TAXINOMISIS

Multidisciplinary approach → stratification of patients with carotid artery disease

TAXINOMISIS plenary meeting
October 8-9, 2020 (virtual)

Extension of the project due to the Covid-19 outbreak
up to June 30,2023

Newsletter 02 September 2020

TAXINOMISIS is a European Commission funded research project which aims to develop a new approach for the stratification of carotid artery disease patients.

TAXINOMISIS takes bold step beyond the state of the art unwinding the pathobiology underlying symptomatic plaques, discriminating distinct disease mechanism-driven states and biomarkers, and developing a multiscale risk stratification model.

TAXINOMISIS will deliver, as a main outcome, a software platform, which can perform the risk stratification.

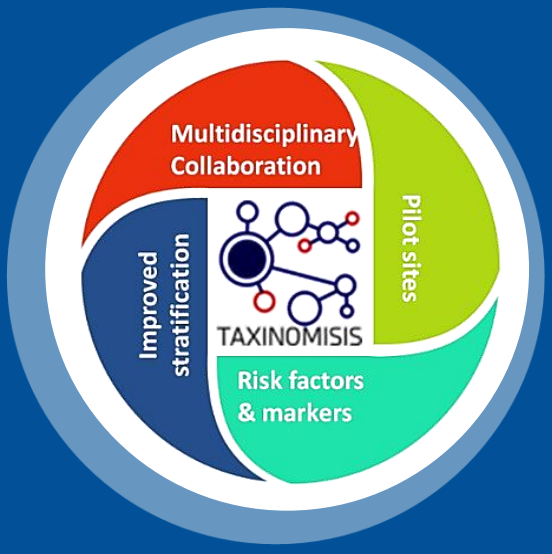
Purposes

Provide novel disease mechanism-based stratification for carotid artery disease patients to address the need for stratified and personalised therapeutic interventions in the current era.

Objectives

- → Investigate the causal relationship of the major pathways and factors identified in symptomatic carotid artery disease
- → Study disease phenotypes and disintegrate them into endotypes according to specific pathobiological mechanisms
- → Integrate a computational model and an agent based model of plaque progression in the risk stratification tool
- → Perform a test for determining the presence of single Nucleotide Polymorphisms and predicting drug response
- → Evaluate the risk model of carotid artery disease stratification in an observational multicentre clinical study
- → Present a cost-effectiveness analysis

TAXINOMISIS innovation capacity



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 755320

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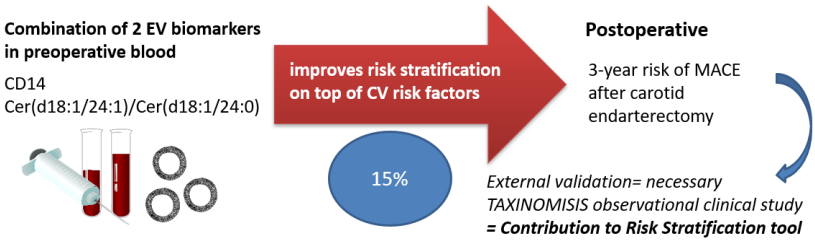
Project activities

Characterization of symptomatic and asymptomatic carotid atherosclerotic plaques lesions, and identification of risk and susceptibility factors through the exploitation of longitudinal cohort data and multiomics

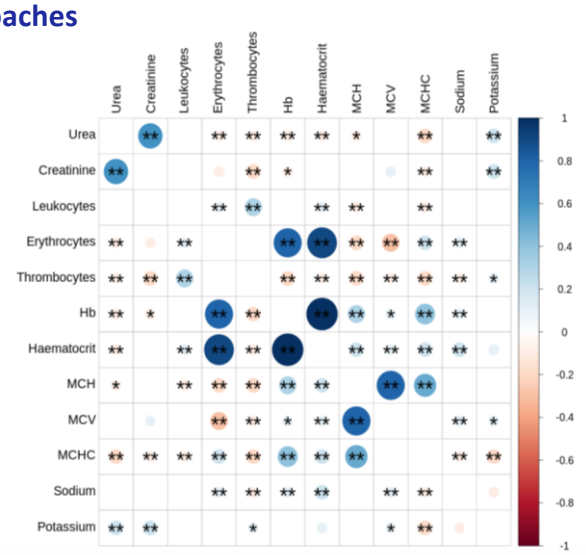
- Combined measurement of both ceramides and extracellular vesicle (EV) proteins on the exact same AtheroExpress large plasma sample set -> identification of the added value of both in prediction of secondary cardiovascular events together with a clinical model, as well as the combined association with plaque histology and symptomatic vs non-symptomatic.
- A plasma ceramide, EV proteins, EV ceramides and EV Ceramides/Plasma Cell (PC) ratios were found to be associated with major adverse cardiovascular events (MACE) occurring within 3 years after inclusion, independent of clinical risk factors.
- This is the first time that both proteins, ceramides and PCs have been measured in plasma and EV subfractions in a large consecutive cohort of carotid artery disease patients and have been associated with MACE.
- This holds great potential for the identification of high risk carotid artery disease patients using a small blood sample before surgical intervention occurs.



