

UNITED EUROPEAN
GASTROENTEROLOGY

ueg journal

An international forum for clinical practice
and research in gastroenterology

21st United European Gastroenterology Week Berlin 2013

Abstract Issue



21st UEG Week 2013

Berlin, Germany, October 12–16, 2013

Accepted abstracts available online at:
<http://www.e-learning.ueg.eu>
<http://ueg.sagepub.com>

Disclaimer: United European Gastroenterology (UEG) is not responsible for errors or omissions in the abstracts. This abstract book was finalized on August 26, 2013, any changes received after this date have not been incorporated. Changes to presenters received after August 26, 2013 have been included in the online version of the programme and can be obtained at: <http://www.e-learning.ueg.eu>.

Disclosure policy: The United European Gastroenterology (UEG) is committed to ensuring scientific rigour and objectivity in all of its educational activities. These include all aspects of the educational programme at UEG Week 2013. All presenters, whether invited Faculty or abstract presenters are required to make a formal disclosure of financial or other relationships that could influence the content of a presentation in the form of a disclosure statement. Conflict of interests does not preclude an individual from making a presentation providing the conflict was disclosed.

Editor

Jan Tack, *University of Leuven, Belgium*

Associate Editors

Tim Greten, *NIH, USA*

Arthur Kaser, *University of Cambridge, UK*

Oliver Pech, *St John of God Hospital, Regensburg, Germany*

Editorial Board

Alberto Arezzo, *University of Turin, Italy*

David Armstrong, *McMaster University, Canada*

Michael Bourke, *Westmead Hospital, Australia*

Guido Costamagna, *Catholic University of the Sacred Heart, Italy*

Carlo Di Lorenzo, *Children's Hospital of Columbus, USA*

Wouter De Jonge, *Academic Medical Center, The Netherlands*

Doug Drossman, *University of North Carolina at Chapel Hill, USA*

Mohamad Eloubeidi, *American University of Beirut School of Medicine, Lebanon*

Johanna C Escher, *Erasmus MC, The Netherlands*

Ronnie Fass, *The Neuro-Enteric Clinical Research Group, USA*

Richard Hunt, *McMaster University, Canada*

Michael P Jones, *Macquarie University, Australia*

John Kellow, *The University of Sydney, Australia*

Markus Lerch, *University Medicine Greifswald, Germany*

Lars Lundell, *Karolinska Institute, Sweden*

Hendrik Manner, *HSK Wiesbaden, Germany*

Helmut Neumann, *University of Erlangen-Nuremberg, Germany*

Qin Ouyang, *West China Hospital, China*

Stefan Schreiber, *UKSH Campus Kiel, Germany*

Vincenzo Stanghellini, *University of Bologna, Italy*

Jaap Stoker, *Academic Medical Centre, The Netherlands*

Hidekazu Suzuki, *Keio University School of Medicine, Japan*

Michael Vieth, *University of Bayreuth, Germany*

Michael Wallace, *Mayo Clinic, USA*

Heiner Wedemeyer, *Hannover Medical School, Germany*

Frank Zerbib, *CHU Bordeaux, France*

Aims and scope

Launched in 2013, *United European Gastroenterology Journal* is the official Journal of United European Gastroenterology (UEG), a professional non-profit organisation combining all the leading European societies concerned with digestive disease. UEG's member societies represent over 22,000 specialists working across medicine, surgery, paediatrics, GI oncology and endoscopy, which makes UEG a unique platform for collaboration and the exchange of knowledge.

United European Gastroenterology Journal provides an international forum for research in gastroenterology, publishing original articles which describe basic research, translational and clinical studies of interest to gastroenterologists and researchers in related fields. Articles from across all fields of gastroenterology are welcomed by the Editor-in-Chief, including luminal, liver and pancreatic diseases, gastrointestinal surgery, gastrointestinal oncology, paediatric gastroenterology and nutrition as well as endoscopy.

Published article types include original research, reviews, guidelines papers and news items. The journal is a member of the Committee on Publication Ethics (COPE).

2014 annual subscription rates

United European Gastroenterology Journal ISSN: 2050-6406 (print) 2050-6414 (online) is published in February, April, June, August, October and December by SAGE Publications (London, Thousand Oaks, CA, New Delhi, Singapore and Washington DC).

Annual subscription (2014) including postage: Institutional Rate (combined print and electronic) £673/US\$1246. Note VAT might be applicable at the appropriate local rate. Visit <http://www.sagepublications.com> for more details. To activate your subscription (institutions only) visit <http://online.sagepub.com> online. Abstracts, tables of contents and contents alerts are available on this site free of charge for all. Student discounts, single issue rates and advertising details are available from SAGE Publications Ltd, 1 Oliver's Yard, 55 City Road, London EC1Y 1SP, UK, tel. +44 (0)20 7324 8500, fax +44 (0)20 7324 8600 and in North America, SAGE Publications Inc, PO Box 5096, Thousand Oaks, CA 91320, USA.



