are needed

- Enabling technologies including all Omics technologies paves the way to understanding disease etiology.
- Key to insight remains the ability to find good answers to relevant clinical questions
- Why responders and non-responders?

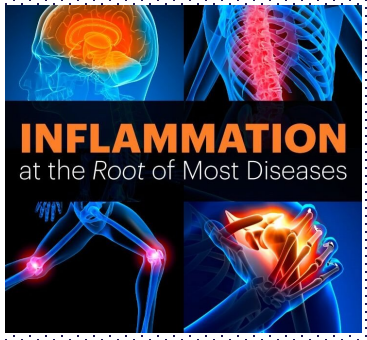
BIOMARKER



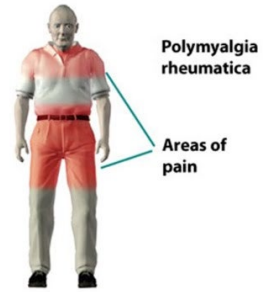


Disease risk (prognosis/Diagnosis/ prevention)

Patient stratification (Translational biomarkers)

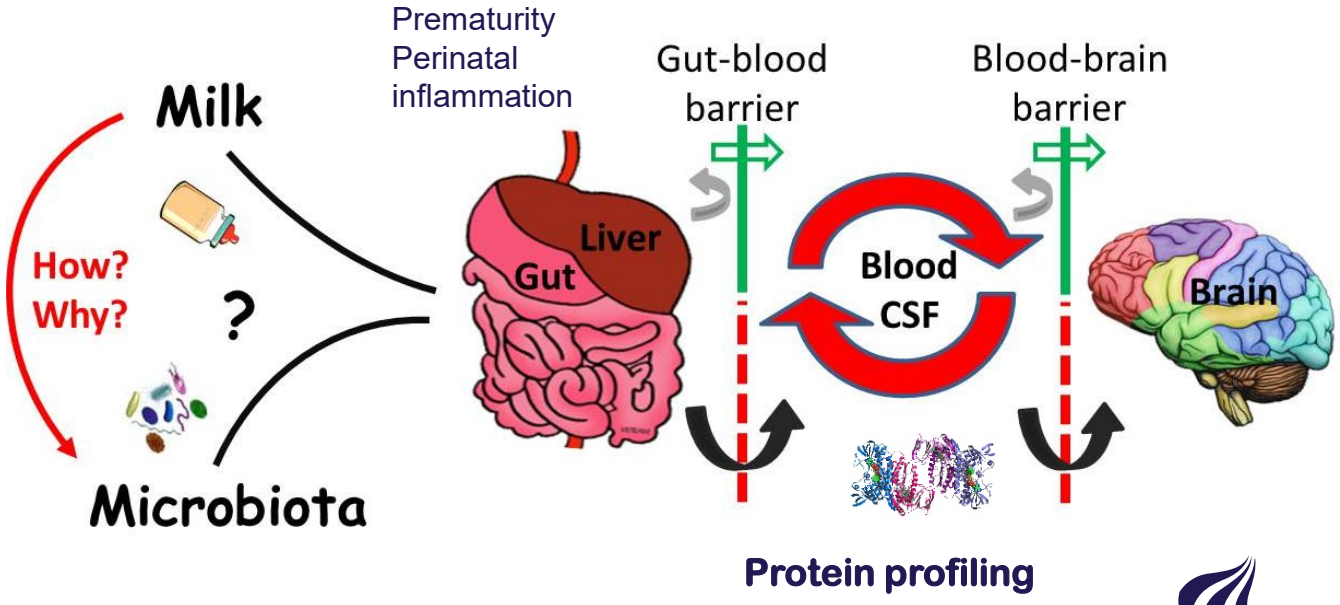


Treatment response (Prediction/monitoring)

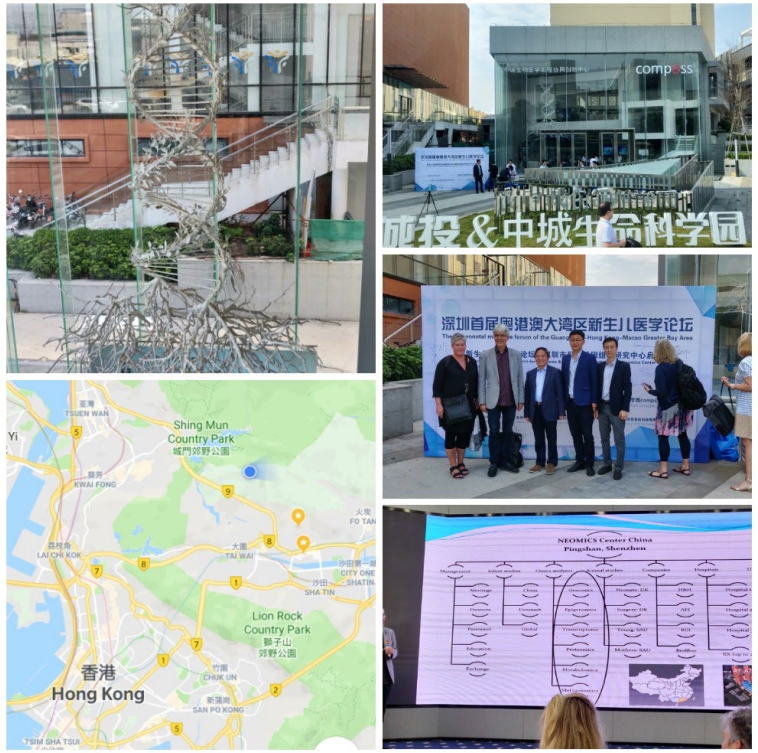


Omics technologies for premature newborns – Challenges & Opportunities

Insight into treatment and long-term outcome for healthy and perfect miracle babies if born premature

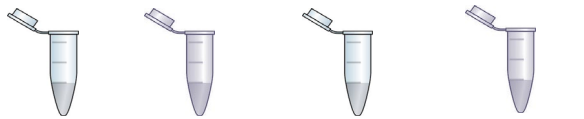


Systems Biology at Sino-Danish NEOMICS Center

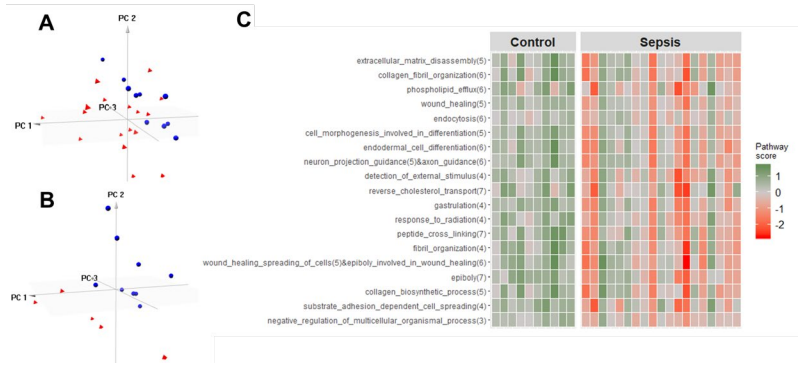


Sepsis-induced changes in cerebrospinal fluid affect proteome of the developing hippocampus - correlation to systemic changes

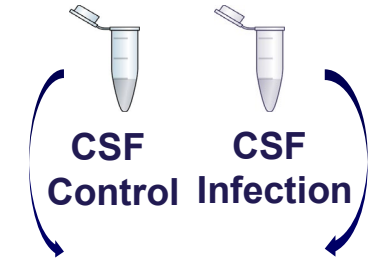
Preterm infant (GA<32 wk)



CSF Control | CSF Sepsis | Plasma Control | Plasma Sepsis

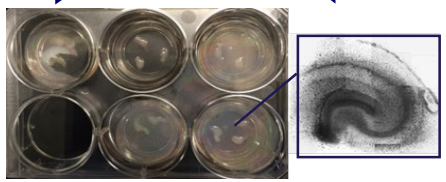


Formula-fed 5d preterm pigs (90% GA)



CSF Control | CSF Infection

in vitro stimulation

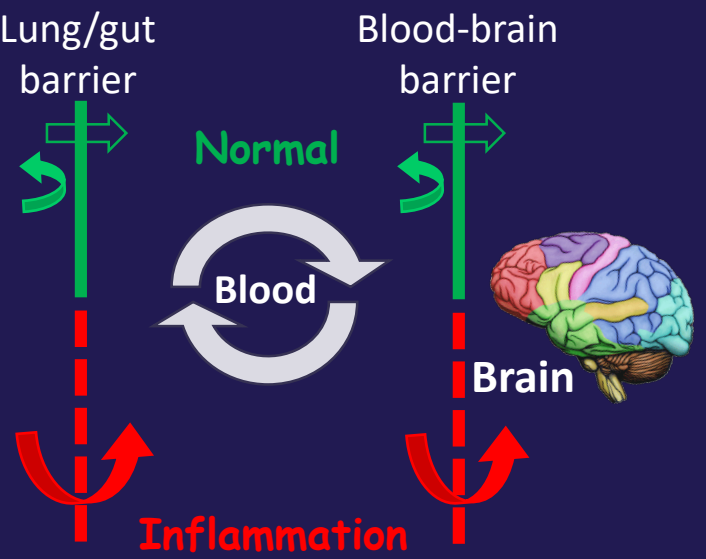


Primary hippocampal slices derived from preterm pigs

Collect culture medium and tissue

Hippocampus

Secretome



- *How systemic infection affects brain development and functions is poorly understood.*
- *Good biomarkers for early diagnosis and treatment for sepsis-induced brain injury are lacking.*

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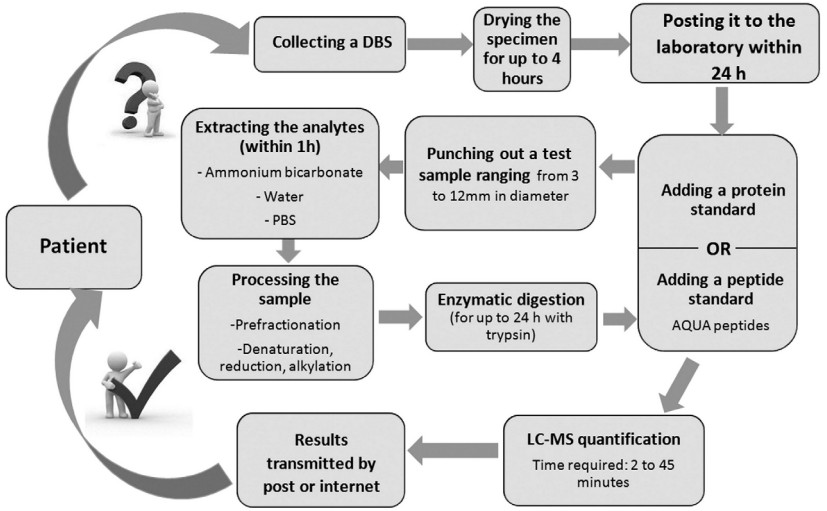
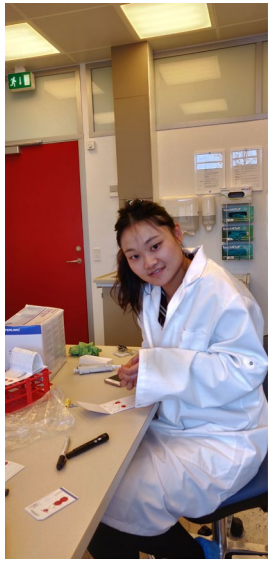
Omics analysis of Dried whole blood samples – Whole blood analysis

- *Dried blood spots offer many advantages as a sample format including ease and safety of transport and handling.*
- *Dried blood spots are a potentially rich source of protein biomarkers, an area that has been overlooked.*



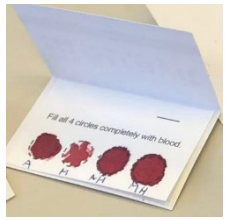


Tik Muk

Finger puncture whole blood

Pig

Human

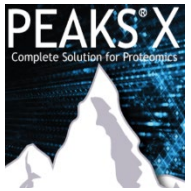


FASP extraction

5% SDC

S-TRAP

Single column setup (25cm Ionoptiks) and Bruker timsTOF PRO PASEF



Data analysis

Accession	-10lgP	Coverage	Cov
Proteins			
P02768|ALBU_HUMAN	699.93	95%	
tr|A0A0C4DGB6|A0A0...	697.05	94%	
tr|B7WNR0|B7WNR0_H...	660.45	94%	
tr|H0YA55|H0YA55_HU...	658.12	98%	
ows identified peptides R2_HU...	643.05	92%	
P04114|APOB_HUMAN	566.65	60%	
P01024|CO3_HUMAN	557.08	90%	
P68871|HBB_HUMAN	649.59	100%	
P69905|HBA_HUMAN	716.46	100%	
P02549|SPTA1_HUMAN	560.99	82%	
P01023|A2MG_HUMAN	539.93	84%	
tr|G3V1N2|G3V1N2_HU...	703.30	100%	
P11277|SPTB1_HUMAN	529.64	74%	
P02042|HBD_HUMAN	528.02	100%	
P02787|TRFE_HUMAN	497.14	88%	
P16157|ANK1_HUMAN	540.23	72%	
P02647|APOA1_HUMAN	467.12	95%	
P0C0L5|CO4B_HUMAN	512.95	68%	
P0C0L4|CO4A_HUMAN	511.77	68%	
tr|A0A0G2JPR0|A0A0G...	510.96	68%	
tr|A0A2R8Y7C0|A0A2R...	629.68	66%	
tr|A0A0G2JL54|A0A0G...	510.46	68%	

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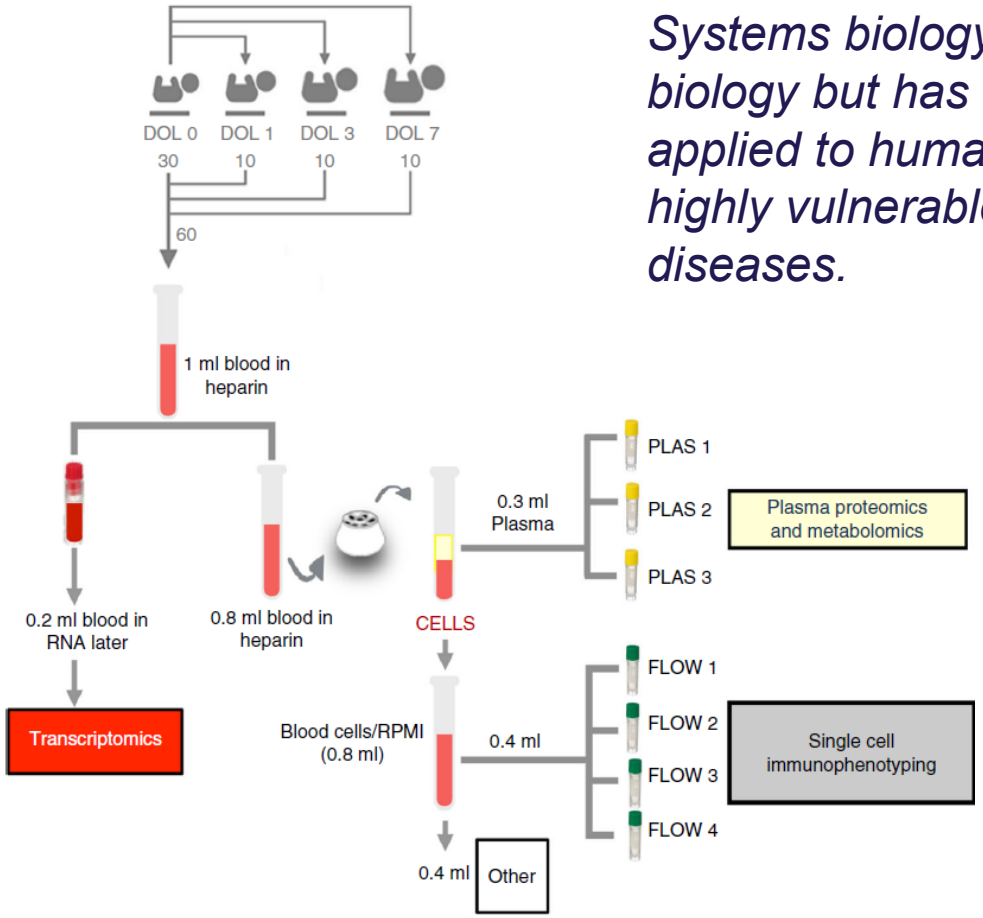
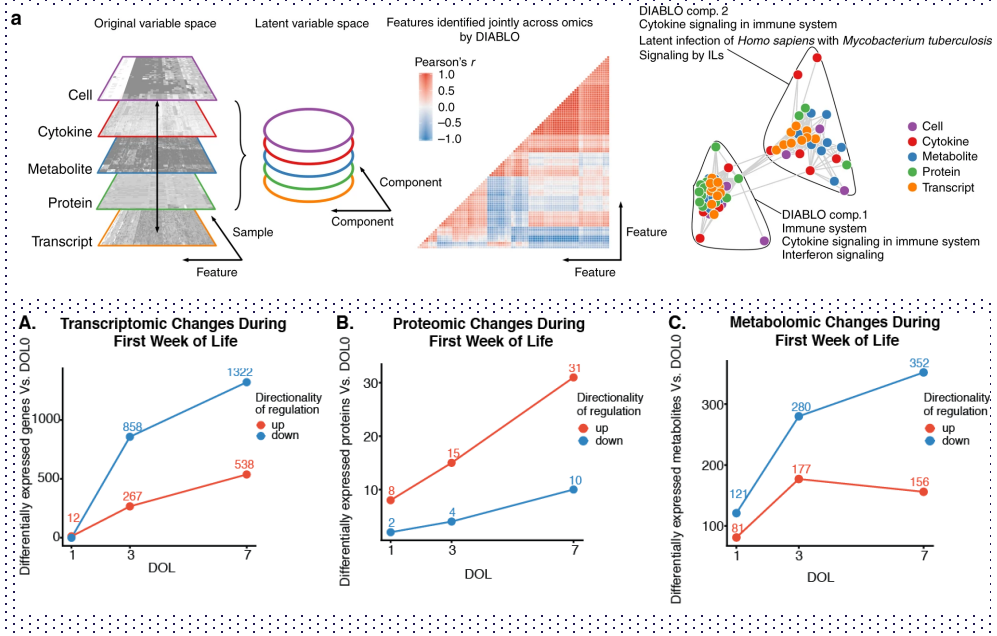
Deep proteome coverage reducing missing values for diagnostics and prognostics