- Further analysis will be performed in combining proteins, ceramides and PCs with optimal cut-offs including c-statistics and net reclassification improvement.

Disintegration of carotid artery disease phenotypes into endotypes through joint modelling of multiple omics datasets and systems medicine approaches

- Evaluation of potential biomarkers that differ between symptomatic and asymptomatic patients, as well as plaque types.
- Initial results indicate that mmp-8, mmp-9, pcsk9, gdf15, pdgf_bb, urea and potassium have statistically significant difference between asymptomatic and symptomatic patients.
- Models for the classification of patients with carotid artery disease have shown that many markers which had been characterized as non-important when examined individually, could play an important role when examined together with a set of other markers.
- The models used for the classification analysis of certain data sets were of high predictive value reaching an accuracy score close to 80%, whereas for other data sets they were less accurate.



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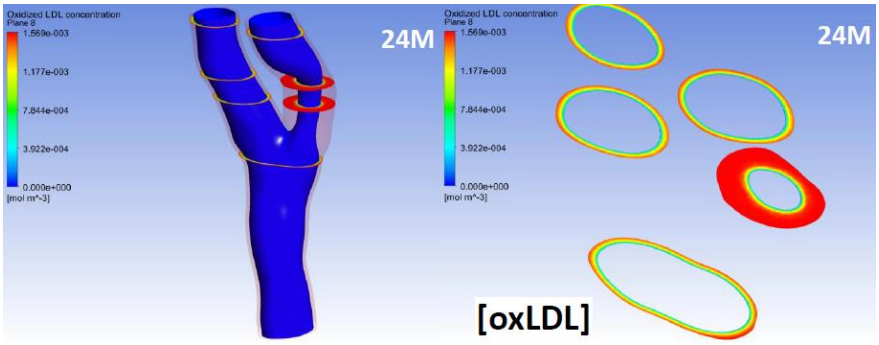
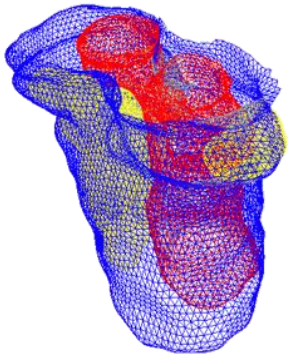
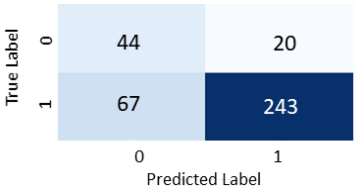
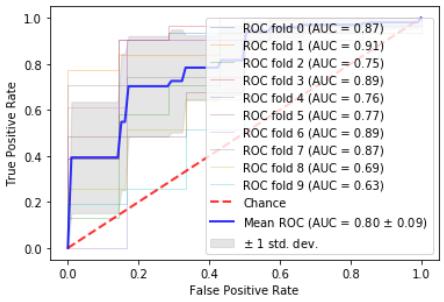
Risk stratification model

- The architecture of the Risk Stratification Tool has been established.
- The first version of the computational model of plaque progression has been developed using both retrospective data and data from the prospective clinical study.

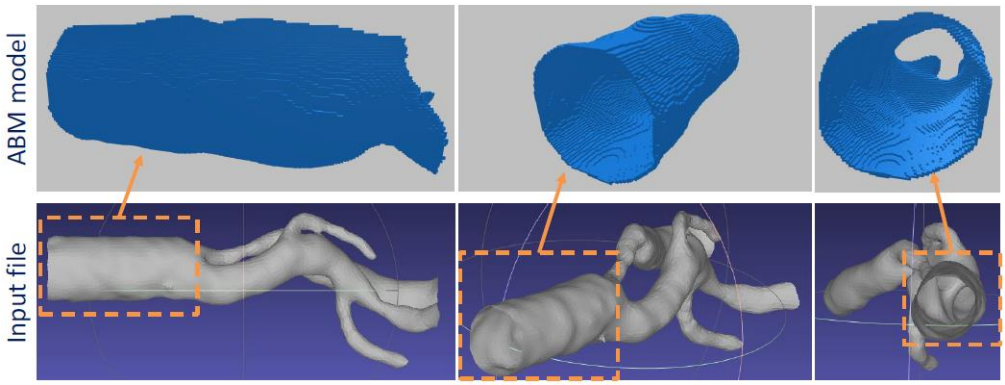








- The first version of the agent based model (ABM) of plaque progression has been developed presenting an artificial 3D model of the carotid artery.