SAGE Publications is a member of CrossRef

Periodicals postage paid at Jamaica, NY. POSTMASTER Send address corrections to *United European Gastroenterology Journal*, c/o Worldnet Shipping NY Inc., 155-11 146th Street, Jamaica, New York, NY 11434, USA.

Manuscript submission guidelines

To view the manuscript submission guidelines, please visit the Manuscript Submission link at <http://ueg.sagepub.com>

Peer review policy

United European Gastroenterology Journal operates a conventional single-blind reviewing policy in which the reviewer's name is always concealed from the submitting author. Papers will be sent for anonymous review by at least two reviewers who will either be members of the Editorial Board or others of similar standing in the field. The Editors' decision is final and no correspondence can be entered into concerning manuscripts considered unsuitable for publication in *United European Gastroenterology Journal*. All correspondence, including notification of the Editors decision and requests for revisions, will be sent by email.

Commercial sales

For information on reprints and supplements please contact reprints@sagepub.co.uk and for advertising, please contact UKAdvertising@sagepub.co.uk.

Abstracting and indexing

Please visit <http://ueg.sagepub.com> and click on more about this journal, then Abstracting/Indexing, to view a full list of databases in which this journal is indexed.

© UEG 2013

Cover image:

© Shutterstock

Apart from fair dealing for the purposes of research or private study, or criticism or review, and only as permitted under the Copyright, Designs and Patents Act 1988, this publication may only be reproduced, stored or transmitted, in any form or by any means, with the prior permission in writing of the Publishers, or in the case of reprographic reproduction, in accordance with the terms of licences issued by the Copyright Licensing Agency or your equivalent national blanket licencing agency. Enquiries concerning reproduction outside of those terms should be sent to SAGE Publications.

Disclaimer: The authors, editors, and publisher will not accept any legal responsibility for any errors or omissions that may be made in this publication. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper by Page Bros., Norwich, UK.



Contents

Letter of Thanks	v
Thanks to Partners, Sponsors and Exhibitors	vii

UEG Week 2013 Oral Presentations

Monday, October 14, 2013

Opening Plenary Session – Hall 1	A1
Today’s science; tomorrow’s medicine: From genes to disease in IBD – Hall 2	A2
Paediatric IBD – Hall Helsinki	A3
<i>H. pylori</i> treatment – Hall 7	A4
Endotherapy via the submucosal space – Hall 6	A6
Improving colonoscopic practice – Hall 9	A8
Advances in biliopancreatic imaging – Hall 10	A9
Oesophageal cancer: Treatment, prognosis and prognosticators – Hall 8	A11
Hepatocellular carcinoma – Salon 11/12	A13
Getting more out of anti-TNF therapy in IBD – Hall 2	A16
Management of GI bleeding: A case based discussion – Hall 3	A18
IBD: Extraintestinal manifestations and complications – Hall Prague	A18
Improving survival in colon cancer: Lessons learned from rectal cancer – Hall Oslo	A20
Colorectal sensory and motor dysfunction in constipation: Lessons for the management of adult and paediatric patients – Roof Garden	A20
Coeliac disease: From the tip of the iceberg to deep water – Hall Helsinki	A21
Prevention and early detection of upper GI cancer – Hall 7	A23
Endoscopy towards, into and through the stomach – Hall 6	A25
Today’s science; tomorrow’s medicine: Genetics of functional disorders – Hall 9	A26
Multimodal therapies in biliopancreatic diseases – Hall 10	A28
Basic Science Workshop 1: The metagenomic approach to GI disease – Hall 8	A30
Aids to improving endoscopic practice – Salon 11/12	A31
Clinical challenges in the anorectal region – Hall 3	A32
Long-term outcomes in IBD – Hall Prague	A33
IBD: Top late breaking trials and other major advances – Hall Helsinki	A35
Clinical management of pancreatic diseases: Important updates – Hall 8	A37
Update on Barrett’s oesophagus – Hall 7	A38
Endoscopic techniques which will change tomorrow’s practice – Hall 6	A40
Today’s science; tomorrow’s medicine: Genetics and pathogenesis – Hall 9	A42
New developments in upper GI imaging – Hall 10	A44
Basic mechanisms of GI motor and sensory dysfunction – Salon 11/12	A45