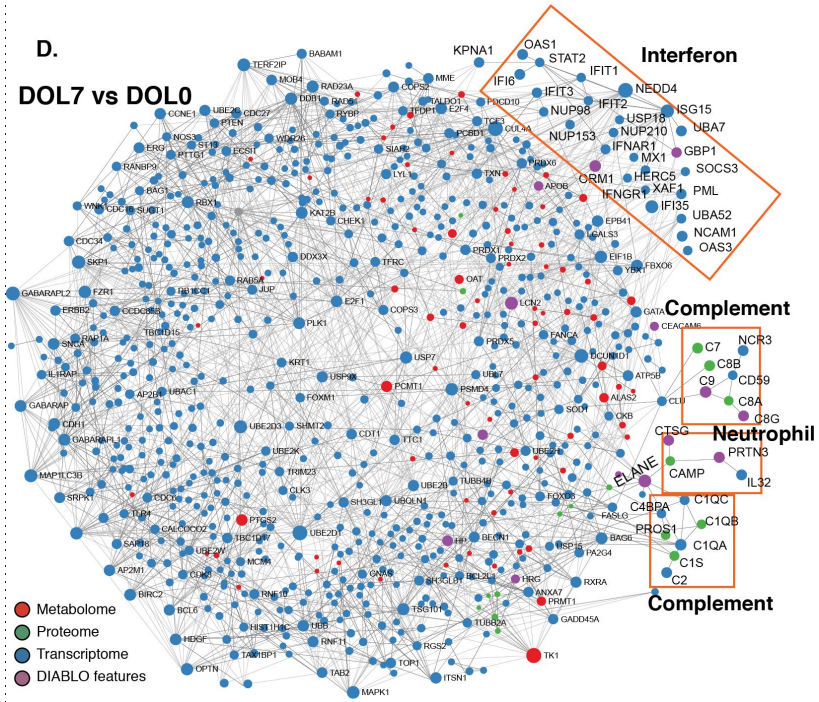
Dynamic molecular changes during the first week of human life follow a robust developmental trajectory

Tue B. Bennike

Systems biology can unravel complex biology but has not been extensively applied to human newborns, a group highly vulnerable to a wide range of diseases.







Amy H. Lee, Casey P. Shannon*, Nelly Amenyogbe*, Tue B. Bennike* et al. Nat. Commun.* ***10****, 1092 (2019).*

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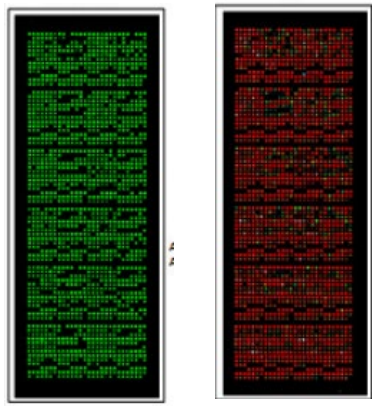
Improved phenotyping of disease subtypes by Immunome array

- Elevated levels of autoantibodies are present before the clinical diagnosis of auto immune diseases
- *State-of-the-art* personalized protein array technology allows phenotyping of autoantibodies.

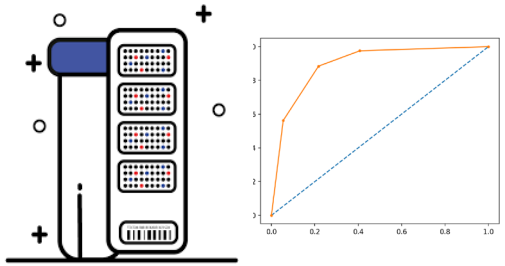
plasma/serum, synovial fluid cerebrospinal fluid

Array 50-1636 Control

Array 50-1636 Disease



Personalized arrays optimized for highly improved disease subtyping prognostics compatible with routine clinical laboratory settings



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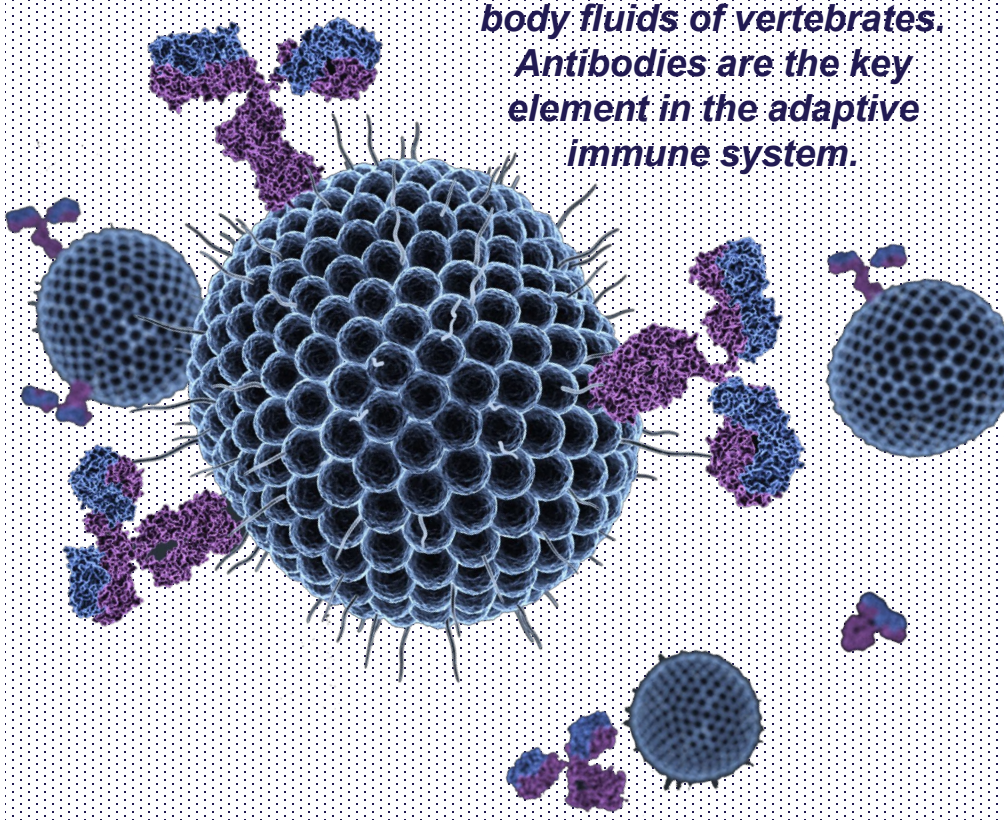
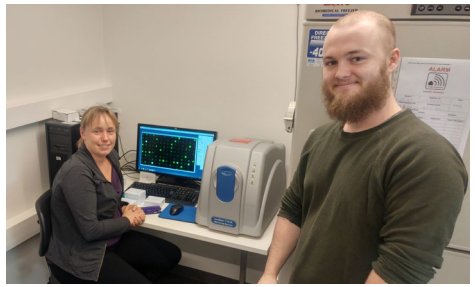
Antibodies (also called immunoglobulins) are large Y-shaped proteins. They are found in the blood or other body fluids of vertebrates. Antibodies are the key element in the adaptive immune system.



Proportion of Patients with Positive Antibody Tests Relative to the Time of Diagnosis or Appearance of the First Clinical Manifestation of Systemic Lupus Erythematosus

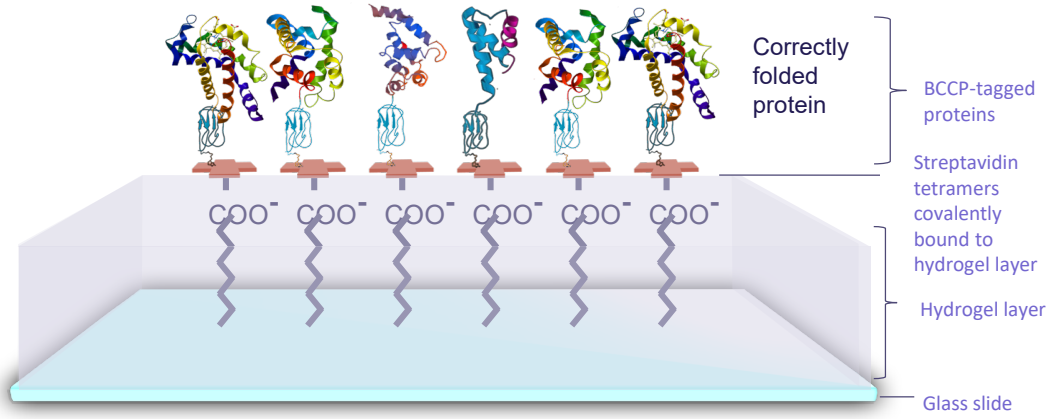
- *Systemic Lupus Erythematosus Up to 28yr*
- *Rheumatoid Arthritis – Up to 16yr*
- *Multiple sclerosis - Up to 14yr*

Digging deeper into the autoantibody-ome in biofluids



Thomas BG Poulsen
Malene M. Jørgensen

- IMMUNOME Discovery Array is a protein array which utilizes the patented Sengenics KREX™ functional proteomics technology.
- The array contains human proteins from biologically significant protein families including kinases, signalling molecules, cytokines, interleukins, chemokines and cancer antigens.



KREX technology enables autoantibody panels from single to 1600+ individual antigens.

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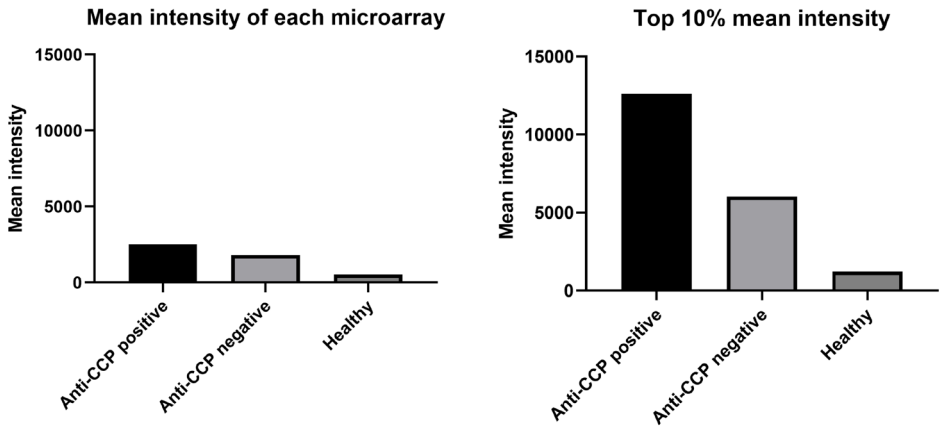
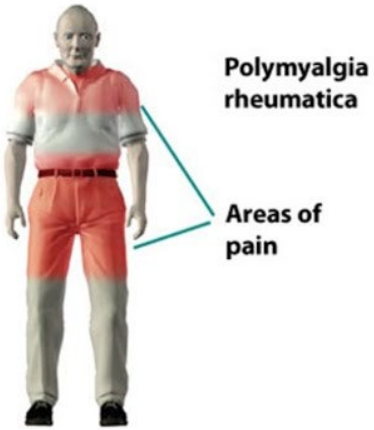
Discover diagnostic autoantibody biomarkers

Low noise of array technology enabling



Glucocorticoid Responsive mechanisms in plasma from Polymyalgia Rheumatica patients

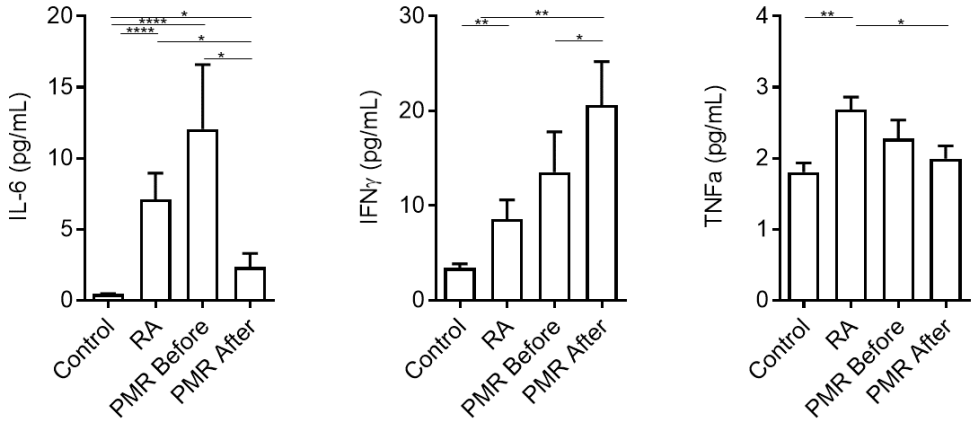
Michael Kruse Meyer

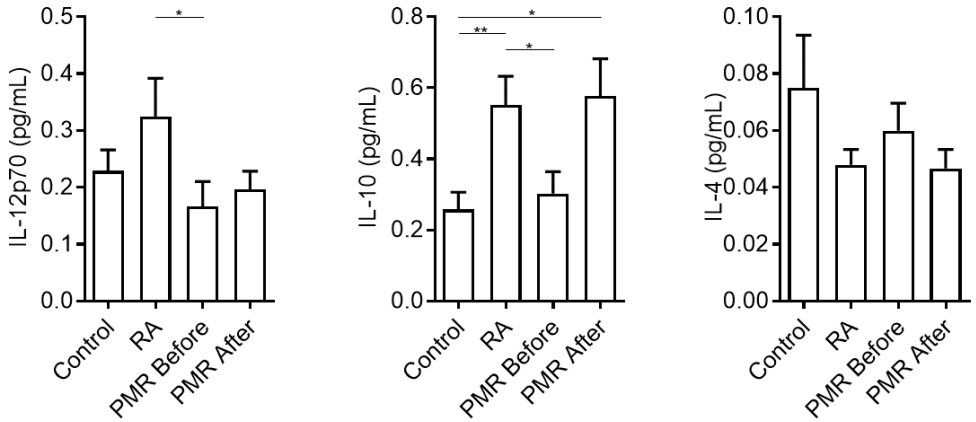


Polymyalgia rheumatica is a relatively common inflammatory rheumatic disease.

There are no validated international guidelines available for the diagnosis and treatment of PMR; however, diagnostic and classification criteria are currently being developed.