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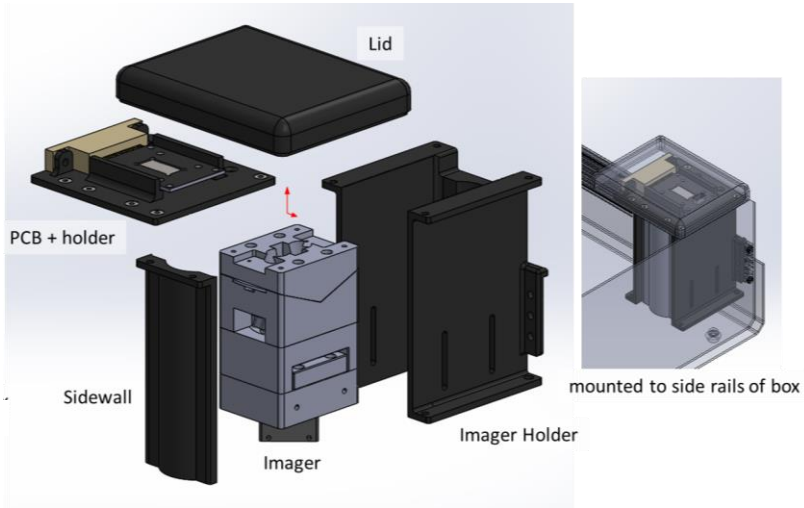
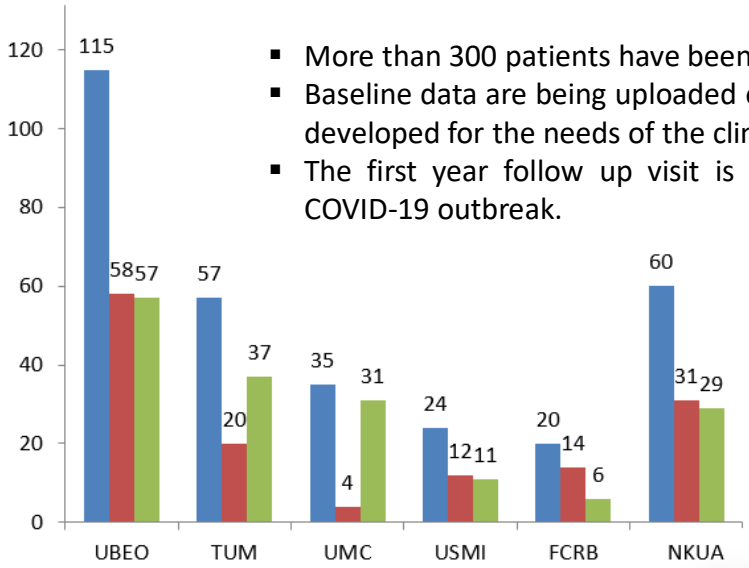
Pharmacogenomics analysis and development of a new lab-on-a-chip for further stratification of patients and personalization of medical treatment

- Final run for open fluidics multicavity PCR chips.
  - 4 different designs allowing further optimization of the closure of the central channel, imaging markers and optional controls.
  - Chip fabrication 12 wafers out, 200 chips/wafer.
- Chips were wire-bonded, awaiting calibration.



From research to the clinic: Evaluation of the new risk stratification tool in a prospective observational clinical study



- More than 300 patients have been recruited.
- Baseline data are being uploaded on the specialized electronic case report form developed for the needs of the clinical study of the project.
- The first year follow up visit is ongoing, although delays occur due to the COVID-19 outbreak.

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Consortium

TAXINOMISIS encompasses a highly multidisciplinary group of researchers with remarkable track record and complementarity from 12 world-leading institutions of clinical and research excellence and 3 pioneering SMEs including:

- ✓ Medical experts
- ✓ Vascular surgeons
- ✓ Cardiologists
- ✓ Neurologists
- ✓ Biologists
- ✓ Software engineers
- ✓ Biomedical engineers
- ✓ Lab-on-a-chip experts
- ✓ Health research experts

TAXINOMISIS researchers are international leaders in their respective fields and have contributed to our current understanding of:

- the **clinical medicine surrounding carotid artery disease** (UMC, TUM, UBEO, USMI, FCRB, NKUA),
- **the molecular mechanisms** driving atherosclerosis in carotid and coronary arteries (UMC, TAUH, BRFAA, ZORA, USMI, UOXF),
- the **immuno-inflammatory processes involved** (UMC, BRFAA, USMI, UOXF, UBEO),
- the identification of **diagnostic markers and treatments** for cardiovascular disorders (TAUH, ZORA, IMEC, UMC, TUM, USMI, FCRB),
- **the development of new algorithms and simulation tools for atherosclerotic plaques and CVDs** (UOI, BIOIRC, END),
- **the development of risk prediction models** (UOI, BIOIRC),
- the design and production of **lab-on-a-chip devices** based on nanoelectronics (IMEC) and
- the provision of **retrospective data and cohorts** (NIVEL, TAUH, UMC)

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