Tuesday, October 15, 2013

New treatments for functional GI disorders – Hall Prague	A47
New tools for IBD diagnosis and monitoring – Hall Oslo	A50
Treatment of rectal cancer in 2013 – Roof Garden	A53
Management of pancreatic cancer – Hall Helsinki	A53
Upper GI interventions and advanced endoscopy: Top late breaking abstracts – Hall 7	A53
<i>H. pylori</i> and gastric cancer risk – Hall 9	A54
Beneficial and detrimental effects of bacteria in the GI tract – Hall 10	A56
Nutrients, gut function and obesity – Hall 8	A59
Endoscopic interventions in pancreatic diseases – Salon 11/12	A61
IBD therapy: Safety issues – Hall 2	A64
Non-invasive diagnosis and staging of liver disease – Hall Stockholm	A66
Faecal calprotectin as a diagnostic tool in IBS and IBD – Hall Oslo	A66
Role of gut microbiota in GI diseases – Hall Helsinki	A68
Colonoscopic screening: Top late breaking abstracts – Hall 7	A69
Viral hepatitis B – Hall 6	A70
Gastro-oesophageal cancer: The science behind the medicine – Hall 9	A71
Challenges in diagnosis and treatment of colorectal cancer – Hall 10	A73
Nutrition and gut function – Hall 8	A75
Pancreatitis: Lessons from animal models – Salon 11/12	A76
Difficulties in the diagnosis of colitis – Hall Copenhagen	A78
IBD: Therapy beyond anti-TNFs – Hall Helsinki	A78
Recent developments in upper GI and small bowel bleeding – Hall 7	A81
Complications of cirrhosis – Hall 6	A82
Prevention, detection and management of gastric tumours – Hall 9	A84
Optimising colonic polyp detection – Hall 10	A85
Basic Science Workshop 2: Autophagy a common pathway in GI-inflammation – Hall 8	A87
Pancreatic cancer: Pre-clinical models – Salon 11/12	A88
Video Cases – Hall 1	A90
Inherited liver diseases – Hall Stockholm	A92
Controversies in oesophageal squamous cell cancer – Hall Prague	A93
Interactions between <i>H.pylori</i> and epithelial cells – Roof Garden	A94
IBD epidemiology: New insights – Hall Helsinki	A94
Screening for colorectal cancer: The facts and the future – Hall 7	A96
NAFLD and general hepatology: Important updates – Hall 6	A98
Improving EUS-guided diagnosis – Hall 9	A100
Identifying high risk colonic polyps – Hall 10	A101
Gastroduodenal and small intestinal tumours – Hall 8	A103
Autoimmune pancreatitis: Mechanism and treatment – Salon 11/12	A104

Wednesday, October 16, 2013

Safety profile of immunosuppressive therapy in IBD – Hall 2	A106
East meets West: Colorectal cancer screening – Hall Stockholm	A107
Understanding new technologies: A session for the general gastroenterologist – Hall Oslo	A107
New insights into the pathophysiology of functional GI disorders – Hall 6.	A108
GORD: From diagnosis to treatment – Hall 9.	A111
Viral hepatitis C – Hall 10	A113
Therapeutic ERCP update – Hall 8.	A116
Management of early oesophageal tumours – Salon 11/12.	A118
Unravelling new pathways in IBD pathogenesis – Roof Garden	A121
Oesophageal motility disorders and eosinophilic oesophagitis – Hall 9	A123
Capsule endoscopy: From mouth to anus – Hall 10	A125
Management issues in pancreatic and biliary cancers – Hall 8	A127
Colorectal cancer: Back to the basics – Salon 11/12	A128
Optimizing clinical outcomes in IBD – Roof Garden	A130
GI Surgery: What's new in 2013? – Hall 6.	A132
Nutrition: From the nursery to the nursing home – Hall 10	A132

UEG Week 2013 Poster Presentations**Monday, October 14, 2013**

POSTER PLUS VIDEO I – Poster Area	A135
GENETICS OF GI AND LIVER DISEASES I – Poster Area	A141
LIVER & BILIARY I – Poster Area	A145
PANCREAS I – Poster Area	A158
ENDOSCOPY AND IMAGING I – Poster Area	A165
SURGERY I – Poster Area	A196
IBD I – Poster Area	A201
OTHER LOWER GI DISORDERS I – Poster Area	A228
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS I – Poster Area.	A248
<i>H. PYLORI</i> I – Poster Area.	A267
SMALL INTESTINAL I – Poster Area	A273
NUTRITION I – Poster Area	A280

Tuesday, October 15, 2013

POSTER PLUS VIDEO II – Poster Area	A283
GENETICS OF GI AND LIVER DISEASES II – Poster Area	A288
LIVER & BILIARY II – Poster Area	A292
PANCREAS II – Poster Area	A304
ENDOSCOPY AND IMAGING II – Poster Area.	A312

SURGERY II – Poster Area	A345
IBD II – Poster Area	A351
OTHER LOWER GI DISORDERS II – Poster Area	A379
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS II – Poster Area	A398
<i>H. PYLORI</i> II – Poster Area	A420
SMALL INTESTINAL II – Poster Area	A425
NUTRITION II – Poster Area	A431