A quantitative proteome study design to compare with DMARD naïve RA patients and matched controls





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Temporal Changes Of Inflammation In Multiple Sclerosis Related To The Evolution Of Enhancing Lesions On The MRI

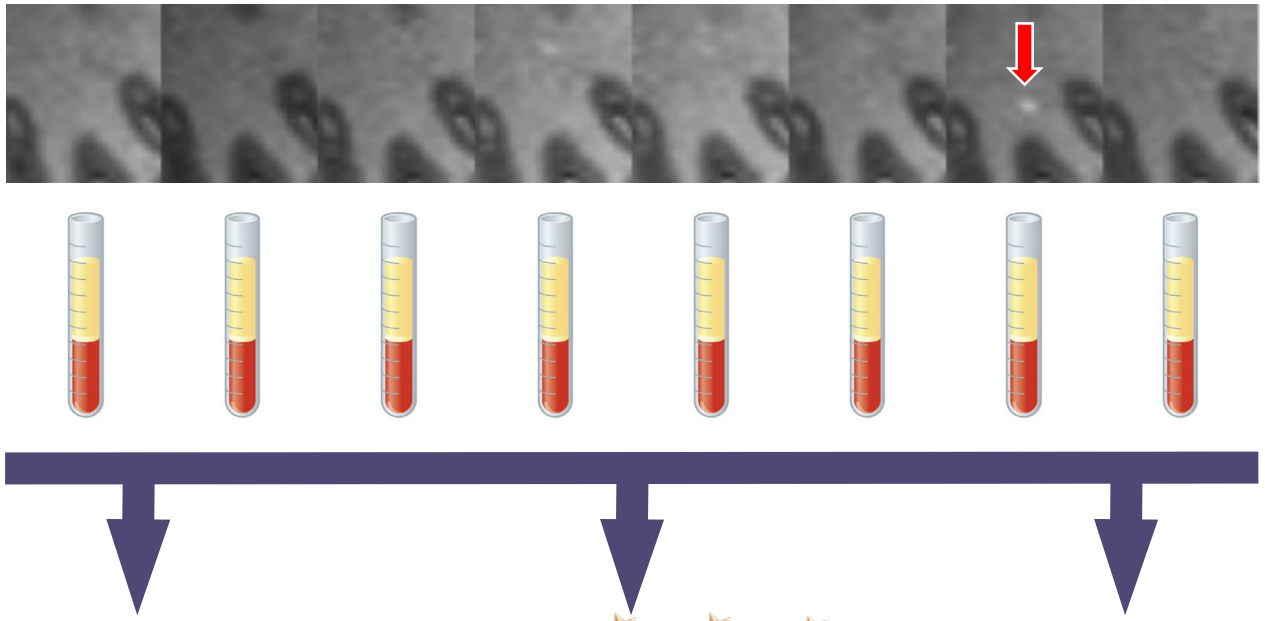
MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Multiple sclerosis lesion formation and early evolution revisited: A weekly high-resolution magnetic resonance imaging study

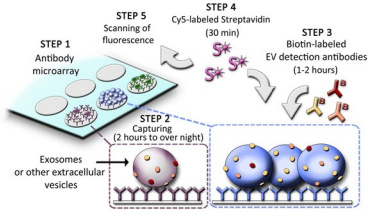
Charles RG Guttmann*, Matthieu Rousset*, Jean A Roch, Salem Hannoun, Françoise Durand-Dubief, Boubakeur Belaroussi, Michele Cavallari, Muriel Rabilloud, Dominique Sappey-Marinier, Sandra Vukusic and François Cotton

- Multiple Sclerosis patients were monitored for MS lesion activity, onset frequency, and early disease evolution.
- We investigated the inflammatory profile for correlation of disease status and biomarkers



Weekly MRI scanning (8 weeks)

Patient plasma



Endothelial stress optimized EVArray

Multiplex Immunoarray

Discovery Proteomics

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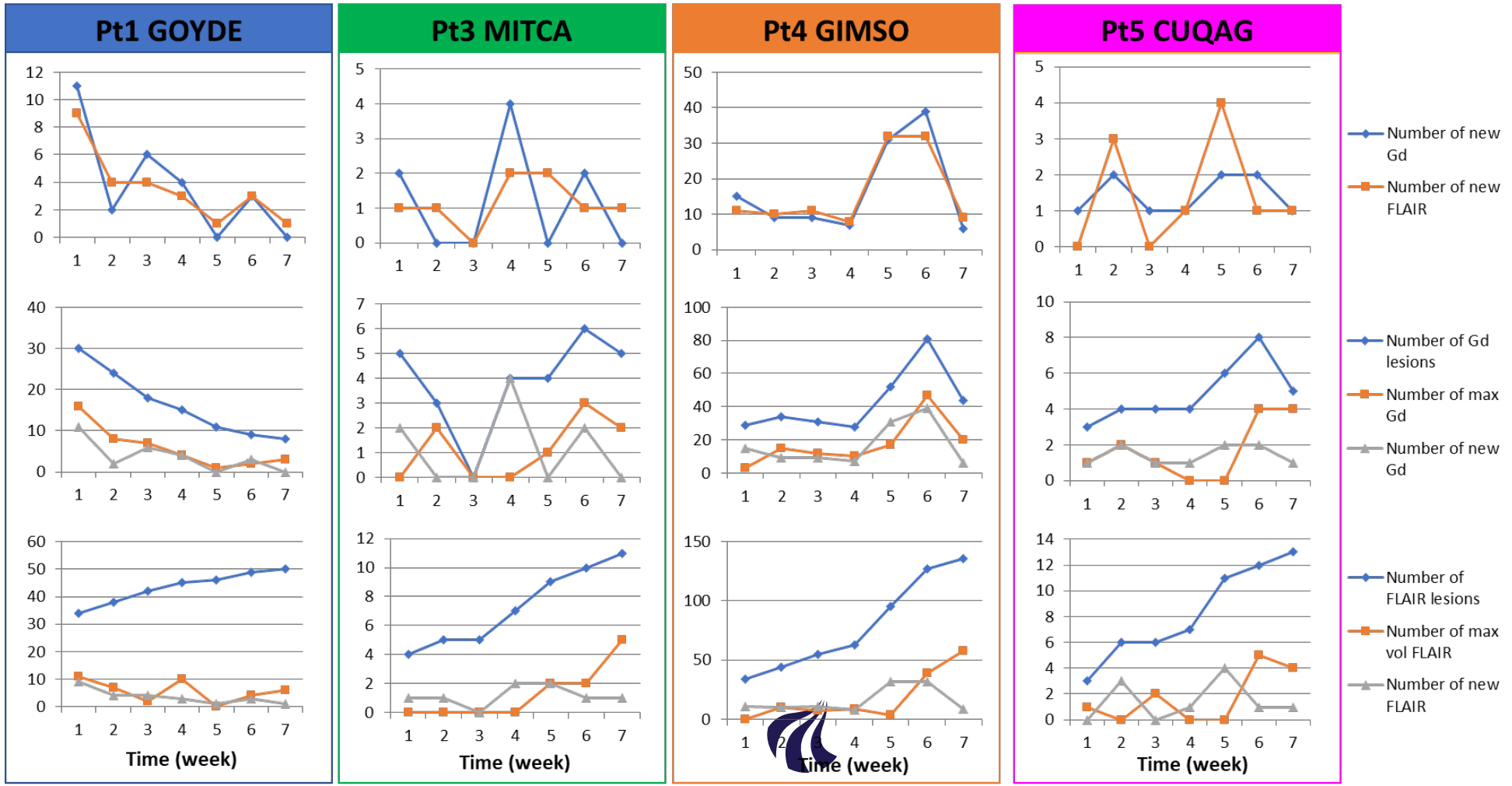
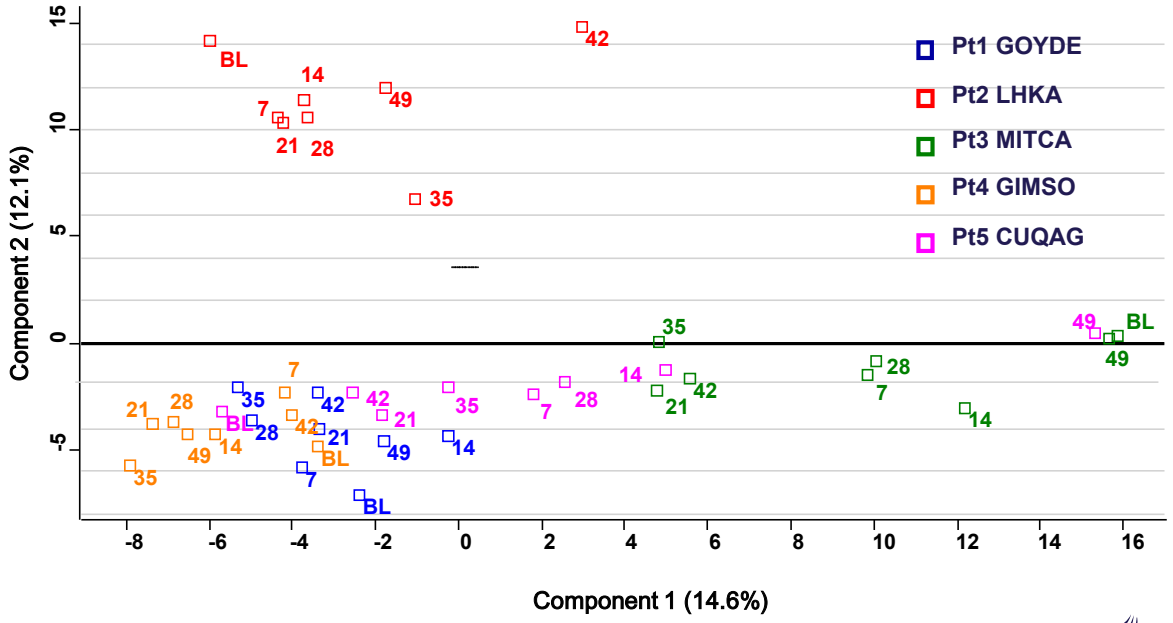
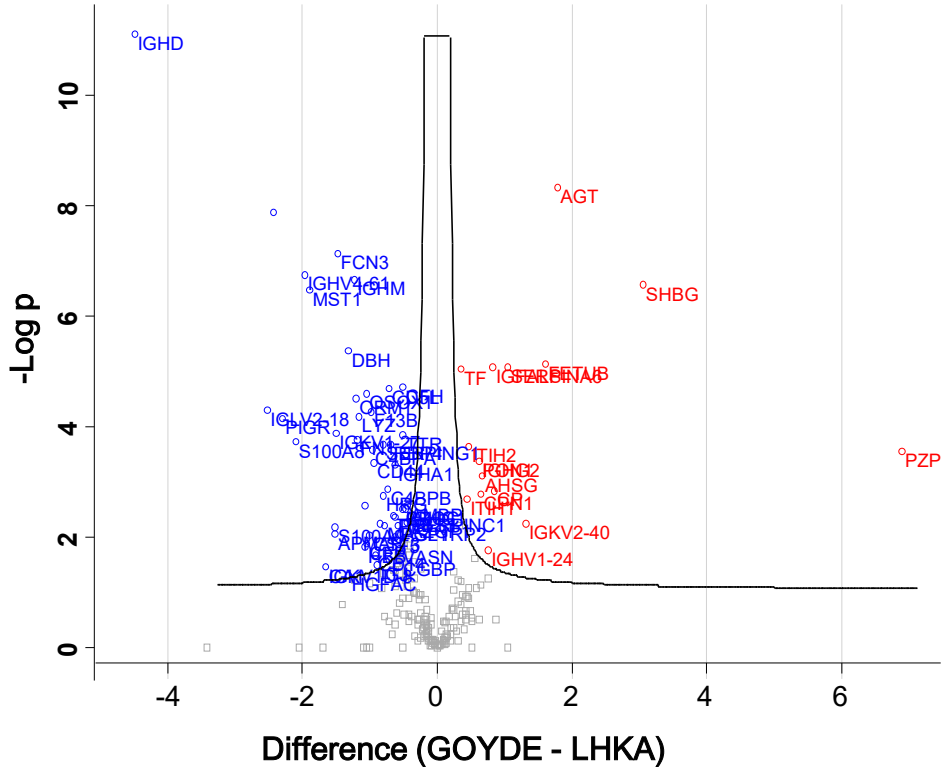
Temporal Changes Of Inflammation In Multiple Sclerosis Related To The Evolution Of Enhancing Lesions On The MRI



Temporal Changes Of Inflammation In Multiple Sclerosis Related To The Evolution Of Enhancing Lesions On The MRI

Quantitative proteomics reveals individualized plasma profiles and FLAIR intensity related markers





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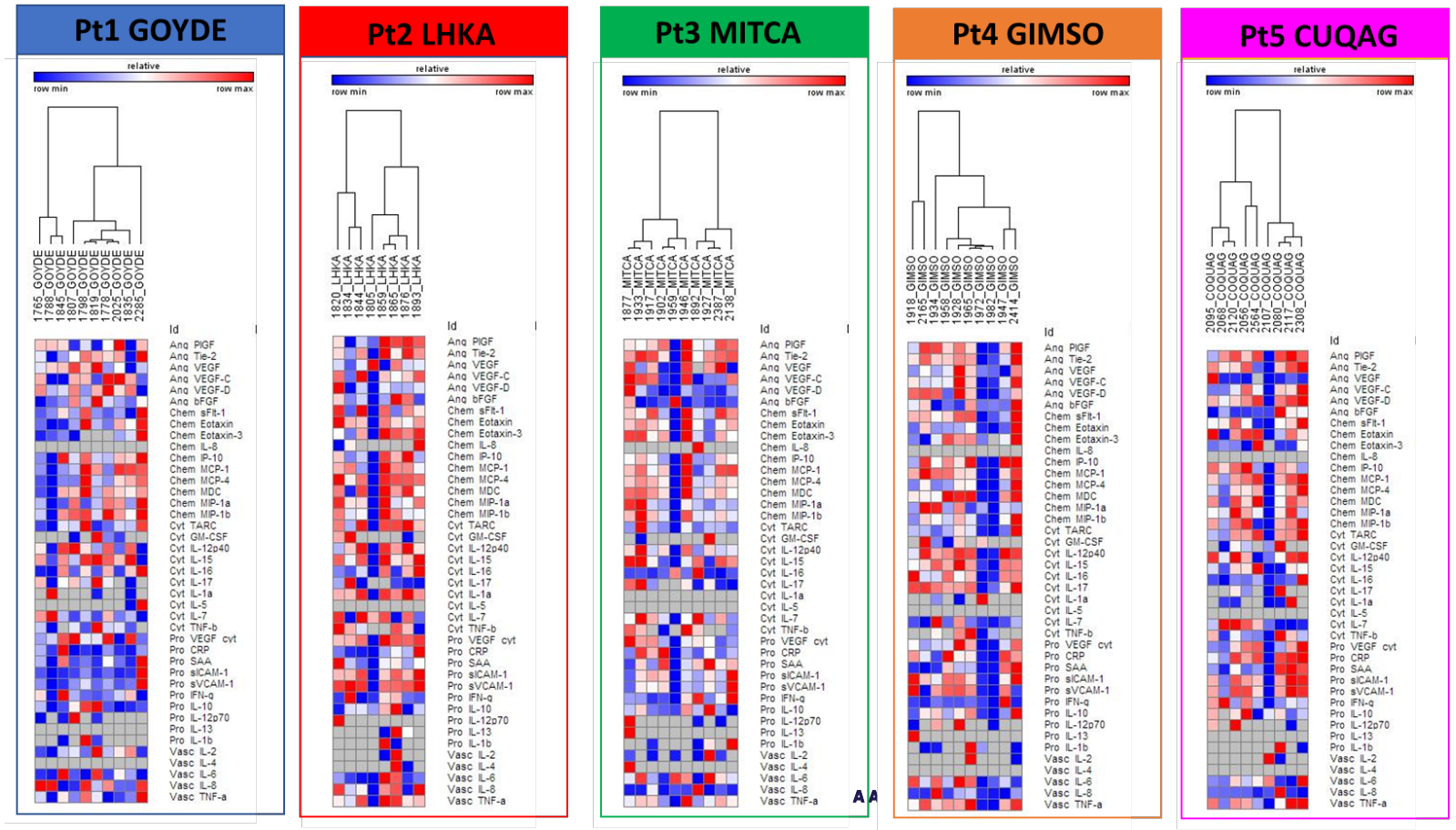
Temporal Changes Of Inflammation In Multiple Sclerosis Related To The Evolution Of Enhancing Lesions On The MRI

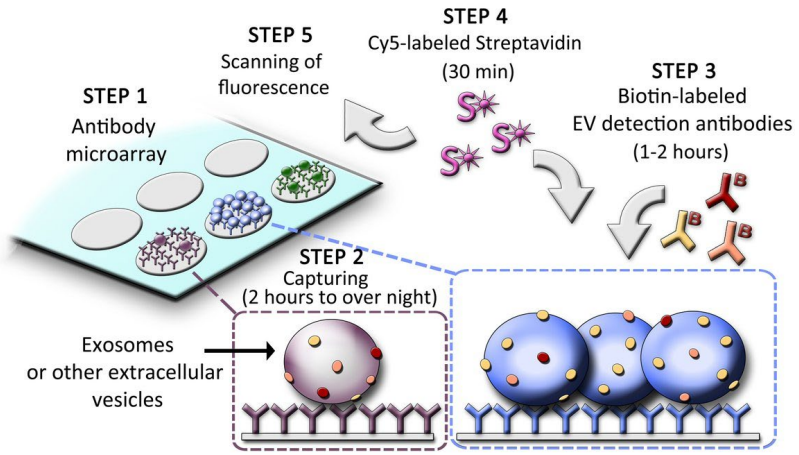
Quantitative assessment of cytokine and chemokine revealed patient to patient variation not correlating to FLAIR profiles

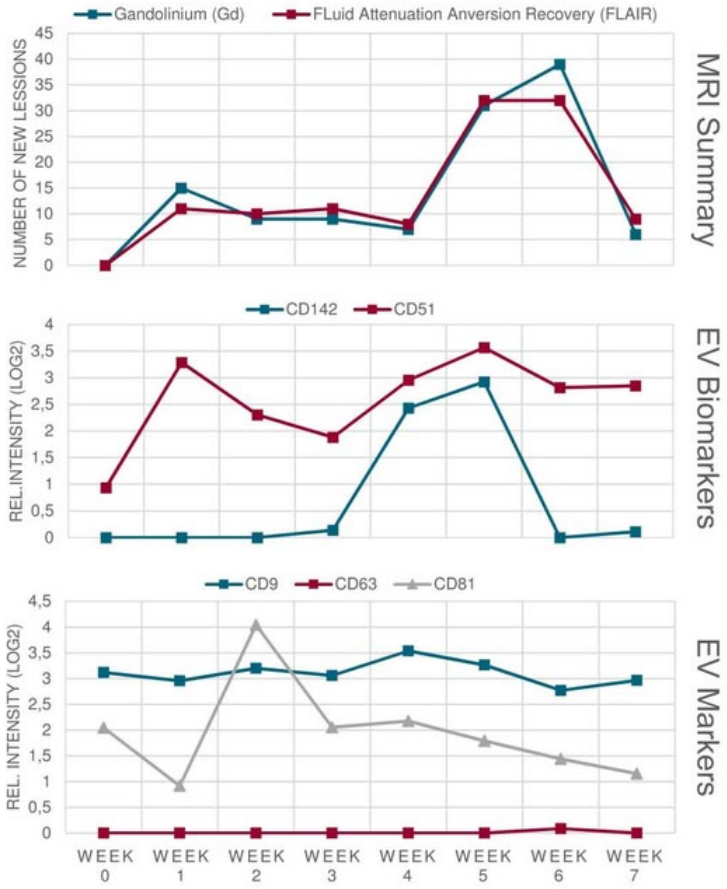


Temporal Changes Of Inflammation In Multiple Sclerosis Related To The Evolution Of Enhancing Lesions On The MRI

