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GSGH2022

Global Summit on Gastroenterology and Hepatology

March 17, 2022

Virtual

The Scientistt
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FOREWORD

Dear Colleagues,

It is a great pleasure to announce that The Scientistt will host the Global Summit on Gastroenterology and Hepatology (GSGH2022) as a virtual conference during March 17-19, 2022.

GSGH2022 aims to bring together renowned researchers, scientists, and scholars to exchange ideas, present sophisticated research works to discuss hot topics in the field, and share their experiences on all aspects of Gastroenterology and Hepatology.

The GSGH2022 will be a 3 days event that means gathering the key players of the Gastroenterology and Hepatology community and related sectors. This event is launched with the aim to become an established event, attracting global participants, intent on sharing, exchanging, and exploring new avenues of Gastroenterology and Hepatology-related scientific and commercial developments.

A wide-ranging scientific program consisting of plenary lectures, keynote lectures, Invited lectures, parallel sessions, as well as poster sessions for young scientists covering all topics in Gastroenterology and Hepatology will be scheduled. This conference provides a wonderful opportunity for you to enhance your knowledge about the newest interdisciplinary approaches in Gastroenterology and Hepatology.

Moreover, the conference offers a valuable platform to create new contacts in the field of Gastroenterology and Hepatology, by providing valuable networking time for you to meet great personnel in the field.

We look forward to seeing you at the GSGH2022 webinar.

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Index alphabetical order

SPEAKERS

P: Plenary Speaker
K: Keynote Speaker
I: Invited Speaker

Index alphabetical order

Virtual Presentations

Amedeo Amedei
University of Florence, Italy

The Role of Microbiota-Immunity Axis in Gastrointestinal Disorders

Abstract

The interplay between the immune system and gut microbiota (GM) is also well-known.Since the intestinal tract is the main point of contact of the host immune system and microorganisms, the microbiota influence on systemic immune function may have a crucial impact in pathogenesis of gastrointestinal disorders and in the variability of the disease course.We have recently explored the impact of microbiota-immunity axis (MIA) in colorectal cancer (CRC) and Crohn disease (CD).
In the first observational study, we collected tumor (CRC) and healthy (CRC-S) mucosa samples from 45 CRC patients. We characterized the tissue infiltrating lymphocytesubset profile and the GM composition. Subsequently, we evaluated the CRC and CRC-S molecular inflammatory response and correlated this profile with GM composition, using Dirichlet multinomial regression.

CRC samples displayed higher percentages of Th17, Th2, and Tregs. Moreover, CRC tissues showed significantly higher levels of MIP-1α, IL-1α, IL-1β, IL-2, IP-10, IL-6, IL-8, IL-17A, IFN-γ, TNF-α, MCP-1, P-selectin, and IL-9. Compared to CRC-S, CRC samples also showed significantly higher levels of the following genera: Fusobacteria, Proteobacteria, Fusobacterium, Ruminococcus2, andRuminococcus. Finally, the abundance of Prevotella spp. in CRC samples negatively correlated with IL-17A and positively with IL-9. On the contrary, Bacteroides spp. presence negatively correlated with IL-9.

In conclusion, our data consolidated antitumor immunity impairment and the presence of a distinct microbiota profile in the tumor microenvironment compared with the healthy mucosa counterpart. Relating the CRC cytokine profile with GM composition, we confirmed the presence of bidirectional crosstalk between the immune response and the host's commensal microorganisms. Indeed, we documented, for the first time, that Prevotella spp. and Bacteroides spp. are, respectively, positively and negatively correlated with IL-9, whose role in CRC development is still under debate.

Regarding the Crohn diseasestudy, we aimed to characterize the molecular immune response distribution within the ileal layers and to evaluate the correlated microbiota in pathological/ healthy settings comparing first surgery/relapse clinical conditions.We enrolled 12 CD patients. A comprehensive analysis of an ileal mucosa, submucosa and serosa broad-spectrum cytokine panel was performed through a multiplex approach. In addition, ileal microbiota composition was assessed through next generation sequencing.

We observed a distinct profile [of IL1-α, IL-1β, IL-4, IL-8, ICAM-1, E-Selectin, P-Selectin, IP-10, IL 6 and IL 18] across the CD vs healthy ileal layers; and a different distribution of IFN- γ, P-Selectin, IL-27 and IL-21 in first surgery vs relapse patients. In addition, the phylum Tenericutes, the family Ruminococcaceae, and the genera Mesoplasma and Mycoplasma were significantly enriched in the pathological setting. Significant microbiota differences were observed between relapse and first surgery patients regarding the class Bacteroidia, and the genera Prevotella, Flavobacterium,

Tepidimonas and Escherichia/Shigella. Finally, the abundance of the genus Mycoplasma was positively correlated with IL-18.

In conclusion, we described a dissimilarity of cytokine distribution and microbiota composition within CD and adjacent healthy ileal tissue layers and between first operation and surgical relapse. Our results give potential insight into the dynamics of the gut microbiota-immune axis in CD patients, leading to detection of new biomarkers.