Wednesday, October 16, 2013

POSTER PLUS VIDEO III – Poster Area	A436
GENETICS OF GI AND LIVER DISEASES III – Poster Area	A441
LIVER & BILIARY III – Poster Area	A445
PANCREAS III – Poster Area	A458
ENDOSCOPY AND IMAGING III – Poster Area	A464
SURGERY III – Poster Area	A496
IBD III – Poster Area	A503
OTHER LOWER GI DISORDERS III – Poster Area	A532
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS III – Poster Area	A554
<i>H. PYLORI</i> III – Poster Area	A574
SMALL INTESTINAL III – Poster Area	A578
NUTRITION III – Poster Area	A584
Author Index	A588

enhancing cell sensitivity to 5-FU. Furthermore, 5-FU exposure markedly decreased the levels of endogenous ERK5 and MEK5 expression ($p < 0.05$), while inducing p53 and p21 expression ($p < 0.05$).

CONCLUSION: Overall, our results indicate that overactivation of MEK5/ERK5 pathway may contribute to CC aggressiveness and chemoresistance, suggesting that ERK5-targeted inhibition, via siRNA, miRNA or small-molecule inhibitors, may provide a promising therapeutic approach for CC treatment, warranting further investigation.

(Supported by PTDC/SAU-ORG/119842/2010, PEstOE/SAU/UI4013/2011, Sociedade Portuguesa de Gastroenterologia, SFRH/BD/88619/2012 and SFRH/BD/79356/2011. The authors thank Dr. Robert Doebele for the kind gift of pWPI-MEK5AA and pWPI-MEK5DD constructs.)

Contact E-mail Address: dampereira@ff.ul.pt

Disclosure of Interest: None Declared

Keywords: 5-Fluorouracil, Chemosensitization, Colon Cancer, MEK5/ERK5 Signalling

TUESDAY, OCTOBER 15, 2013

11:00-12:30

Nutrition and gut function – Hall 8

OP246 PPARGAMMA IS A MASTER REGULATOR OF LACTASE PRODUCTION BY INTESTINAL EPITHELIAL CELLS

M. Fumery¹, A. Langlois¹, S. Specia¹, C. Dubuquoy¹, M. Figeac², R. Christel³, L. Dubuquoy¹, S. Bellinvia⁴, P. Desreumaux¹, B. Bertin^{1,7}. ¹Inserm U995, ²Genomic platform IFR-114, ³Inserm U995, Université Lille-Nord de France, Lille, France, ⁴GiulianiSpA, Milano, Italy

INTRODUCTION: Lactose intolerance is a frequent condition that causes abdominal discomfort and diarrhea, resulting from lactase (LCT) enzyme deficiency produced by intestinal epithelial cells (IEC). Except for lactose free diet, no treatment can cure lactose intolerance and the regulation of LCT enzyme expression remains unknown. Peroxisome proliferator-activated receptor γ (PPAR γ) is a nuclear receptor highly expressed by IEC playing a key role in gut homeostasis and metabolism regulation.

AIMS&METHODS: Aim: To evaluate the roles of PPAR γ in the regulation of lactase production *in vitro* in IEC and *in vivo* in rodents. **Methods:** Caco2 cells were treated 24 hours with Pioglitazone (Pio; 1 μ M) and with a new PPAR γ modulator named GED (amino-phenyl-methoxy-propionic acid; 1mM) or 5-aminosalicylate (5ASA; 30mM). Transcriptomic profiling was done using Agilent 2-colors 44K Gene Expression Microarrays. LCT mRNA and protein expression was assessed by quantitative RT-PCR and immunostaining. LCT activity was evaluated *in vitro* by standard method measuring the amount of glucose after lactose digestion. Involvement of PPAR γ was confirmed using RNA interference, antagonist treatment (GW9662) and intestine-specific PPAR γ knock-out C57BL/6 mice (PPAR^{ΔIEC}). *In vivo*, LCT expression and activity were determined in the duodenum and jejunum of wild-type rodents orally treated with GED.

RESULTS: Both in microarray and qRT-PCR analysis, LCT mRNA expression was upregulated by GED, Pio and 5ASA compared to control cells with a mean fold of 5.7 ($p < 0.0001$), 14.7 ($p < 0.0001$) and 9.5 ($p < 0.0001$) respectively. LCT protein upregulation was also observed by immunostaining of stimulated Caco-2 cells. Importantly, GED and Pio treatments significantly increased LCT enzyme activity of Caco-2 cells (2.5 to 3 fold; $p < 0.05$). LCT mRNA ($p = 0.0022$), protein expression and lactase activity ($p = 0.0043$) were decreased in PPAR γ knock-down Caco2 cells. In PPAR^{ΔIEC} mice, LCT mRNA expression was significantly decreased both in duodenum ($p = 0.028$) and jejunum ($p = 0.05$) compared to control mice. Both LCT expression and activity were increased in the duodenum ($p < 0.05$) and jejunum ($p < 0.01$) of weaned C57BL/6 mice and Sprague-Dawley rats treated one week with GED compared to animals receiving vehicle.