Quantitative assessment of EV marker profiles revealed patient to patient variation and multiple markers correlating to FLAIR profiles

EV	Immune	Endothelial	Platelet	Other
Annexin V	CD3	CD31	CD42a	LAMP2
CD9	CD8α	CD51	CD62 E	TNF RII
CD63	CD19	CD146	CD62 E/P	Tspan8
CD81	CD28	tPA	CD142	AKAP3
CD82	CD80	Thrombospondin-1		CD106
TNF RI	MIC A/B	VE-Cadherin		CD151
TSG101	CTLA4			
Alix	ICAM-1			
	HLA DR/DP/DQ			





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- Azra Karamehmedovic
- Joakim Bastrup
- Ditte Kristensen
- Kenneth Kastanjegaard
- Michael Kruse Meyer
- Christopher Aboo

Sangild Lab

- Tik Muk
- Ping ping Jiang
- Ninh Duc Nguyen

Other Important People for the presented work

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- Rikke Bæk
- Rikke Gry Nielsen (vet)
- Jonathan Blackburn - Sengenics

Danish National Hospital

- Claus H. Nielsen
- Dres Damgaard

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HORIZON 2020
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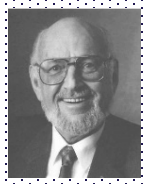


Svend Andersen-Fonden

Lundbeck

DET FRIE FORSKNINGSRÅD
DANISH COUNCIL FOR INDEPENDENT RESEARCH

LUNDBECK FOUNDATION

spar Nord FONDEN

CARLSBERG FOUNDATION

DET OBELSKE FAMILIEFOND

The transition at birth and the preterm problem

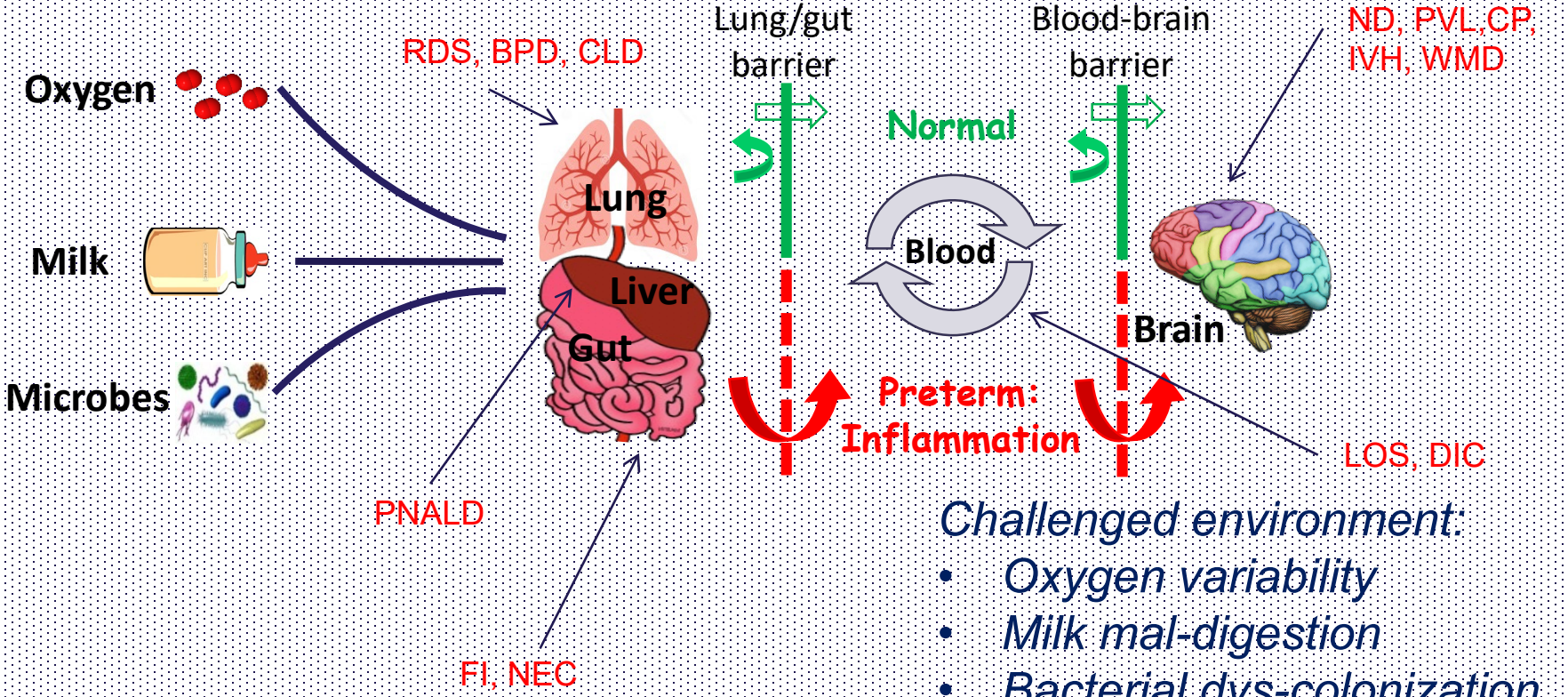
Tik Muk

Azra Karamehmedovic

NEOMICS

Preterm infants are susceptible to sepsis, which in turn may lead to neurodevelopmental disorders

Milk and microbiota effects on immunity, gut and brain development is poorly understood

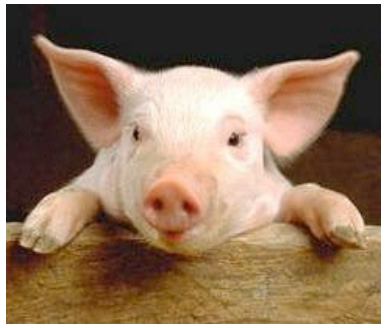


Challenged environment:

- *Oxygen variability*
- *Milk mal-digestion*
- *Bacterial dys-colonization*

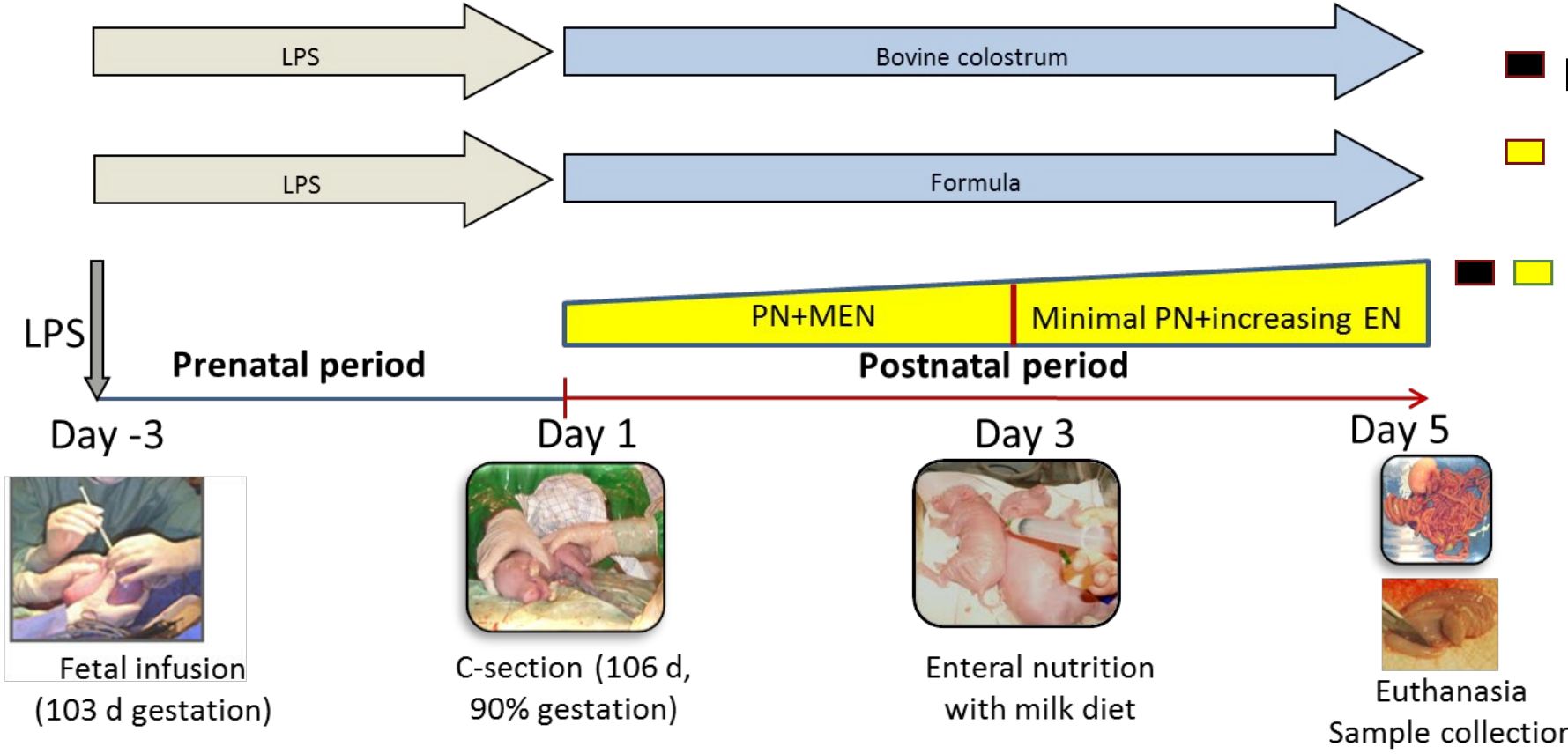
Proteomics - From pigs to humans infants

- *Many years of porcine to human proteomic work made available to facilitate future research with pigs as model system.*
- *Porcine model systems are feasible to study human diseases including immunological systems – by far better than rodents*
- *Proteomics findings can be translated between species using big data investigations*
- *Neonatal Omics necessitate focus on ethical restrictions and sample availability*

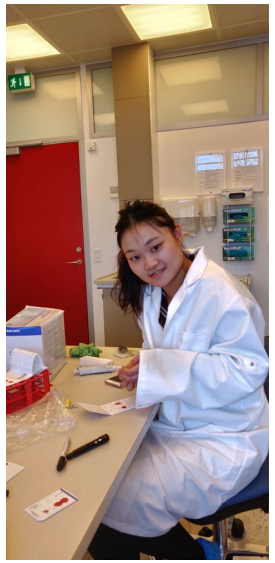


Pig model for neonatal sepsis

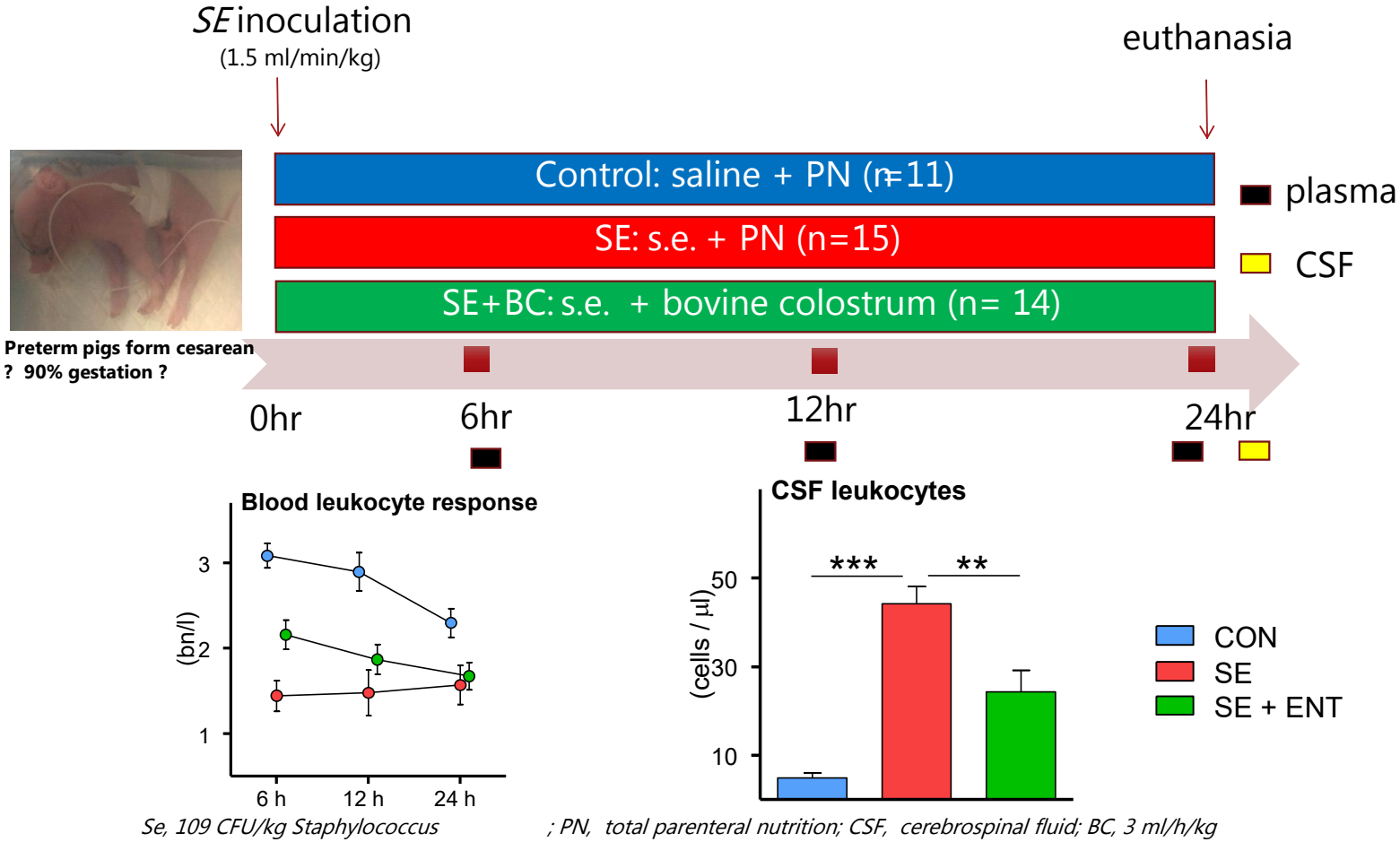
Postnatal dietary effects following prenatal inflammation



Pig model for neonatal sepsis



Tik Muk



Se, 109 CFU/kg Staphylococcus epidermidis ; PN, total parenteral nutrition; CSF, cerebrospinal fluid; BC, 3 ml/h/kg

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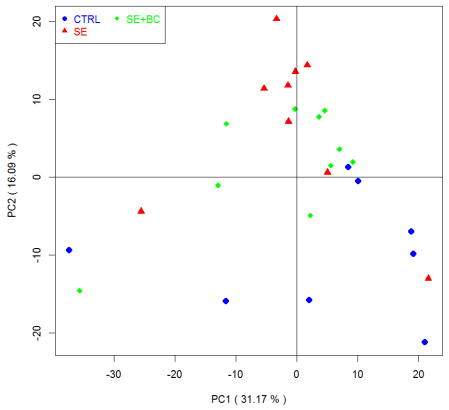
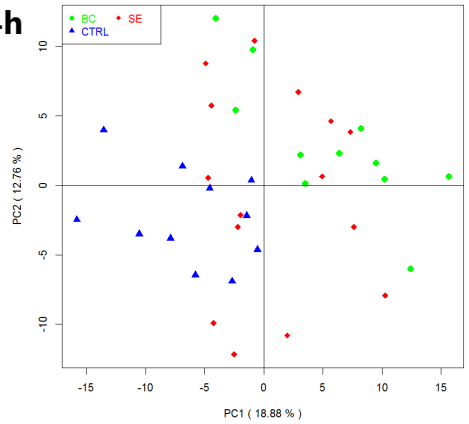
Proteomics workflow for determination of diet and sepsis markers

Effect" markers:

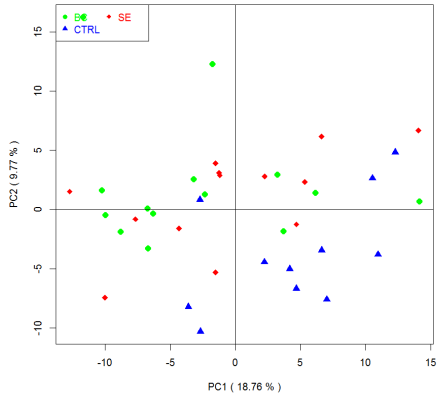
In CSF



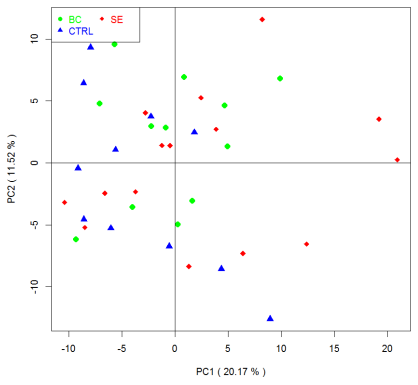
In 24h



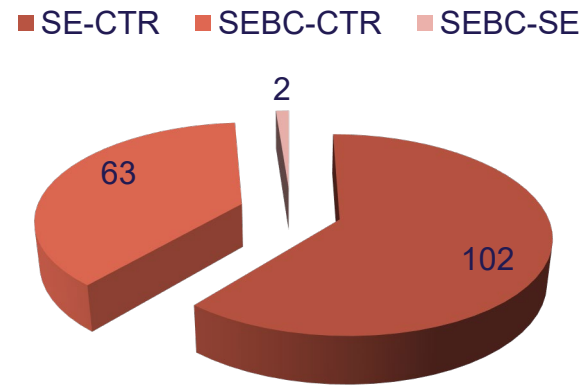
In 12h



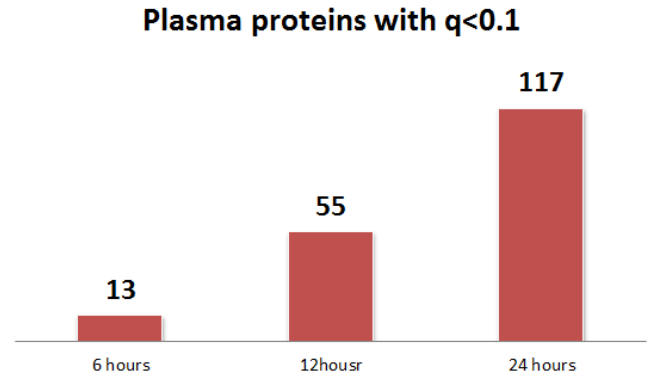
In 6h



114 out of **1960** proteins with q<0.1 found in CSF.



