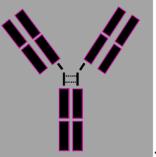
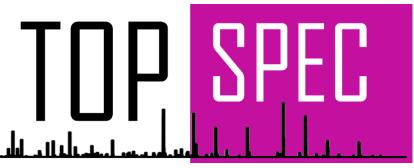
9.30 - 9.45 Welcome and brief introduction of partners







# **Project Review Meeting**

FET OPEN Project number: 829157

Next generation precision antibody profiling from science fiction to reality

Brussels, February 6th 2020



**Call**: Future Emerging Technologies OPEN

**Duration**: January 1, 2019 – December 31, 2021

**Budget**: 3, 991, 550 €

## **Grand challenge to address:**

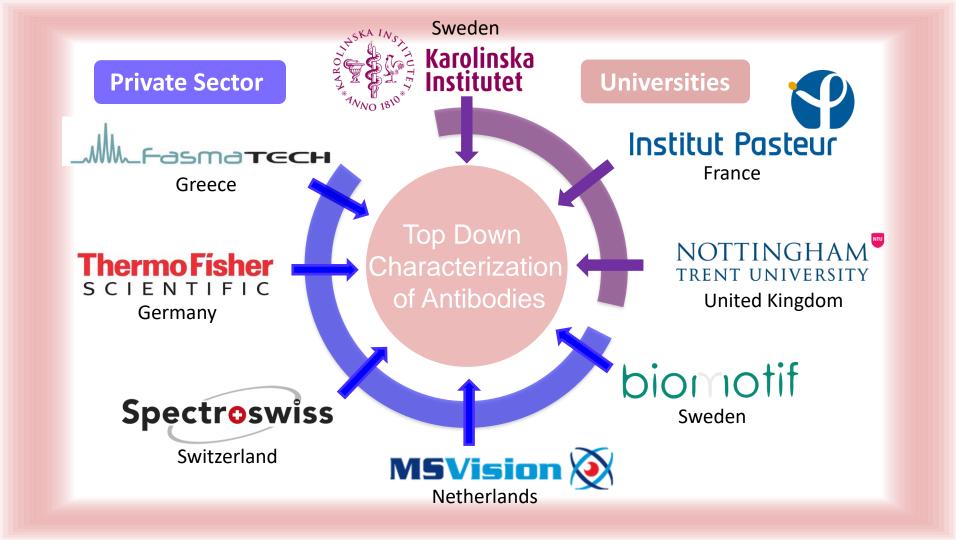
A major and growing challenge in the EU health system is the cost of drugs and targeted therapies. Reducing time taken to develop novel therapies will reduce costs to the health system.

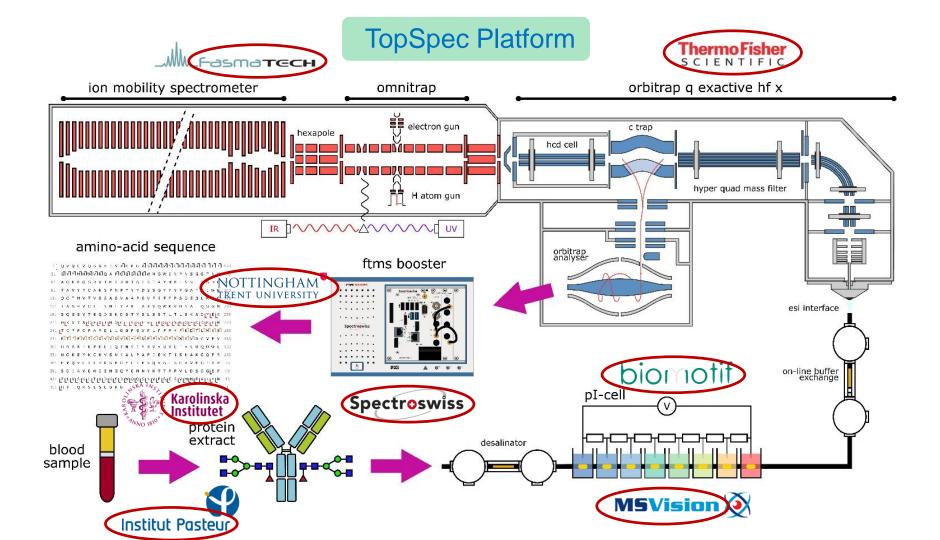
## **Proposed solution:**

To address this grand challenge, it is imperative to better understand how the human organism defends itself against diseases. The biggest mystery is the human immune system; and, understanding this ultimately requires knowledge of the sequence repertoire of human antibodies and their respective antigens.

### **FET program:**

To create a top-down antibody sequencing tandem mass spectrometry technology based on novel molecule separation techniques, ion fragmentation reactions, signal processing and data analysis approaches.







