Newsletter No 2/2016

Dear GENIEUR partners and followers, Heidelberg/Gothenburg, December 16, 2016

It is time for the second up-date 2016 right before the holiday season.

With great pleasure we continue to report major outputs generated by GENIEUR-*reloaded* members who recently published the following manuscripts:

Epigenetics

Teams in Barcelona (Vicario and Santos et al.) and Heidelberg (Martinez and Niesler et al.) published their research based on the first joint venture initiated at the GENIEUR Starter Meeting in Bologna in 2012 in Gut.

Martinez et al. 2016 performed comparative expression analysis which revealed distinct miRNA and mRNA profiles in the jejunum of IBS-D patients compared to healthy controls. In addition, tight junction signalling was associated with the IBS-D expression profile. Further validation of selected genes showed consistent up-regulation in 75% of genes involved in epithelial barrier function. Specifically, hsa-miR-16 and hsa-miR-125-b were found to be de-regulated in IBS-D and lead to compromised barrier function by disturbed fine-tuning of claudin-2 and cingulin. Furthermore, bowel dysfunction, perceived stress, depression and number of mast cells correlated with the expression of hsa-miR-125b and hsa-miR-16 and their respective target proteins. This emphasized again the role of impaired barrier function in IBS and the potential of targeting this in therapeutic interventions.

Genetics

Henström et al. 2016 Mauro D'Amato and colleagues from Sweden, Italy and USA analysed the sucrose-isomaltase gene *SI* known to be disturbed in a congenital sucrose isomaltase de ficiency (*CSID*) presenting with disaccharide malabsorption and characterised by symptoms well known in IBS: diarrhoea, abdominal pain and bloating. Sequencing of the *SI* gene in *CSID* familial cases revealed a higher mutation load and a common SNP p.Val15Phe. This SNP was followed up in a multicentre study analyzing more than 1800 cases and controls and was shown to be associated with IBS-D. The dosage of the associated allele correlated with stool frequency and *Parabacteroides* faecal microbiota abundance and 35% reduced enzymatic activity of the recombinant protein. This underlines the power of genetics by stratification of *SI* SNP carriers which may enable a personalized therapy in the future.

Furthermore, we congratulate Mauro D'Amato to his *Bellygenes initiative* which was recently launched. The Bellygenes initiative is coordinated by researchers at Karolinska Institutet and the University Medical Centre Groningen and aims to study the genetic makeup of 800,000 Europeans in relation to IBS and associated symptoms.

At the UEGW2016 in Vienna the first GENIEUR-*reloaded* Common Interest Group Meeting (CIG) took place which was well attended. Within the scheduled 90 minutes, an up-date was given on the current status of GENIEUR-*reloaded*, ongoing collaborations and grant proposals including one proposal within a HORIZON2020 call. Major outputs have been highlighted, such as a position paper with recommendations for deep phenotyping in IBS and biobanking which has been published open access in *Neurogastoenterology and Motility:* Phenotyping of subjects for large scale studies on patients with IBS. Actually, the METC of the GENIEUR protocol has been approved in three additional countries, Poland, Romania and Germany, thereby increasing the number of approvals to 10 of the 21 European GENIEUR member countries. Furthermore, GENIEUR has been highlighted in two articles within a Nature-*Outlook* issue on IBS: And three reviews by GENIEUR members have been

included there and in a Nature online collection on IBS. Moreover, a status report on the UEG LINK Award Project *'Help EU in IBS'* in which groups from the *Netherlands, Germany, Norway, Bosnia and Herzegovina, Serbia and Malta* are involved was given by Daisy Jonkers. The LINK Award Project had its successful *kickoff* meeting in March 2016 in Sarajevo (Bosnia and Herzegovina) and groups involved have started to work on this. A report on collaborative genetics and epigenetics projects within GENIEUR was given by Beate Niesler as well as progress on the microbiota pilot study was reported by Mirjana Rajilić-Stojanović.

In order to further lobby for our mission, a leaflet as a basic information resource on GENIEUR in lay language has been prepared for patients and patient support groups. This has been translated into all national languages of partners involved in GENIEUR and is available in the GENIEUR repository. We are currently working on a concerted dissemination plan to your National Contact Points and update you on the further strategy in order to lobby for the GENIEUR network and IBS research. In addition, the *Major Outcome Brochure* is currently produced combining publications with SOPs in a brochure for clinicians and scientists to be distributed at conferences. Both, the brochure and the leaflet will be available on the website (www.GENIEUR.eu).

The next GENIEUR-reloaded Meeting will take place at the NeuoGASTRO2017 in Cork, Ireland.

We are looking forward to our future collaborations and hope to see you again in Cork.

Merry Christmas and all the best wishes for 2017!

With kind regards,

Beate Niesler and Magnus Simrén

Chair and Co-Chair of GENIEUR reloaded

www.GENIEUR.eu

This newsletter can also be found on our website and the CIG Meeting presentations and the patient leaflets are available in the GENIEUR repository.