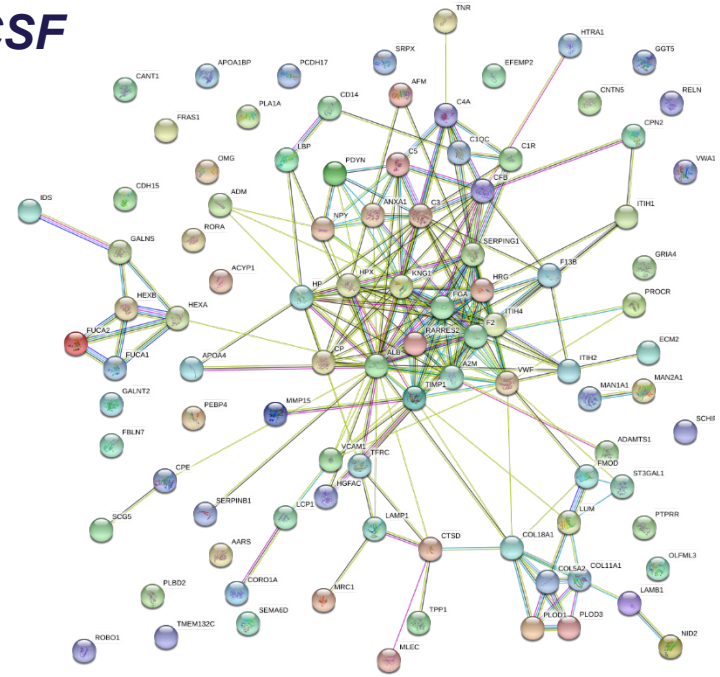
180 out of **735** proteins with q<0.1 found in plasma.



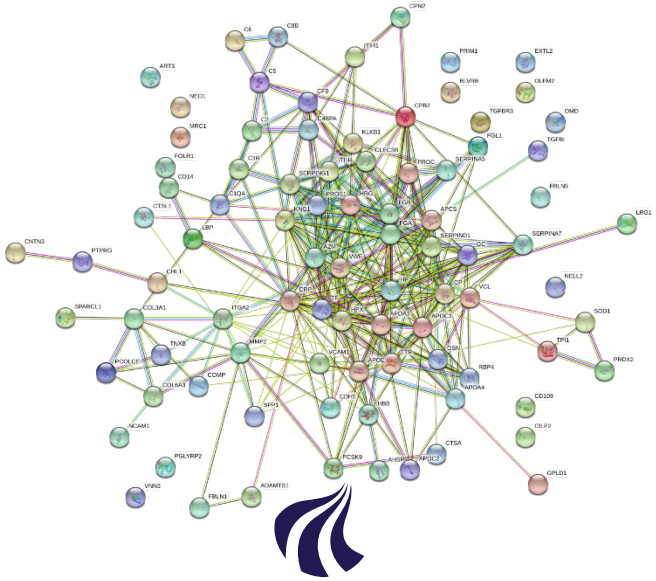
Proteomics workflow for determination of diet and sepsis markers

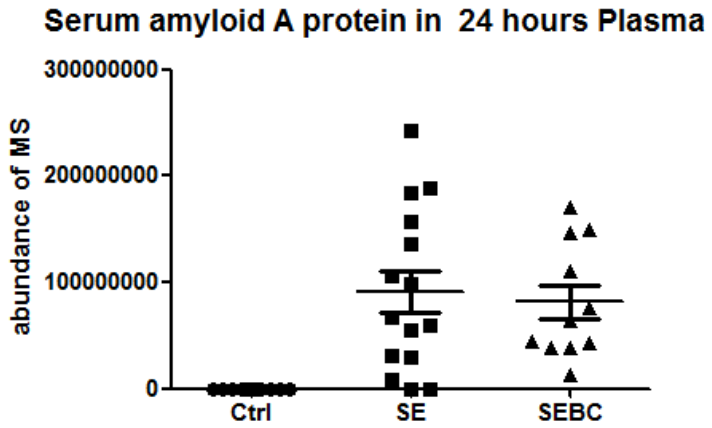
Effect and exposure markers
Inflammation related protein
Complement system
Neural proteins
Transportation proteins

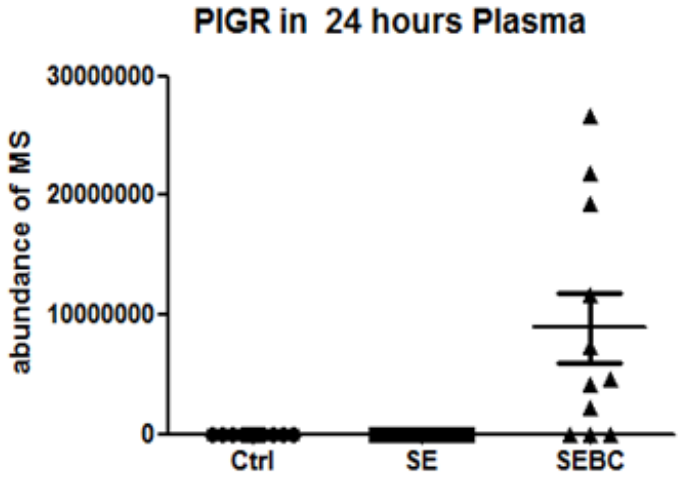
In CSF



In Plasma at 24 hours

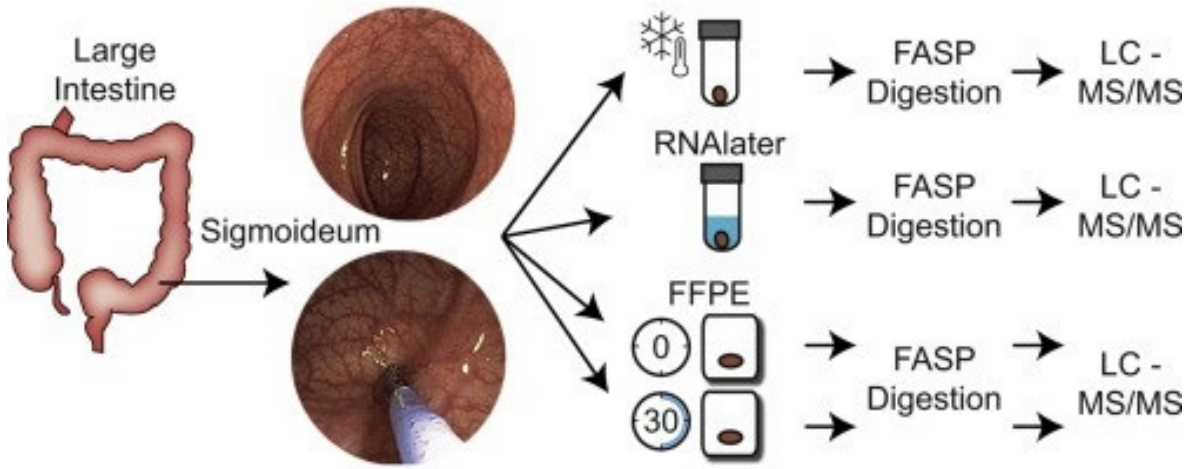


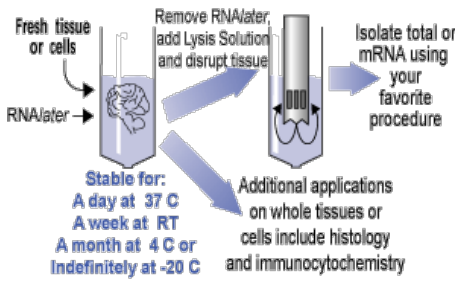


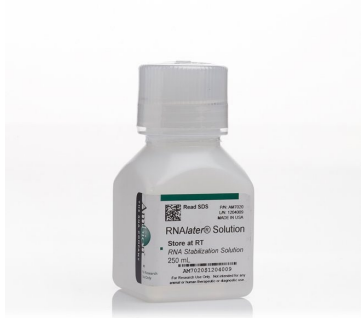


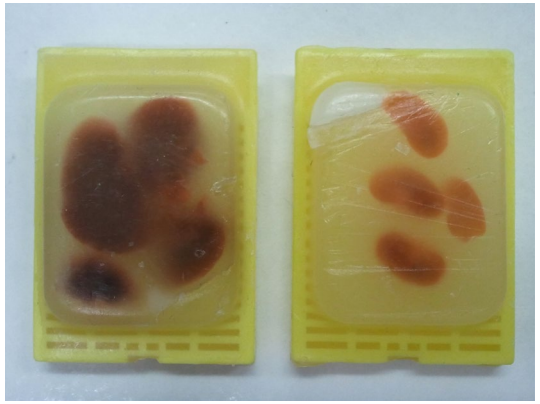
Improved sample preparation from Biobank samples

- Most biological samples are preferably snap-frozen and stored at -80C
- Typical samples are serum, plasma, tissue and immune cells









Bennike, T.B., Kastaniegaard, K., Padurariu, S., Gaihede, M., Birkelund, S., Andersen, V., and Stensballe, A. (2015). Comparing the proteome of snap frozen, RNAlater preserved, and formalin-fixed paraffin-embedded human tissue samples. EuPA Open Proteomics.

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Improved sample preparation from Biobank samples

FFPE biopsy

↓

Optimized FFPE removal and NaDOC based protein extraction

↓

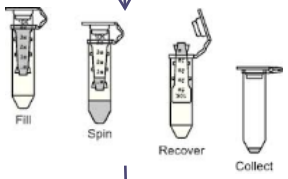
In solution digest (trypsin/; IAM)

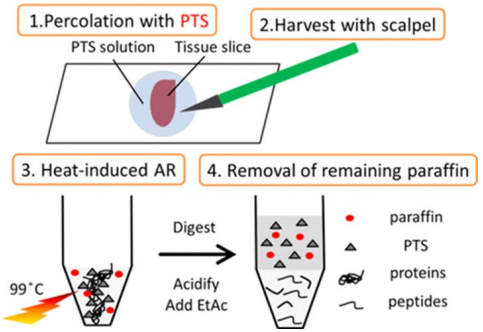
↓

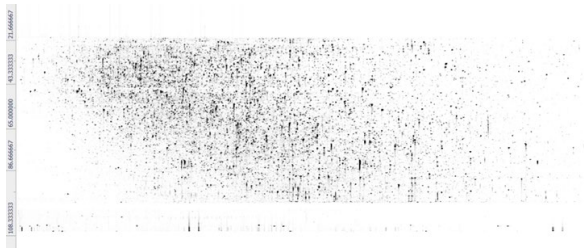
UPLC tandem MS (Qexactive 2hr gradient)