CONCLUSION: PPAR γ agonists are able to increase lactase expression and activity *in vitro* and *in vivo*. These findings identify PPAR γ as a new master regulator of LCT production by IEC and suggest that modulating PPAR γ activity may be a new therapeutic strategy for the management of lactose intolerance.

Contact E-mail Address: benjamin.bertin-2@univ-lille2.fr

Disclosure of Interest: M. Fumery Financial support for research from: Giuliani SpA, A. Langlois Financial support for research from: Giuliani SpA, S. Specia Financial support for research from: Giuliani SpA, C. Dubuquoy Financial support for research from: Giuliani SpA, M. Figeac: None Declared, R. Christel Financial support for research from: Giuliani SpA, L. Dubuquoy Financial support for research from: Giuliani SpA, S. Bellinvia Directorship(s) for: Giuliani SpA, P. Desreumaux Financial support for research from: Giuliani SpA, B. Bertin Financial support for research from: Giuliani SpA

Keywords: intestinal epithelial cells, lactase gene, lactose intolerance, PPARGamma, small intestine

OP247 DISTURBED INTESTINAL INTEGRITY IN PATIENTS WITH COPD; EFFECTS OF ACTIVITIES OF DAILY LIVING

K. Lenaerts^{1*}, E. Rutten², W. Buurman¹, E. Wouters². ¹Department of Surgery, Maastricht University Medical Centre, Maastricht, ²Centre of expertise for Chronic Organ Failure (Ciro), Horn, Netherlands

INTRODUCTION: Chronic obstructive pulmonary disease (COPD) is accepted to be a multicomponent disease with various comorbidities. The contribution of the gastrointestinal tract to the systemic manifestation of COPD has never been investigated. This metabolically active organ may experience recurring local oxygen deficits during daily life, leading to disturbed intestinal integrity in COPD patients.

AIMS&METHODS: 18 patients with moderate COPD (mean FEV1: 55±3%pred) and 14 matched healthy controls were tested on two occasions, a

baseline measurement at rest and, at another day, during the performance of activities of daily living (ADLs). To assess enterocyte damage, plasma intestinal fatty acid binding protein (IFABP) levels were determined, whereas urinary excretion of orally ingested sugar probes was measured using liquid chromatography and mass spectrometry to assess gastrointestinal permeability.

RESULTS: Plasma IFABP concentrations were not different between COPD patients and healthy controls at rest. In contrast, 0-3h urinary lactulose/rhamnose and sucralose/erythritol ratios and 5-24h urinary sucralose/erythritol ratios were significantly higher in COPD patients compared to controls, indicating increased permeability of the small intestine and colon. Furthermore, the performance of ADLs led to significantly increased plasma IFABP concentrations in COPD patients but not in control subjects. In line, the intestinal permeability difference between COPD patients and controls was intensified.

CONCLUSION: Besides an altered intestinal permeability in COPD patients at rest, performing ADLs led to enterocyte damage in addition to intestinal hyperpermeability in COPD patients but not in controls, indicating functional alteration in the gastrointestinal tract. Hence, intestinal compromise should be considered as a new component of the multisystem disorder COPD.

Contact E-mail Address: kaatje.lenaerts@maastrichtuniversity.nl

Disclosure of Interest: None Declared

Keywords: Chronic disease, Intestinal epithelial barrier, Intestinal epithelial cells, Intestinal injury, Physical activity

OP248 FOLATE PRODUCTION IN BIFIDOBACTERIA FROM INFANT AND ADULT HUMANS

M. R. D'Aimmo¹, M. Modesto², P. Mattarelli^{2*}, B. Sgorbati², B. Biavati², T. Andlid¹. ¹DEPARTMENT OF CHEMICAL AND BIOLOGICAL ENGINEERING, Chalmers University of Technology, Goteborg, Sweden, ²DIPSA, BOLOGNA UNIVERSITY, Bologna, Italy

INTRODUCTION: Folates – the natural chemically reduced forms of folic acid (vitamin B9) – are cofactors in essential metabolic pathways such as DNA synthesis and methylation pathways. Humans cannot synthesize folate and depend on intake both from the diet (green vegetables, cereals, rice, milk, fermented milk products, etc.) and from indigenous folate synthesizing bacteria of the intestinal microbiota. Low folate levels increase the risk for neural tube defects and may increase the risk for e.g. certain cancer forms, cardiovascular disease and Alzheimer's.

AIMS&METHODS: Screening for folate production of the bifidobacteria isolates from human adult and infant (1-6 month old) was performed. Strains typical of infants, such as *Bifidobacterium longum* subsp. *infantis* and *B. breve*, and of adults (*B. adolescentis*) were selected for characterization. The aim of the present work was to investigate bifidobacteria from human host of different age with different feeding habits in order to establish a possible correlation between diet and the folate production. Folate is present in many different forms in humans. The detectable forms studied in the present work are 5-CH3-H4, H4 and total folate content. Bifidobacteria strains were cultivated in folate free synthetic media. Validated HPLC method was used to analyze deconjugated folates extracted from bacterial biomass.