- Karolinska Institutet, (KI) Stockholm/ Sweden (<u>www.ki.se</u>), founded in 1810
- World leading medical university accounting for over 40% of Swedish medical academic research
- Elects the Nobel laureates in Physiology or Medicine
- Department of Medical biochemistry and Biophysics (MBB)
- One of the academically most successful Dpt (three Nobel prize laureates)
- Oldest mass spectrometry facility in biomedical sciences in Europe (from 1947) and the second oldest in the world
- Today the mass spectrometry facility has 10 operational mass spectrometers, including eight high-resolution Orbitrap mass analyzers (one on loan to Fasmatech)
- The research activities of the laboratory have a broad scientific scope, including method development for proteomics





**Roman A Zubarev**, PhD, professor, chair and director of the Chemistry I division, MBB, KI

Main achievement: Discovered Electron capture dissociation (ECD) and other ion-electron reactions for the analysis of polypeptides by mass spectrometry

**Research:** Developing mass spectrometry based tools for studying disease mechanisms and developing novel proteomics tools



# Main Tasks in TopSpec:

KI is the main coordinator and manager of the project. KI plays central role, integrating all the parts developed by other partners, providing samples, helping develop novel fragmentation techniques, analyzing antibodies using novel fragmentation techniques, creating software for seamless operation of the whole TopSpec platform.

# Thermo Fisher

Thermo Fisher Scientific (TF) (Bremen) GmbH/Germany:

- a world market leader in high-resolution mass spectrometry for organic analysis, isotope ratio analysis, elemental analysis, and life science.
- Following development of breakthrough hybrid Linear Trap- Orbitrap MS of LTQ Orbitrap family in 2000s, recent products of the company include an Orbitrap-only MS and hybrid Quadrupole-Orbitrap MS (Q Exactive family and Orbitrap Exploris 480 instruments).
- The team in Bremen works together with a team at Thermo Fisher, San Jose, CA, one of the latest results being launch of tribrid Quadrupole-Linear Trap- Orbitrap instrument Orbitrap Eclipse in 2019.
- Both sites are also collaborating with the team at Thermo Fisher, Germering, Germany on development on nanoand micro-flow LC.





Alexander Makarov: PhD, Professor (Utrecht Univ.), Director of Global Research in Life Science Mass Spectrometry business of Thermo Fisher Scientific (TFS), Germany, Bremen.

**Main achievement:** invention of the Orbitrap mass analyzer and its numerous improvements transformed modern mass spectrometry

**Research:** Instrumentation and methods of operations of high-resolution and tandem mass spectrometry; hyphenation of mass spectrometry to other techniques.



# **Main Tasks in TopSpec:**

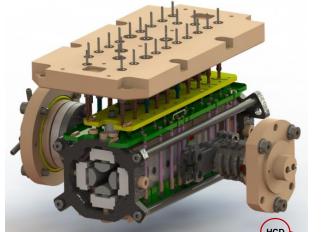
TF is the lead partner in WP 6 (Modification of the Orbitrap mass spectrometer), and will provide a state of the art hybrid instrument to be integrated with the Omnitrap. TF will support also other WPs, especially dissemination and communication activities in WP 8.

# 

- Fasmatech, (FASM) Athens/Greece (<u>www.fasmatech.com</u>), founded in 2009
- Custom engineering mass spectrometry SME
- Extensive know-how in ion optics design, gas dynamics, mechanical, electronics and software engineering
- Strong IP portfolio
- Novel instrumentation designs for a wide range of applications (from experimental physics and planetary sciences to bioanalytical chemistry and process analysis)
- Customer base expanding worldwide



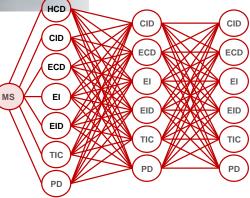




#### Omnitrap<sup>™</sup> platform

A unique linear ion trap design supporting an extensive ion activation network – A top-down oriented device for in-depth characterization of proteins





# Main Tasks in TopSpec:

Fasmatech is responsible for the development of the omnitrap platform and extensions-enhancements to the ion activation network for processing gas phase ions. Key aspects of the project include developments in electron and hydrogen atom sources, ion mobility devices, software tools and top-down tandem MS methods.

# Spectroswiss

- Spectroswiss, (SPS) Lausanne/Switzerland (www.spectroswiss.ch)
- Founded in 2014 as a spin-out from the Biomolecular Mass Spectrometry Lab at the Swiss Federal Institute of Technology (EPFL)
- Host institution for ERC Starting Grant, 2 ERC PoC grants, Eurostars



- FTMS and tandem MS fundamentals, instrumentation & methods
- World-leading FTMS data acquisition hardware: FTMS Booster
- World-leading data processing software for FTMS: Peak-by-Peak
- Antibody analysis with top-down MS: method development & service
- Founding member of Consortium for Top-Down Proteomics
- Industrial Advisory Board for EU EPIC-XS Proteomics Consortium
- Lead for the Inter-laboratory Study for Top-Down MS of mAbs



















Yury O. Tsybin, PhD, CEO

Main achievement: Pioneered mAb analysis via top-down MS (ETD of intact mAbs on TOF MS and Orbitrap FTMS) and middle-down MS (ETD of mAb subunits produced by digestion with IdeS and KGP)

Research: Method and technique development in high-resolution mass spectrometry and tandem mass spectrometry; data acquisition & processing

# Main Tasks in TopSpec:

SPS is the lead partner for data acquisition and processing from TopSpec platform, spearheading and overlooking the following tasks: (i) maximizing information output from TopSpec platform; (ii) developing novel data processing algorithms; and (iii) managing and co-developing data analysis tools. Contributing to results dissemination.