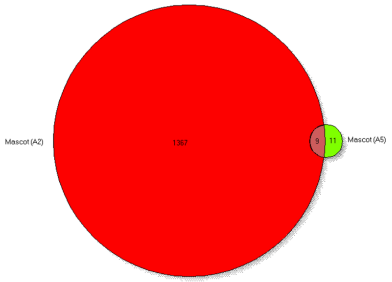
↓

Protein ID

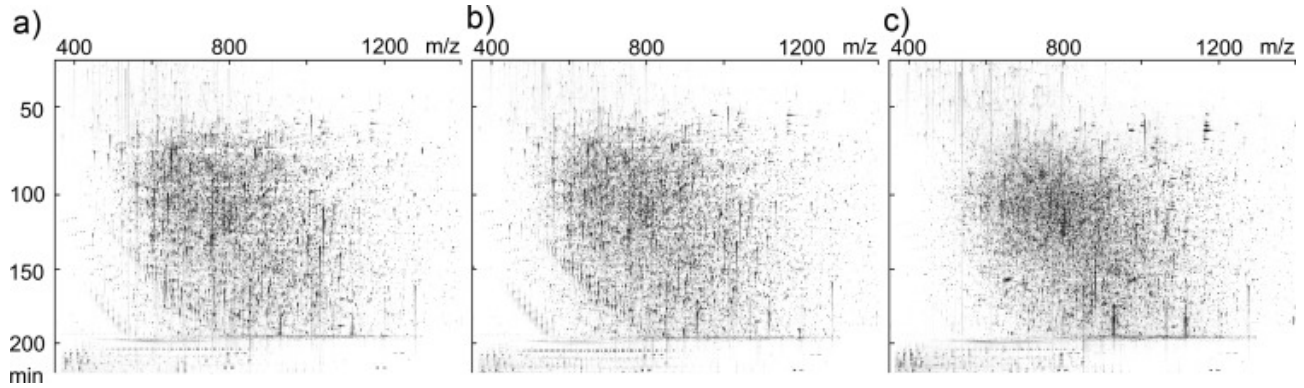


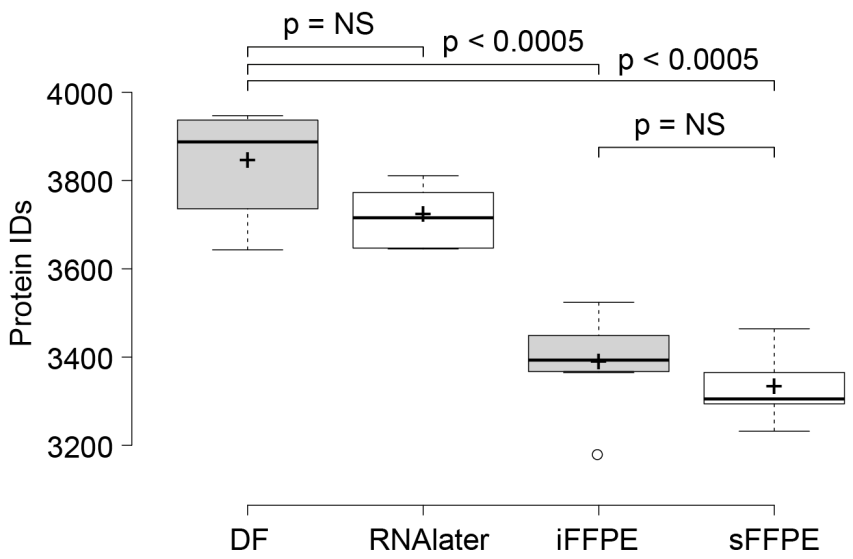


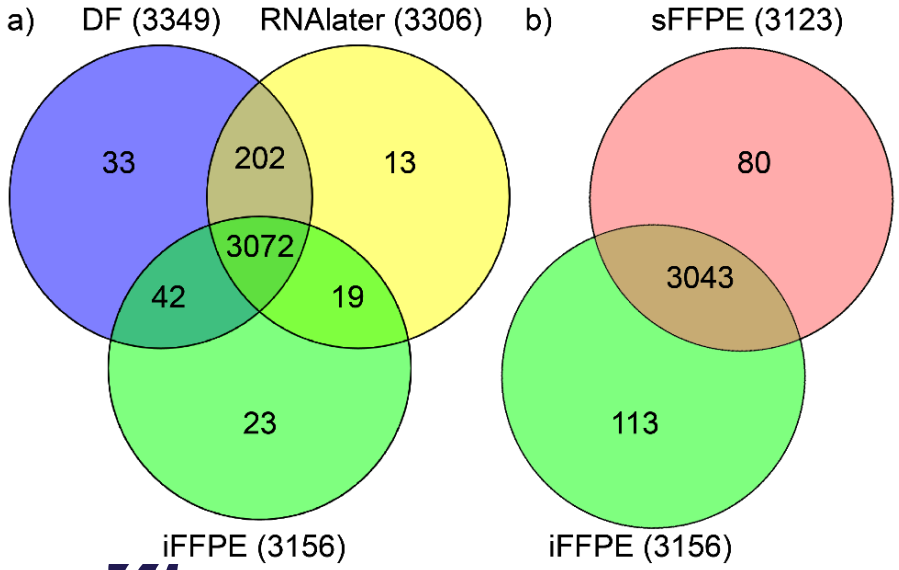




Improved sample preparation from Biobank samples

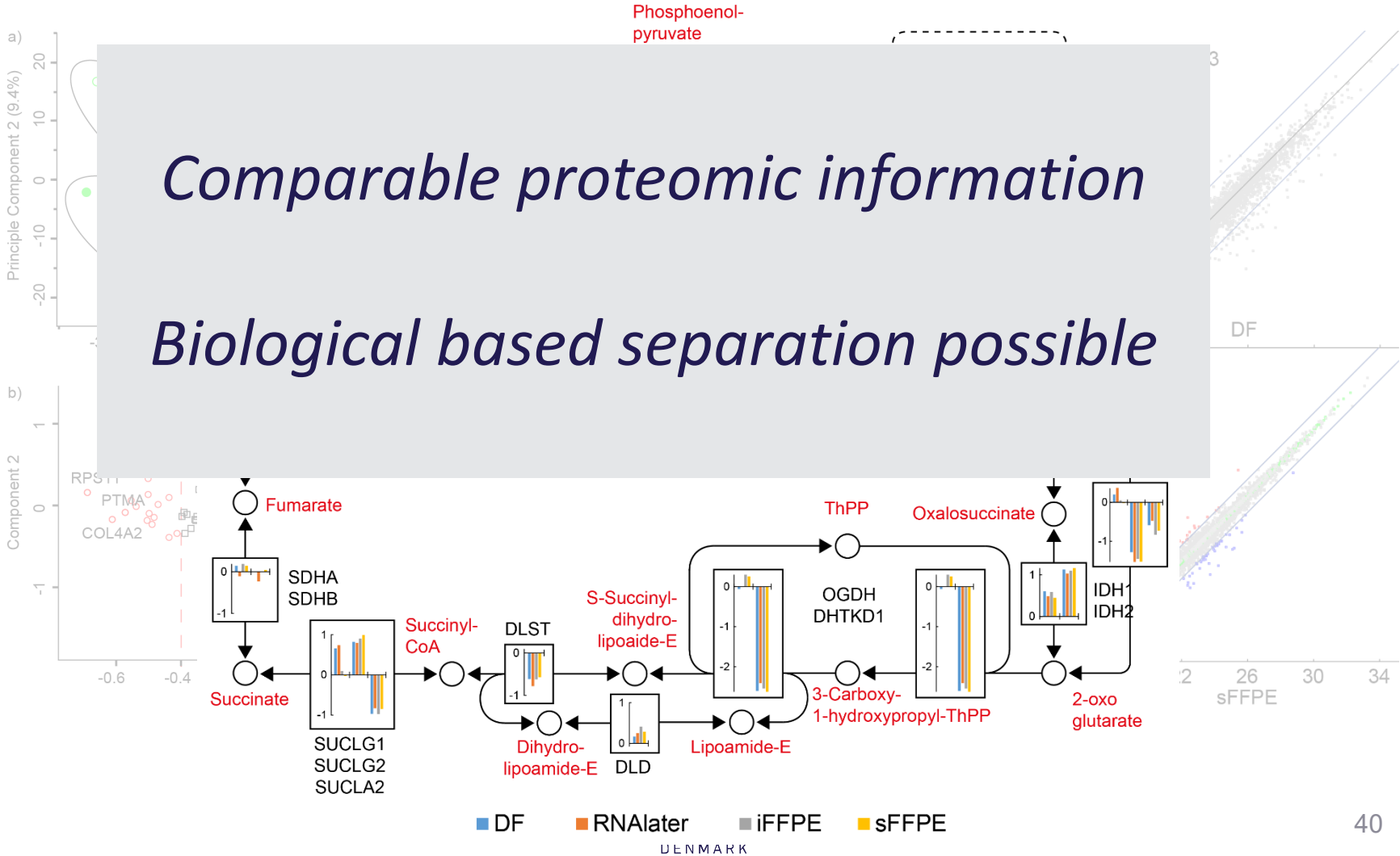






Bennike, T.B., Kastaniegaard, K., Padurariu, S., Gaihede, M., Birkelund, S., Andersen, V., and Stensballe, A. (2015). Comparing the proteome of snap frozen, RNAlater preserved, and formalin-fixed paraffin-embedded human tissue samples. EuPA Open Proteomics.

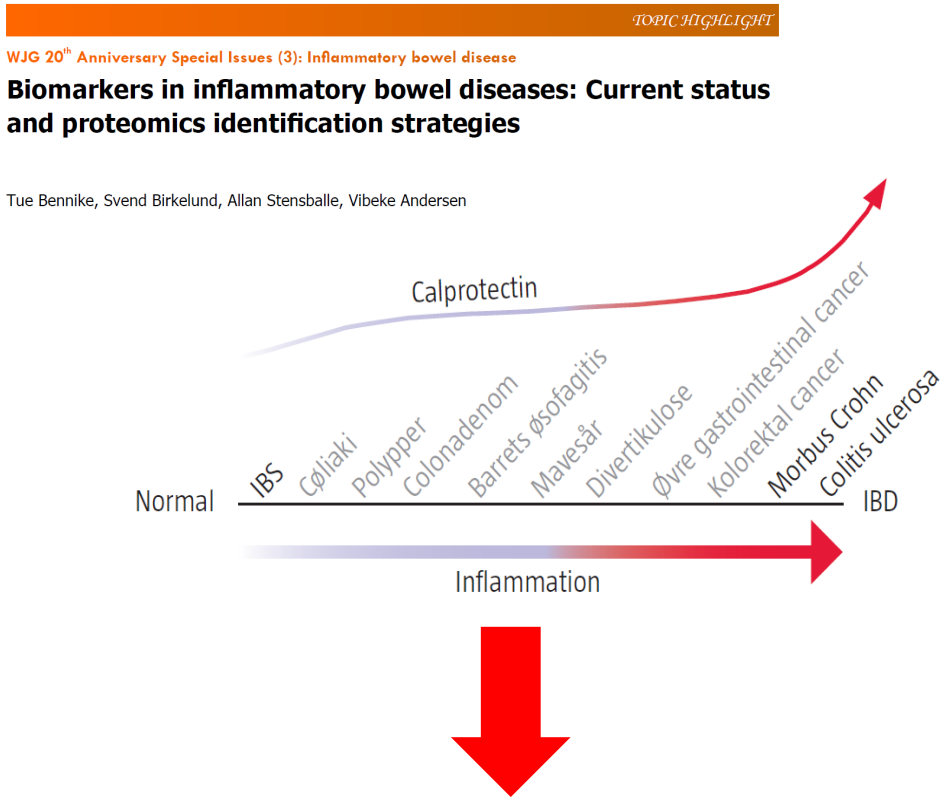
Pathway analysis of quantitative MS data



Assistant Prof. Tue Bennike.

Inflammatory Bowel Diseases vs Rheumatoid Artritis

- Inflammatory Bowel Disease (IBD) comprises two major disease entities, Crohn's disease (CD) and ulcerative colitis (UC)
- IBDs are common diseases with a prevalence of 1% and of raising prevalence
- Diagnosis of IBDs depends on clinical symptoms, endoscopy, histology, MR-scanning, and the exclusion of gut microbes and may be delayed for years
- Diagnosis is difficult and 10-20% change diagnosis or are termed indeterminate colitis



Our Goal:
Investigate the disease related proteome changes of the large intestine associated with IBD and RA

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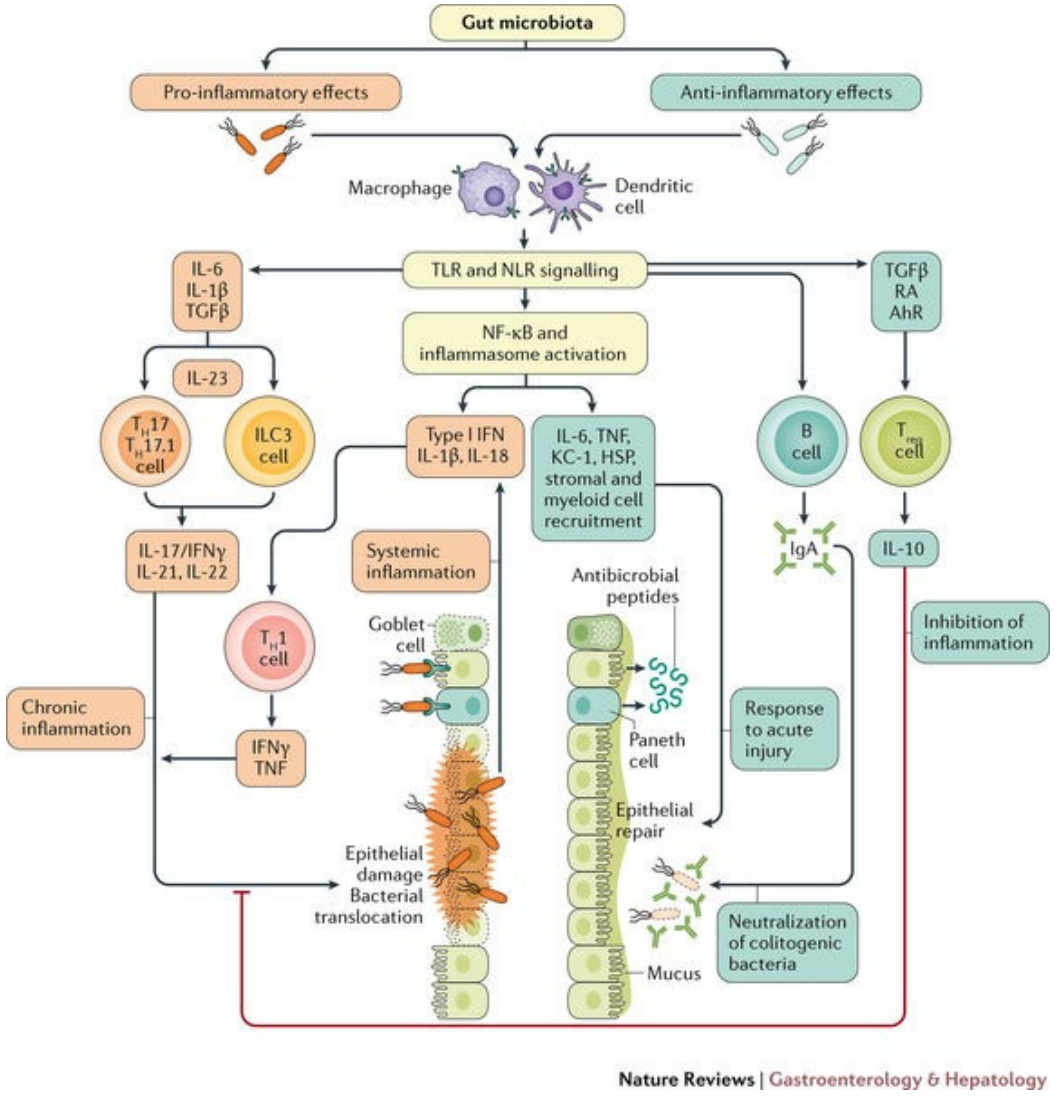
The intestinal barrier in the Gut

- IBD is associated with compositional and metabolic changes in the intestinal microbiota (dysbiosis).
- Several alterations of the barrier function have been identified in IBD, starting from mucus features up to its components, from epithelial junctions up to the Toll-like receptors, and altered immune responses



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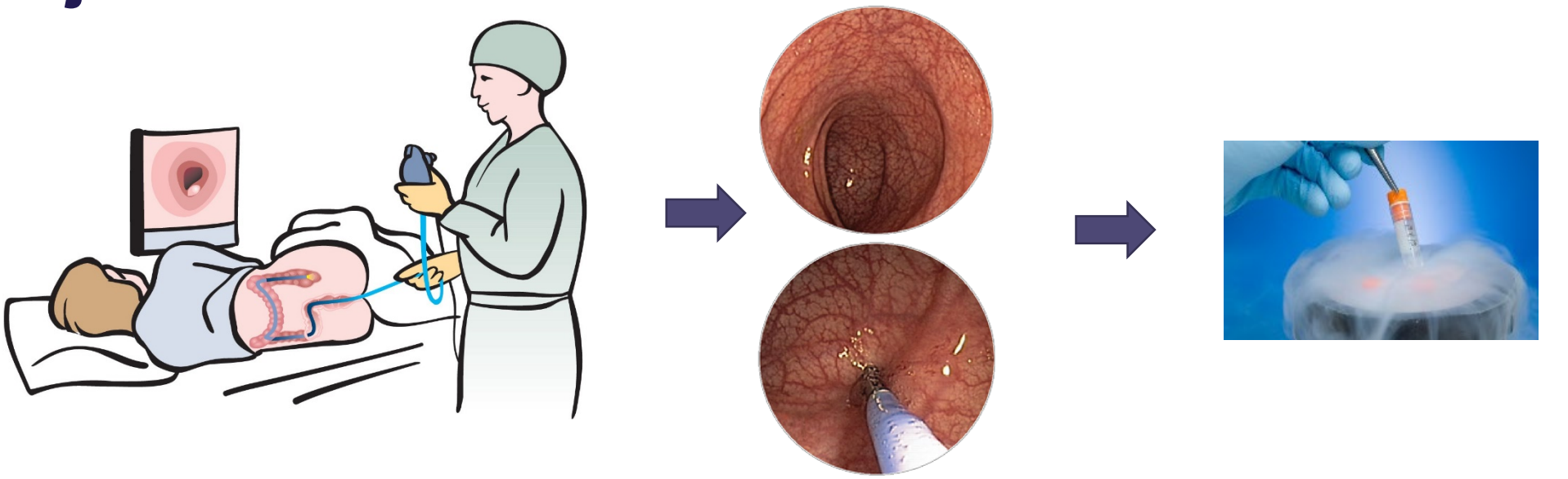
Nature Reviews Gastroenterology & Hepatology
2017 vol: 14 (10) pp: 573

The Silkeborg IBD vs RA Project

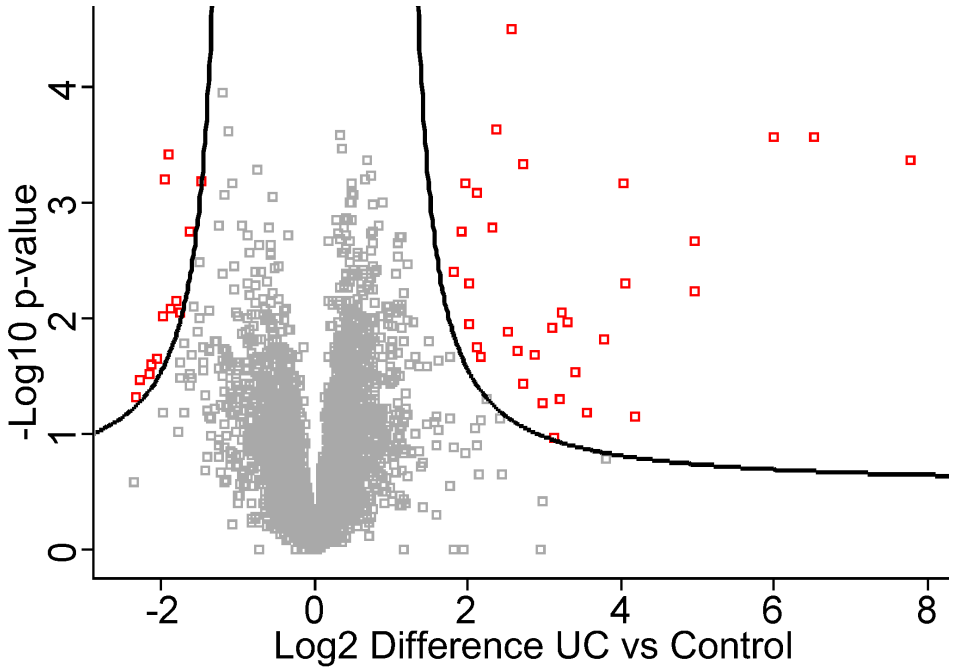


- 10x Ulcerative Colitis
  - Unambiguous diagnosis.
  - Medicated, no disease flairs.
- 10x Reumatoid artritis
  - Unambiguous diagnosis.
  - No gut inflammation detectable by microscopy
- 10x Controls
  - Cancer screenings with no findings

- Proteomics
  - Snap frozen in $N_{2(L)}$, stored at -140C°
  - Mean weight 4.9 mg [3.6-5.9 mg; 25th-75th percentiles]

Proteome analysis reveals activation of innate immune system in ”healthy-looking” UC tissue

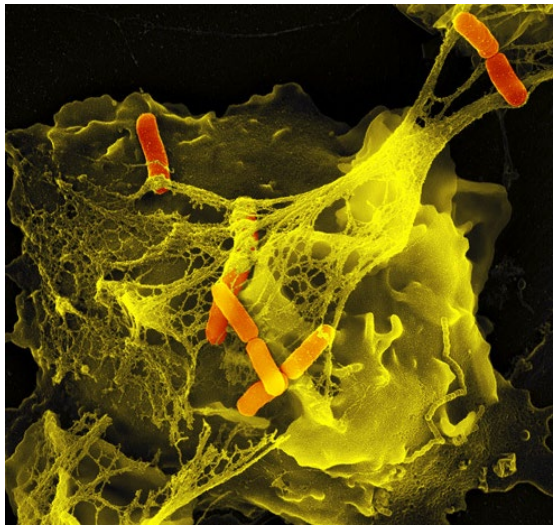
- 5,444 proteins quantifiable!
- T-tests with permutation tests to control false positives.
- 46 proteins with a statistical significant abundance change.
  - 33 more abundant in UC and 13 less.
  - 15% false positives at this cutoff.
  - Statistical significantly changed proteins biological relevant!