RESULTS: All bifidobacteria tested (both from adult and infant) were able to produce folate. Strains derived from adults were the higher producer of total folate (range from 580 to 935 μ g/g dry matter) with the predominance of 5-CH3-H4 folate and a low amount of H4 folate. In infants we obtained the opposite results with strains typical of infant habitat producing low amounts of total folate (range from 35 to 200 μ g/g dry matter) and an inverted ratio of 5-CH3-H4/H4 folate in respect to adults.

CONCLUSION: In agreement with idea of coevolution of host-gut microbiome (Ley et al., 2008) we find that bifidobacteria present in the adult gut were able to produce high amount of folate whereas strains derived from infants were less able to produce folate. These findings correlate with the diet and the folate requirement of the host: in infants, in fact, milk feeding is able per se to fulfill the folate needs of the individuals whereas in adults a more complex diet is sometime not able to cover all the folate need. The relevance of the different ratio of 5-CH3-H4/H4 folate production in adults and infants has being studied only in few strains and further studies are requested in order to complete this finding and provide an ecological explanation.

REFERENCES:

1. Ley RE, et al. (2008) Evolution of mammals and their gut microbes. Science 320:1647–1651

Contact E-mail Address: paola.mattarelli@unibo.it

Disclosure of Interest: None Declared

Keywords: Bifidobacterium adolescentis, Bifidobacterium breve, Bifidobacterium longum subsp. *infantis*, Folate production, Gut microbiota

OP249 UNDISSOCIATED GELATIN TANNATE REDUCES INTESTINAL LEAKINESS AND MUCOSA INFLAMMATION BY FORMING A PROTECTIVE BIOFILM: RESULTS FROM IN-VITRO AND IN-VIVO STUDIES

L. Bueno^{1*}, S. Sekkal¹, V. Theodoru¹, M. Dattilo². ¹INRA, Toulouse, France, ²Biogem, Ariano Irpino, Italy

INTRODUCTION: Gelatine (GEL) stabilised by cross-linking with tannic acid (TA) forms gelatine tannate (GT). GT is approved as medical device for the oral treatment of diarrhoea as Tasetan[®]. GT is considered as a protective biofilm on the gut mucosa and has been shown to cure diarrhoea but the mechanism of action needs further investigation.

AIMS&METHODS: We aimed at investigating the effect of GT and its components (GEL and TA) on the intestinal mucosa using both *in-vitro* and *in-vivo* models.

The *in-vitro* "filming" activity was evaluated by Corrositex[®], a standard measure of chemical aggression, and on Caco-Goblet monolayers. The effect of GT (5 or 20 mg/ml) on Caco-Goblet cell permeability was assessed by Trans-Epithelial Electrical Resistance (TEER) and Lucifer Yellow (LY) before and after apical *S. typhimurium*. The tight-junction (TJ) proteins aquaporin-3 (AQP3) and occludin (OCL) were assayed by RT-PCR as markers of TJ integrity.

In-vivo, Wistar rats received orally either GT (250 mg/kg), Gel (125 mg/kg), or TA (125mg/kg), and 2 h. later were injected IP with LPS from *E. coli*. Jejunal strips were collected 6 hours later for *in vitro* TJ permeability measurement using FITC-dextran and mucosal myelo-peroxidase (MPO) activity as a marker of inflammation.

RESULTS: GT increased the corrosion time (hydrochloric ac. 37%) from 400 to 699 sec ($p < 0.001$) suggesting a chemical biofilm protection. In addition, GT (5 mg/ml) increased TEER of CACO-goblet at 4 hours (from 180.1 to 269.2 ohm*cm², $p < 0.05$) and decreased the basal permeability to LY in basal conditions at both 2 and 4h. The LY permeability increased from 1.18 to 7.54 after 2 hours of exposure to *S. typhimurium* however a pre-treatment with GT suppressed this increase and decreased bacterial invasion by 72%, such been associated with overexpression of AQP3 and OCL at 4 hours (350 and 200% respectively for GT at 20mg/kg).

Six hours after LPS injection in rats, both jejunal TJ permeability and MPO activity were dramatically increased. Oral pretreatment with GT reduced by 78.1% the jejunal increase of permeability whereas GEL and TA did not affected it and subsequently reduced significantly the LPS-induced increase in MPO.

CONCLUSION: Our results confirm that GT acts by mechanical protection of the gut mucosa. The protective biofilm formed by GT prevents the leakiness of the tight junctions both in basal conditions and after insult by bacteria (*in-vitro*) and by LPS (*in-vivo*). These effects cannot be replicated by either tannic acid or gelatine confirming that GT is the active form to prevent gut leakiness and subsequent inflammation.