# NOTTINGHAM TRENT UNIVERSITY

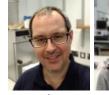
#### Expertise

- NTU is a centre of excellence in instrumental analytical bio/chemistry
- >5 separate research groups related to MS systems and method development alone

#### MS Software

FTMS Transient Data

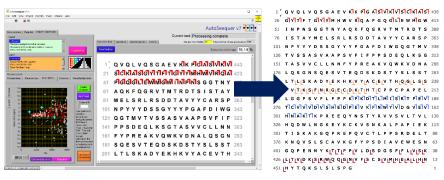
- Developers of AutoVectis Suite
- Suite of MS data processing modules
- Can be combined into many different workflows
- Including Top-down FTMS data processing



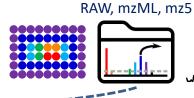


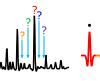
D. Kilgour

X. Wang













# Main Tasks in TopSpec:

NTU is responsible for aspects of the data processing, at both low and higher levels. Additionally, NTU has a key part to play in the dissemination activities.



#### Mass Spectrometry for Biology Unit

- Creation in 2012
- Service & Research activities in proteomics (15 people)
- ISO9001:2015 certification (March 2018)
- Research areas: Infectious diseases & Host-pathogen interactions

#### Expertise & visibility

- Advanced quantitative bottom-up proteomics
- Large-scale top-down proteomics
- Structural proteomics (Cross-linking, Native, HDX)
- International Consortium for Top-Down Proteomics
- EPIC-XS: European Proteomics Infrastructure Consortium
- 1st European Top-Down Proteomics Symposium



### TopSpec team:







J. Chamot-Rooke

J. Dhenin

M. Dupré

#### Relevant expertise for TopSpec

- Characterization of intact proteins (bacterial proteins, biologics)
- Protein fragmentation mechanisms
- First high-throughput large-scale top-down proteomics platform in France

#### Equipment for Top-down proteomics





Q-Exactive HF

**Orbitrap Fusion Lumos** 



# Main Tasks in TopSpec:

Institut Pasteur will evaluate the performance of the complete TopSpec platform on standard antibodies and apply the optimized workflow to the characterization of circulating antibodies and antibody-based biopharmaceuticals.

# biomotif

# Capturing the essence of life

- Biomotif AB, Stockholm, Sweden <u>www.biomotif.com</u>, founded in 2004 as a spin off company from Karolinska Institutet.
- The company develops novel electrophoretic-based methods for protein analysis, which are later developed into analytical instrumentation.
- Biomotif has developed the proprietary pl Trap Åcelus™ for advanced proteomics and biomarker studies. The technology is based on several new inventions including ElectroCapture and Multijunction Base Capillary Isoelectric Focusing.







Thorleif Lavold, Chief Executive Officer, has more than 25 years of experience in the sales, marketing and launching of new mass spectrometers (VG Instruments Ltd., Fisons Plc, Micromass AB (CEO) and Waters AB (Business Development).

He sold the two first Q-Tof hybrid mass spectrometers in the world to Astra Zeneca and Pharmacia.

Juan Astorga-Wells, PhD, Scientific Manager. He is the co-founder of several startups, such as Biomotif AB, HDXperts AB and Capture Device AB, and author of +40 scientific articles including publications in Science Magazine and Molecular Cell Proteomics. Extensive experience in method development with mass spectrometry, microfluidics and isoelectric focusing

# Main Tasks in TopSpec:

Biomotif AB is the responsible for developing the methodologies and instrumentation necessary to combine isoelectric focusing separation with the Omnitrap Mass Spectrometer, and thus facilitating the detection of antibodies. Responsible for WP5.







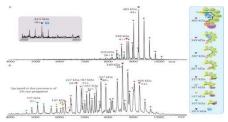


R.Swart

#### MS Vision (https://msvision.com/)

- Based in The Netherlands, Established in 2004, 19 employees
- Independent LC/MS service provider
- LC-MS instrumentation and training
- Native mass spectrometry (structural biology, proteomics, biologics)
- MS technology development
- Separation technology
- International project participation:
- MS SPIDOC H2020 project partner 2019-2021
- TopSpec H2020 project partner 2019-2022
- Supermama H2020 project 2020-2022











# Main Tasks in TopSpec:

MS Vision is responsible for the dissemination, communication & exploitation plan of the project to ensure successful uptake for the TopSpec technologies. MS Vision will also contribute to the integration of all technologies into a TopSpec platform and it's application for model and real-life samples. MS Vision will also provide input for the development of the pl trap system and its components such as the pl cell for protein separations and the buffer exchanger ESI interface.