Discovery of NETs in gut intesitnal tissue

- Neutrophil extracellular traps (NETs) is an important line of defense against microbiota
- Eleven statistically significant proteins involved in NETs
  - all increased in ulcerative colitis!

Fold Change	Protein Description	Peptides	SQ
219.2	*Lactotransferrin	51 (49)	73%
92.1	*Matrix metalloproteinase-9	30 (30)	52%
63.3	*Myeloperoxidase	48 (41)	59%
31.3	*Neutrophil elastase	11 (11)	55%
16.3	*Protein S100-A9	10 (10)	79%
11.8	*Protein S100-A12	5 (5)	36%
9.9	*Neutrophil defensin 3	5 (5)	27%
6.6	*Galectin-10	11 (11)	68%
5.9	*Eosinophil cationic protein	10 (10)	47%
4.5	*Myeloid cell nuclear diff. antigen	17 (17)	39%
3.5	*Cathepsin G	16 (16)	54%



NETs trap the invading microorganisms and facilitates interaction with other effector molecules that kill the microorganisms.

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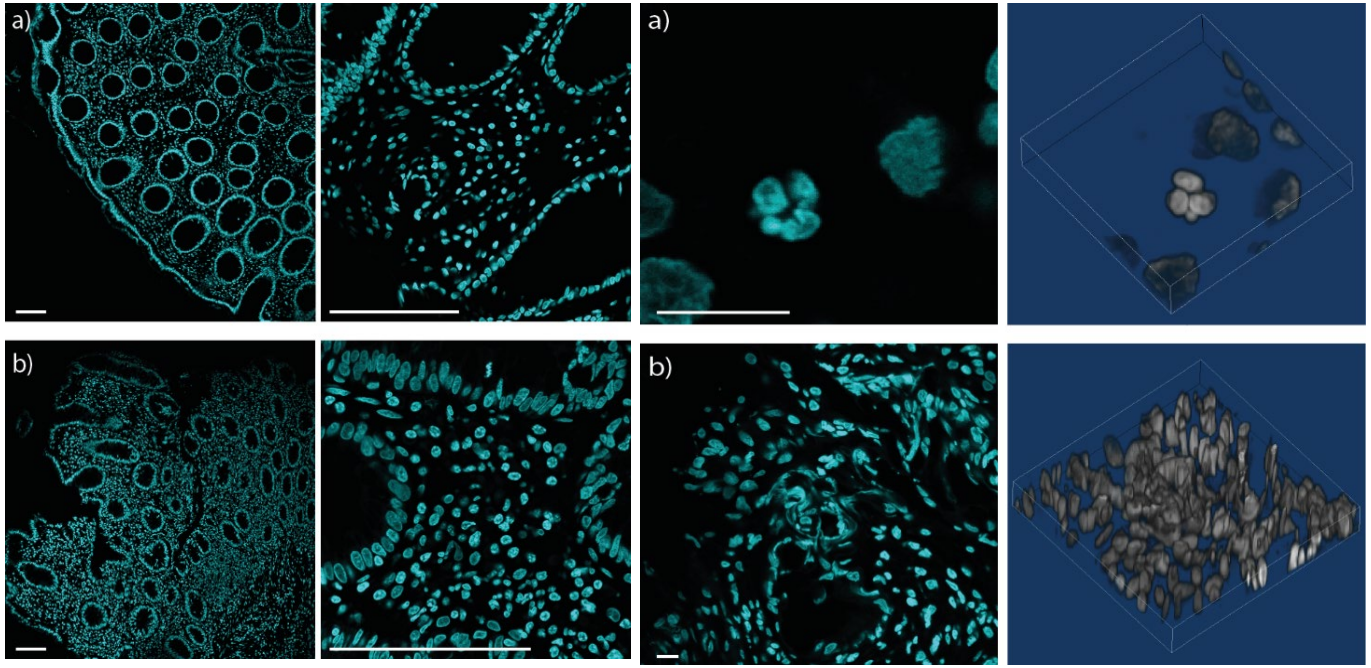
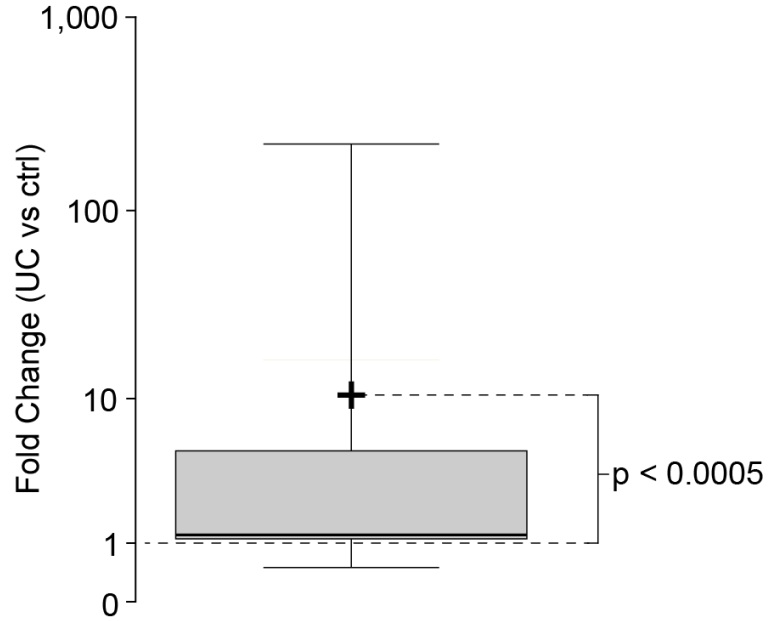
Discovery of NETs in gut intestinal tissue

NETs formation by excretion of the neutrophil DNA (TO-PRO-3 stain).





In total 49 proteins associated with NETs quantified!

Mean fold abundance: 10.9 fold increased in ulcerative colitis tissue.

Proteome analysis of RA Intestinal Mucosa reveals drug induces proteome changes and protein citrullination effects.

To gain new insight into the systemic immune manifestations of RA, we characterized the colon mucosa proteome from RA-patients and healthy controls.

Journal of proteome research

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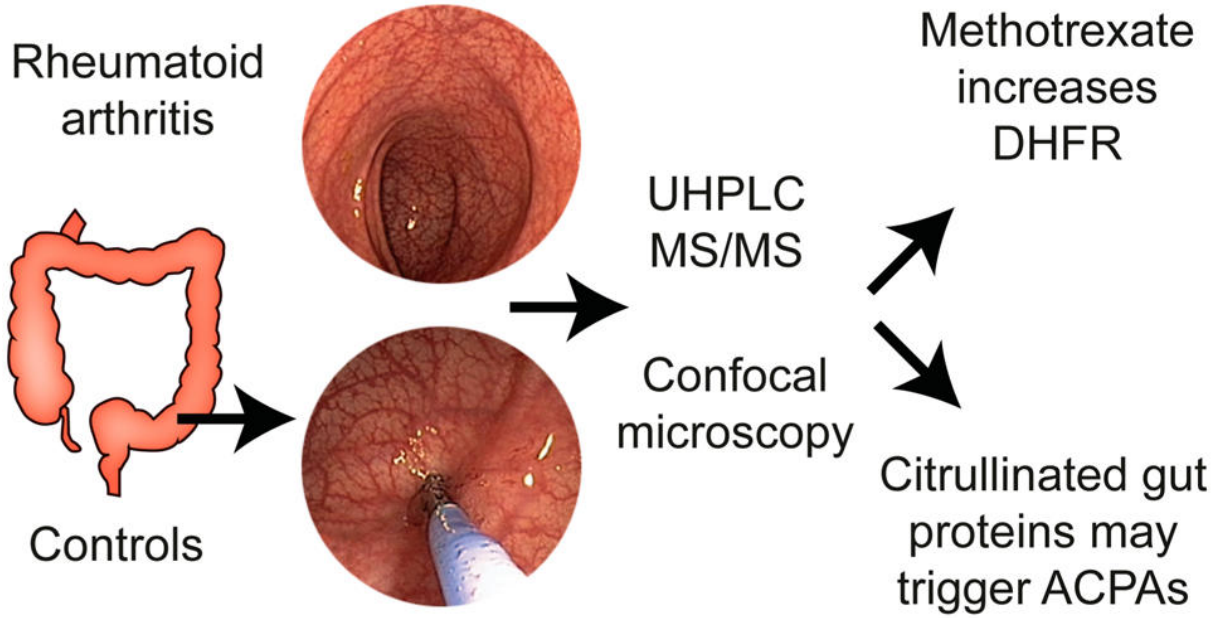
Article

A Proteome Analysis of Rheumatoid Arthritis Gut Mucosa

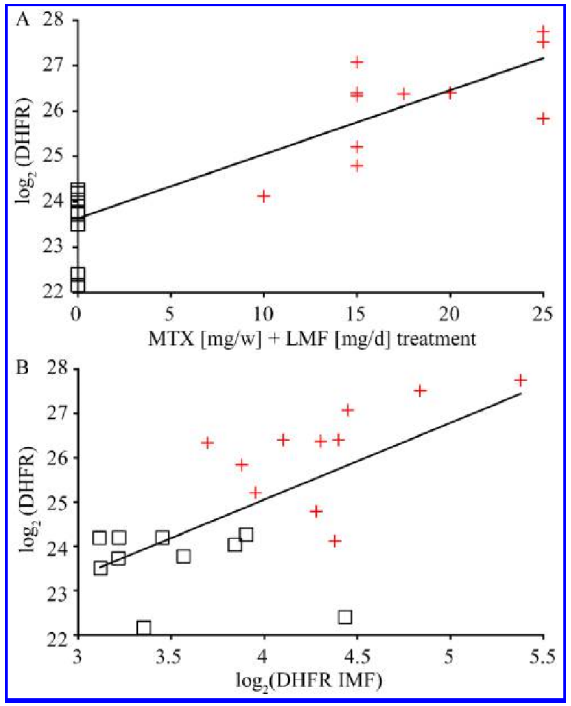
Tue Bjerg Bennike, Torkell Ellingsen, Henning Glerup, Ole Kristian Bonderup, Thomas Gelsing Carlsen, Michael Kruse Kruse Meyer, Martin Bøgsted, Gunna Christiansen, Svend Birkelund, Vibeke Andersen, and Allan Stensballe

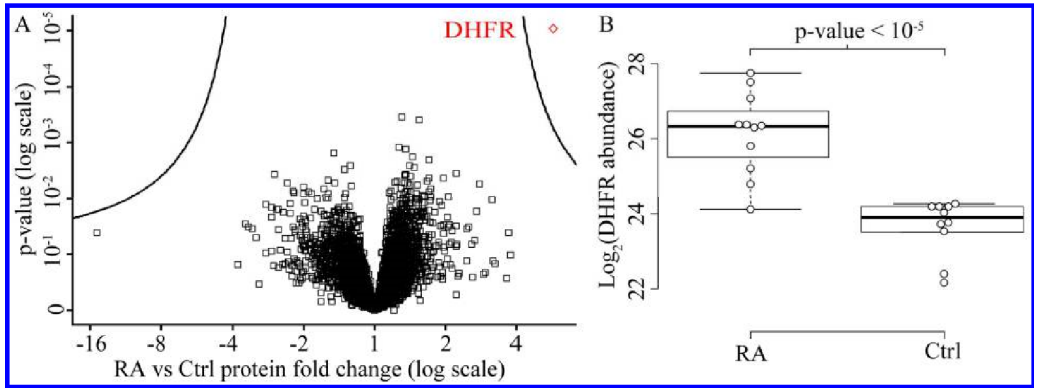
J. Proteome Res., **Just Accepted Manuscript** • DOI: 10.1021/acs.jproteome.6b00598 • Publication Date (Web): 14 Sep 2016

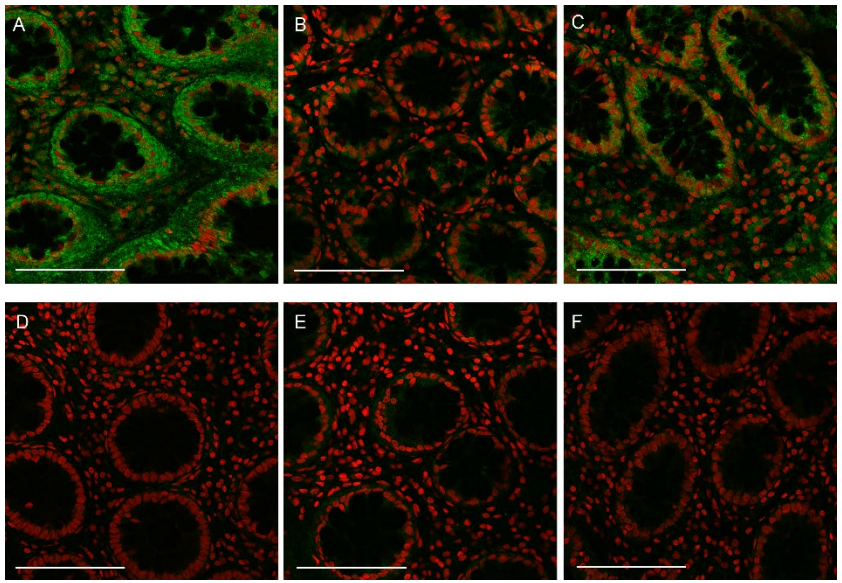


Drug treatment to affect the human immune system that affects the proteome

- Only 1 protein is highly affected by the RA diagnosis.
- The protein DHFR is linked to the treatment with Metrotraxate.







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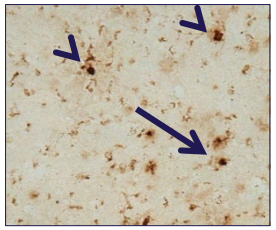
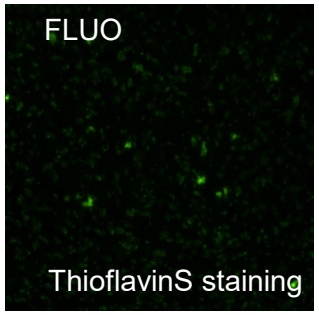
Microproteomics in AD, PD and depression

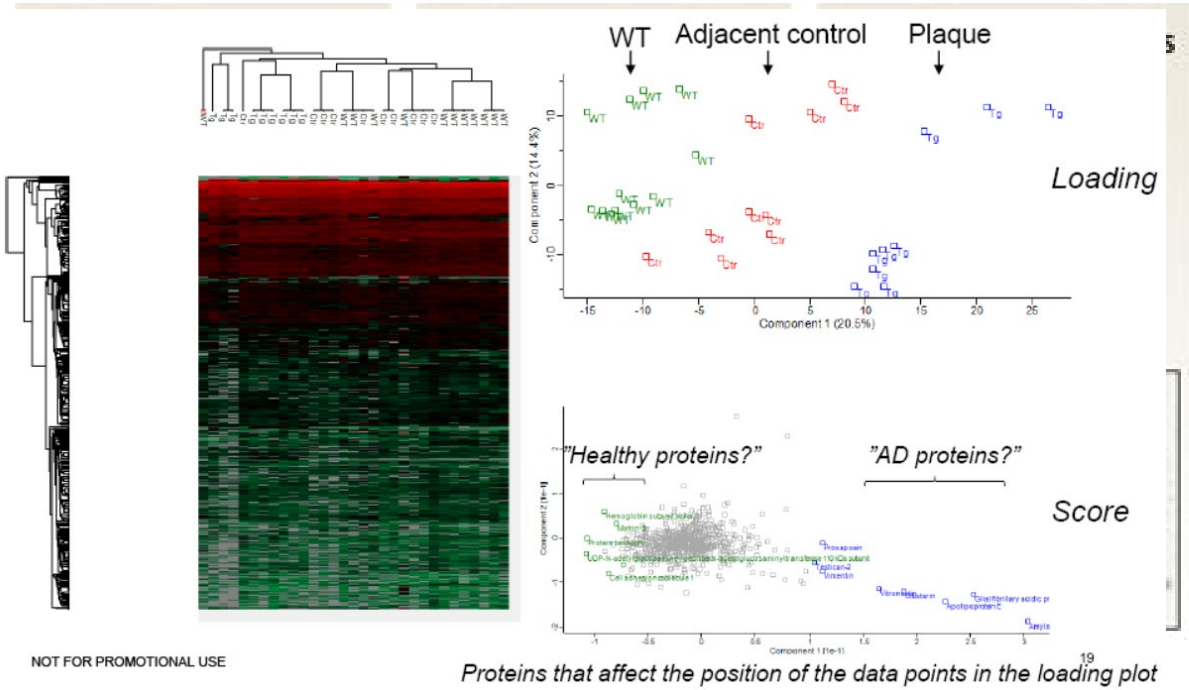
Joakim Bastrup,
PhD student

- Laser Microdissection combined with proteomics allows investigation of minute amounts of protein
- An AD mouse model system was used to investigate the plaque proteome