Contact E-mail Address: maurizio.dattilo@gmail.com

Disclosure of Interest: None Declared

Keywords: Diarrhoea, Gelatin tannate, inflammation, LPS, paracellular permeability

OP250 DIABETES AND GASTROINTESTINAL DISORDERS: THE EFFECT OF INTESTINAL METHANE PRODUCTION ON GLYCEMIC CONTROL

V. Cesario¹, T. A. Di Rienzo¹, D. Pitocco², M. Campanale¹, G. D'Angelo¹, S. Pecere¹, F. D'Aversa¹, A. Tortora¹, F. Barbaro¹, G. Vitale¹, G. Gigante¹, G. Caracciolo¹, A. Gasbarfrini¹, V. Ojetti^{1*}. ¹Internal Medicine, ²Diabetology, POLICLINICO GEMELLI, Rome, Italy

INTRODUCTION: At the state of art it isn't known the correlation between diabetes and lower gastrointestinal disorders. Some studies show a significantly higher prevalence of small intestinal bacterial overgrowth (SIBO) in patients with type I diabetes. No data exists about gastrointestinal methane (CH₄) production in patients with diabetes.

AIMS&METHODS: Aim of our study was to evaluate the effect of methaogenic flora eradications on glycemic control and daily insulin requirements in patients with type 1 diabetes in order to identify a possible role of CH₄ production on diabetes severity.

30 consecutive patients (9 males, 21 females; mean age 45 +/-7yrs) affected by type 1 diabetes underwent H₂/CH₄ lactulose breath test to evaluate the presence of SIBO and CH₄ production (CH₄ concentration at least 3 ppm over that of room air). The glycemic control was evaluated through glycated hemoglobin and daily insulin requirement (ratio between total insulin units in a day and body weight). CH₄ producers were treated with metronidazole (500 mg bid for 10 days) and underwent a control breath test 8 weeks after the end of therapy. Data were analyzed using paired-data t-test.

RESULTS: 12/30 patients (40%) were methane-producers (mean baseline value 6+/-2ppm; mean peak 25+/-8ppm); the mean glycemic control was 7.6% and the daily insulin requirements was 0.68+/-0.12 UI/kg. 9/12 patients (75%) showed a significant ($P < 0.001$) reduction of their glycemic control (mean HbA1c 7.6% vs 6.8%) and daily insulin requirements (0.68+/-0.12 vs 0.49+/-0.08 UI/kg) after metronidazole therapy.

CONCLUSION: Our study showed for the first time a possible role of CH₄ production in diabetes metabolic control. In particular, the most interesting data is that poorly controlled diabetes seems to be related to a gut CH₄ production as confirmed by its significant improvement after eradication therapy.

Contact E-mail Address: valcesario@yahoo.it

Disclosure of Interest: None Declared

Keywords: diabetes mellitus type 1, glycemic control, methanogenic flora

OP251 MEDIUM-CHAIN TRYGlyceride INDUCED LEUKOCYTE ACTIVATION IS NOT MEDIATED BY TOLL-LIKE RECEPTOR 4

E. D. Olthof^{1,*}, A. F. Guelich¹, L. A. Joosten², H. M. Schaap - Roelofs¹, G. J. Wanten¹. ¹Department of Gastroenterology and Hepatology, ²Department of General Internal Medicine, RADOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, Nijmegen, Netherlands

INTRODUCTION: Lipids, as part of parenteral nutrition formulations modulate the function of the immune system. For instance, medium-chain triglycerides (MCTs), but not long-chain triglycerides (LCT), as part of parenteral lipid emulsions activate leukocytes *in vitro* by mechanisms that are still unknown. It has been shown that saturated fatty acids can activate Toll-like receptor 4 (TLR-4) mediated pro-inflammatory signaling pathways in leukocytes.

AIMS&METHODS: Aim of our study was to investigate whether TLR-4 is also involved in MCT-induced leukocyte activation. We assessed the *in vitro* effect of the parenteral mixed lipid emulsion LCT/MCT, at a clinically relevant

triglyceride concentration of 5 mmol/l, on the expression of leukocyte surface membrane activation markers in the presence or absence of the specific TLR-4 inhibitors TAK-242 (0.5 and 5 μmol/l) and *Bartonella quintana* LPS (0.1, 1 and 2.5 μg/ml).

RESULTS: As expected, LCT/MCT activated leukocytes, with an increase in expression of adhesion (55% and 41% in granulocytes and monocytes, respectively), azurophilic and specific degranulation (19% and 22%, respectively in granulocytes) markers, and a decrease in L-selectin (14% and 20% in granulocytes and monocytes, respectively). Inhibition of TLR-4 by TAK-242 and *Bartonella quintana* LPS did not alter the LCT/MCT-induced decrease in L-selectin and increase in adhesion marker expression in granulocytes and monocytes. Furthermore, in granulocytes *Bartonella quintana* LPS did not change the MCT-induced increased expression of specific and azurophilic degranulation markers. The LCT/MCT induced increase in expression of both degranulation markers in granulocytes was abolished during TLR-4 inhibition with 5 μmol/l TAK-242. However, a similar decrease in degranulation marker expression was found after incubation with 5 μmol/l TAK-242 alone.