Plaques in AD brain



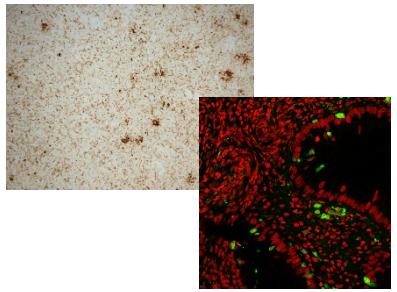


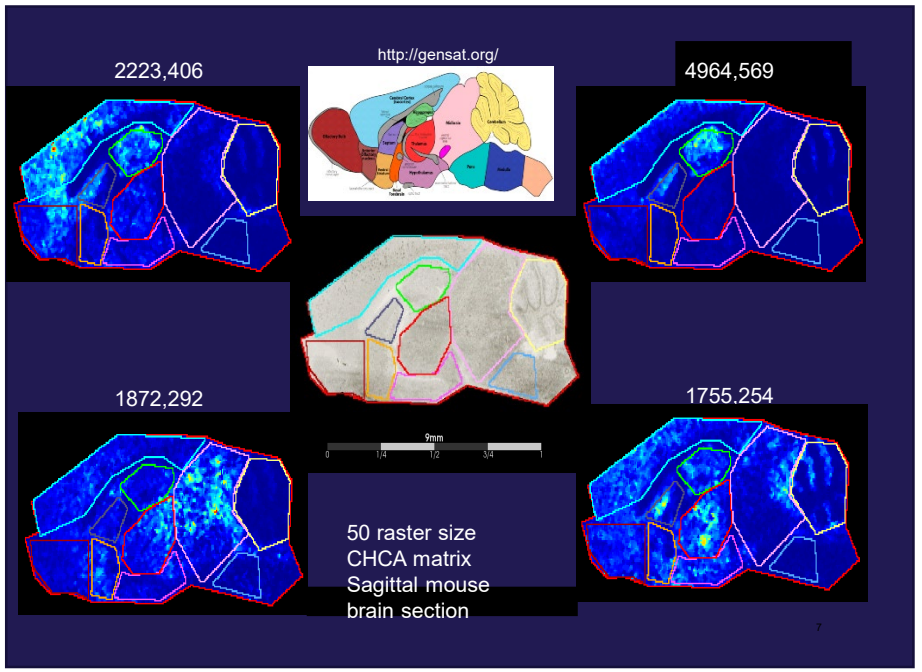
Proteins that affect the position of the data points in the loading plot

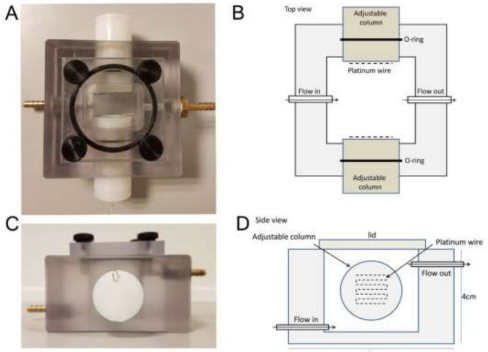
Avanced Imaging by combined MALDI IMS and Expansion /CLARITY microscropy

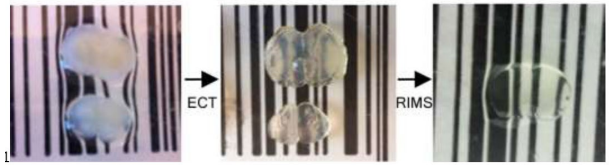
Joakim Bastrup, PhD student

Advanced microscopy



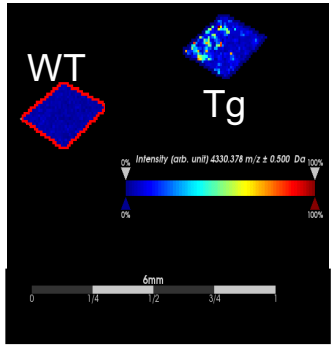




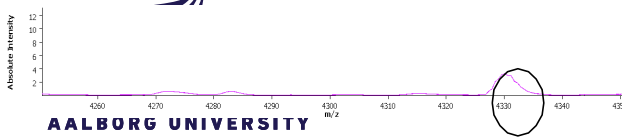


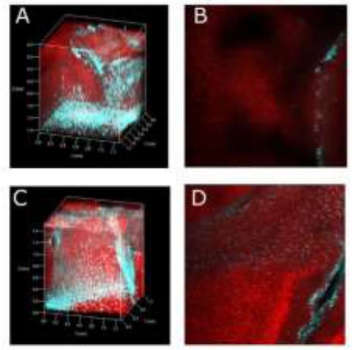
MALDI MS Imaging

DET OBELSKE FAMILIEFOND



Optimized novel sample preparation enhances S/N >100x





Basic research paper

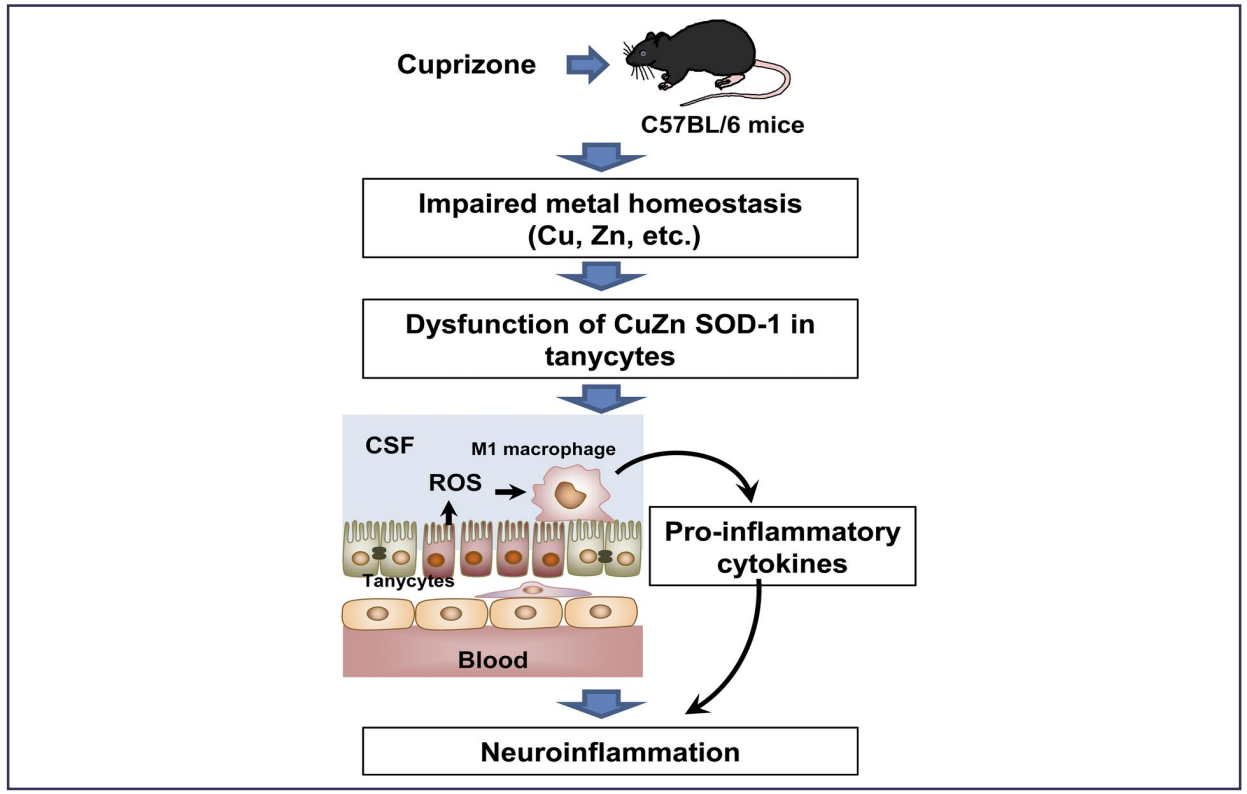
Optimized CLARITY technique detects reduced parvalbumin density in a genetic model of schizophrenia

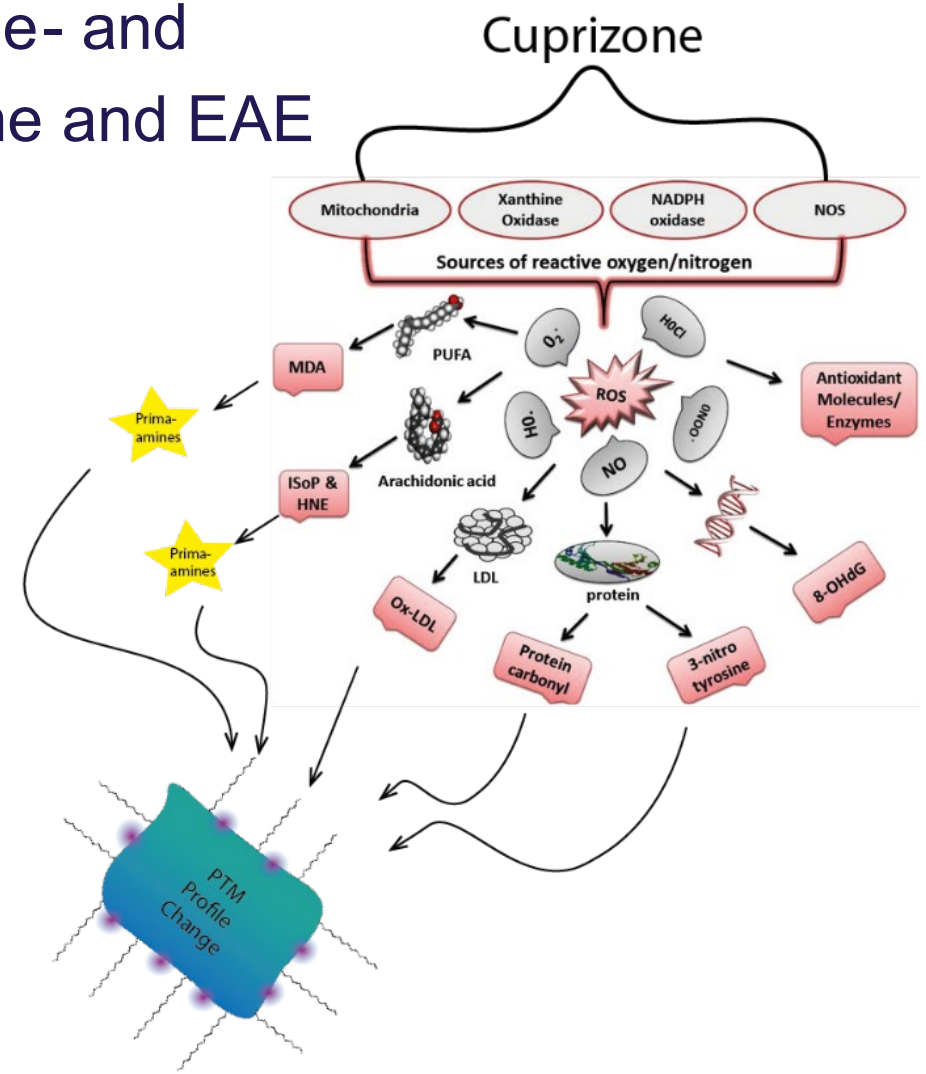
Joakim Bastrup, Peter H. Larsen

Microproteomics of MS models for investigation of disease related PTMs

Kenneth Kastanjegaard

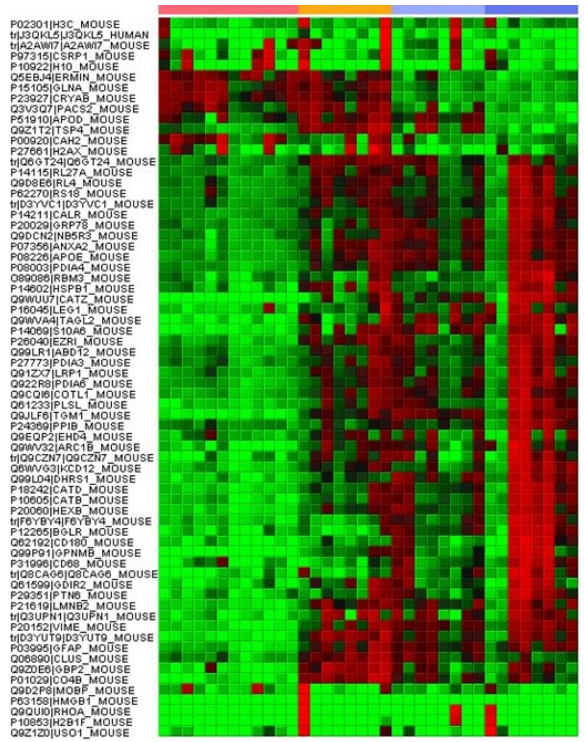
- In order to further understand the pathology of de- and remyelination we have investigated the Cuprizone and EAE mouse models for regional PTM dynamics.



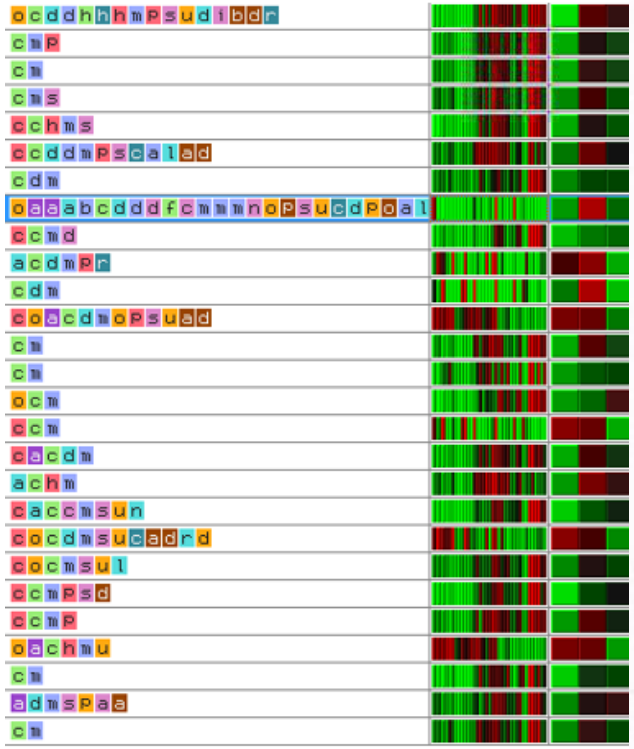


Microproteomics of MS models for investigation of disease related PTMs

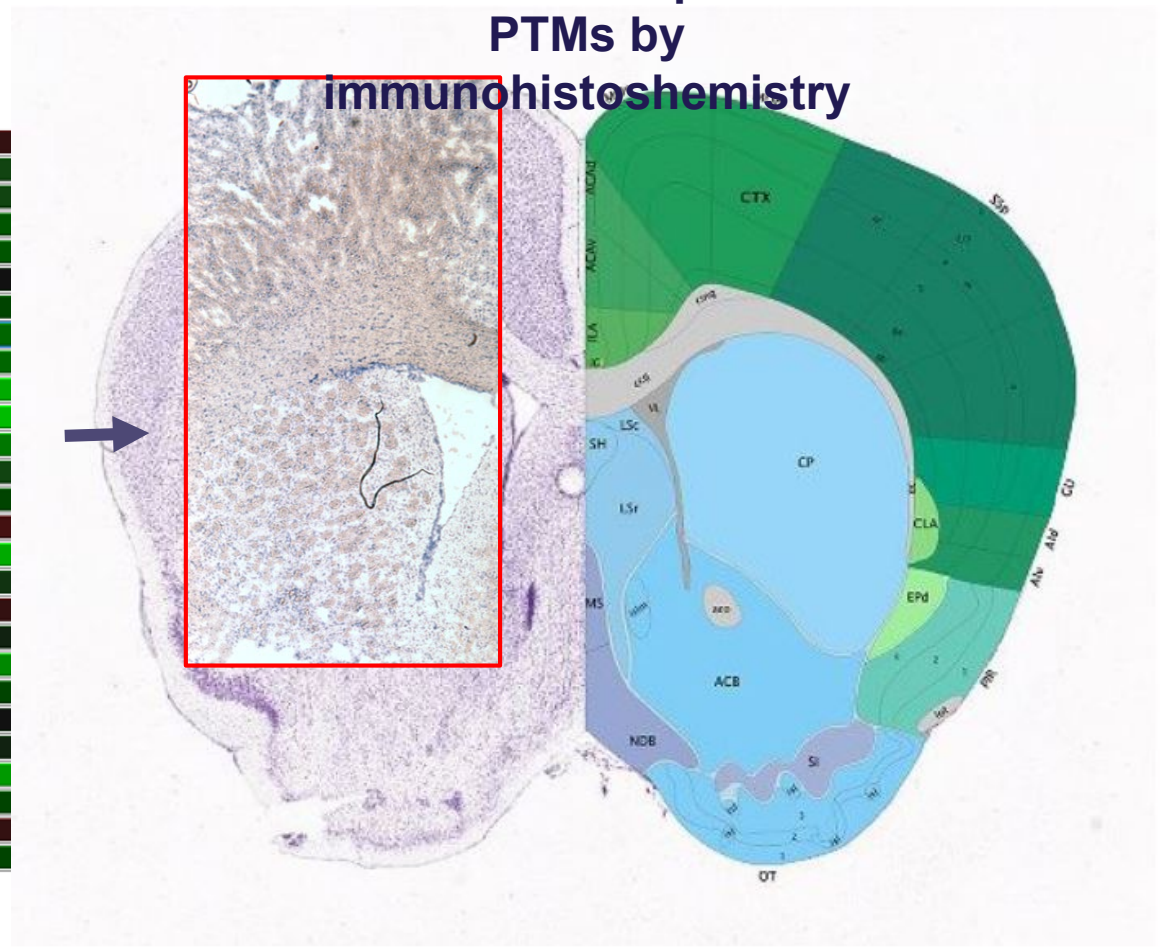
Quantitative proteome alterations



Quantitative profiles of up to 200 PTMs



Validation of specific PTMs by immunohistoshemistry



(Kastaniegaard et. at., in preparation)