CONCLUSION: MCT-induced immune activation is not mediated by TLR-4 signaling.

Contact E-mail Address: e.olthof@mdl.umcn.nl

Disclosure of Interest: None Declared

Keywords: immune activation, medium chain triglyceride, parenteral nutrition, toll like receptor-4

TUESDAY, OCTOBER 15, 2013

11:00-12:30

Pancreatitis: Lessons from animal models – Salon 11/12

OP252 IMPROVEMENT OF ENDOPLASMIC RETICULUM STRESS BY ENHANCED PERK PATHWAY REDUCES MURINE EXPERIMENTAL ACUTE PANCREATITIS

T. Okazaki^{1,*}, A. Nishio¹, T. Masahiro², T. Inoue², Y. Sakaguchi¹, T. Fukui², K. Uchida², K. Okazaki². ¹Gastroenterology and Hepatology, Kansai Medical University, Moriguchi, ²Gastroenterology and Hepatology, Kansai Medical University, hirakata, Japan

INTRODUCTION: Endoplasmic reticulum (ER) stress causes the accumulation of misfolded proteins inside the ER and initiates unfolded protein response (UPR). UPR is activated during pancreatitis to restore ER homeostasis. Although protein kinase RNA-like ER kinase (PERK) is associated with the UPR through phosphorylation of eukaryotic initiation factor 2- α (eIF2- α), the role of PERK signaling pathway in pancreatitis is not fully clarified. We investigated the significance of PERK signaling pathway in severe acute pancreatitis in mice using an eIF2- α dephosphorylation inhibitor, salubrinal.

AIMS&METHODS: Severe acute pancreatitis was induced by intraperitoneal injection of cerulein (CER) at a dose of 50 mg/kg six times at 1 hour intervals. Moreover, LPS was administered at a dose of 10mg/kg as the septic challenge immediately after the completion of CER injections. Salubrinal was administered intraperitoneally immediately after LPS injection and six hours later. Mice were sacrificed at 24 hours after the first injection of CER and the severity of pancreatitis was histologically graded with a scoring system. Serum amylase and proinflammatory cytokine levels were measured. Expression of ER stress-related proteins was examined by western blotting.

RESULTS: The severity of pancreatitis in mice treated with salubrinal was significantly attenuated compared with control mice. Serum amylase and proinflammatory cytokine levels were lower in salubrinal-treated mice than those of control mice. Expression level of 78kDa glucose regulated protein (GRP78), activating transcription factor 4 and phosphorylated eIF2- α protein were elevated in mice treated with salubrinal compared with control groups.

CONCLUSION: Inhibition of eIF2- α dephosphorylation decreased ER stress and reduced severe acute pancreatitis in mice. Augmentation of PERK signaling pathway could be a potential therapeutic option for the treatment of acute pancreatitis.

REFERENCES:

1. Malo A et al. 4-Phenylbutyric acid reduces endoplasmic reticulum stress, trypsin activation, and acinar cell apoptosis while increasing secretion in rat pancreatic acini. *Pancreas*. 2013;42:92-101.
2. Ye R et al. Grp78 heterozygosity regulates chaperone balance in exocrine pancreas with differential response to cerulein-induced acute pancreatitis. *Am J Pathol*. 2010;177:2827-2836.
3. Fazio EN et al. Stanniocalcin 2 alters PERK signalling and reduces cellular injury during cerulein induced pancreatitis in mice. *BMC Cell Biology*. 2011;12:17.

Contact E-mail Address: okazakta@takii.km.ac.jp

Disclosure of Interest: None Declared

Keywords: ER stress, pancreatitis, PERK signaling, Salubrinal

OP253 SEROTONIN REGULATES PROGENITOR CELL-BASED BUT NOT CLONAL REGENERATION IN THE ADULT PANCREATIC ACINAR CELL

E. Saponara^{1,*}, S. Sonda¹, K. Grabliauskaite¹, Y. Tian¹, T. Reding¹, R. Graf¹. ¹Swiss HPB Center, University Hospital Zurich, Zurich, Switzerland

INTRODUCTION: Progenitor cell-based regeneration of acinar cells is activated during cerulein-induced pancreatitis. This process requires a preliminary acinar de-differentiation via secretion of zymogens, followed by expression of progenitor cell markers and formation of acinar-to-ductal metaplasia (ADM). Clonal regeneration without loss of zymogens and cell de-differentiation is observed following 60% pancreatectomy. Previously, we demonstrated that