Vittorio Piloni
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The Use of MR defecography in Rectal Dyschezia

Abstract

Background Existing methods of quantification of rectal emptying by MR defecography have so far failed to obtain both widespread acceptance by researchers and extensive application in the clinical practice.

Aim To describe a technique, to be embedded into routine image processing, by which the quantitation of rectal area decrease is displayed synchronous with its graphic representation together with the image of rectal contrast emptying in a cinematic mode.

Method The imaging series of two-hundred and twenty nine consecutive patients with impaired defecation and prolapse syndromes (191 females, 38 males, mean age and SD, 56.57 ± 14.4 yrs and 50.7 ±16.6 yrs , respectively) who underwent MR defecography between April 2017 and July 2021, are reviewed. The "clearance" of acoustic gel during rectal emptying is calculated planimetrically on MR sagittal images as the value of rectal area before evacuation − the value after evacuation / value before evacuation × 100. In addition, the flow rate, is calculated and given as cm2 divided by t in seconds. Subsequently, values are displayed on the screen as the change of rectal size synchronous with the rectal image and its graphic representation. Thereafter, the shape of the curve and data are compared with clinical findings and presenting symptoms for correlation and subtypes characterization.

Results Average clearance values differed significantly (p, < 0.001) among the three groups i.e, 31.18 cm2 ± 23.34 in the obstructed group, 45.12 cm2 ± 22.53 in the prolapse group, and 58.27 cm2 ± 16.50 in the incontinent group. The same occurred for the flow rate i.e, 0.19 cm2/sec ± 0.15, 0.30 cm2/sec ± 0.16, and 0.83 cm2/sec ± 0.25, respectively. Rectocele accounted for the most frequent abnormality (68%) seen in the obstructed group, and the combination of rectal clearance, flow rate with graphic display and imaging feature allowed recognition of two different sub types.

Conclusions The application of the above method indicates that a better discrimination of categories and subcategories of pathologies can be obtained in patients with functional disorders of defecation, with potential influence on therapy planning.

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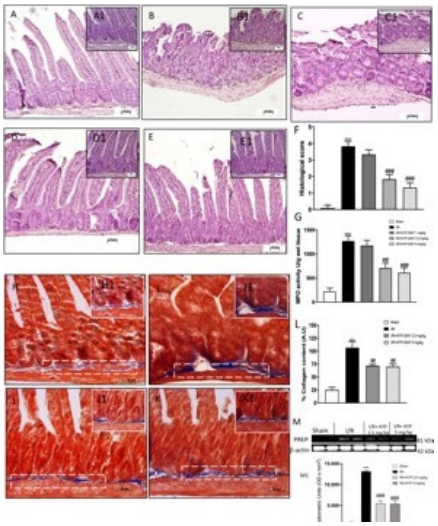
Inhibition of Prolyl Oligopeptidase Prevents Consequences of Reperfusion Following Intestinal Ischemia

Abstract
Intestinal ischemia/reperfusion injury (IRI) remains a clinical event that contributes to high mor-bidity and mortality rates. Intestinal epithelium is exposed to histological and vascular changes following tissue ischemia. Prolyl endopeptidase (PREP), involved in inflammatory responses, could be targeted for recovery from the permanent consequences following intestinal ischemia. Our aim was to investigate the role of PREP inhibitor KYP-2047 in tissue damage, angiogenesis, and endothelial barrier permeability after intestinal IRI in mice. KYP-2047 treatments were performed 5 min prior to intestinal damage. Intestinal IRI was induced in mice by clamping the superior mesenteric artery and the celiac trunk for 30 min, followed by 1 h of reperfusion. PREP inhibition by KYP-2047 treatment reduced intestinal IR-induced histological damage and neutrophil accumulation, limiting inflammation through decrease of NFB nuclear translo-cation and fibrotic processes. KYP-2047 treatment restored barrier permeability and structural alteration following intestinal IRI, attenuating neovascular processes compromised by ische-mia/reperfusion. Additionally, loss of epithelial cells during intestinal ischemia occurring by apoptosis was limited by KYP-2047 treatment, which showed strong effects counteracting apop-tosis and DNA damage. These findings provide the first evidence that PREP inhibi-tion through KYP-2047 inhibitor use could be a validate strategy for resolving alterations of in-testinal epithelium the pathophysiology of intestinal disease.

Keywords
Intestinal ischemia/reperfusion injury; inflammation; angiogenesis; intestinal barrier permeability; apoptosis.



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Marco Maria Pascale
Agostino Gemelli University Policlinic, Italy

Post-transplant Hepatic Graft Function through Bile Analysis

Abstract

Background: The importance of immunosuppressant blood dosage in a transplant patient is widely recognized for detecting the immunosuppressive capacity. In case of Tacrolimus in liver recipients, the drug excretion is carried out by the transplanted graft itself. The aim of the “Tacrolimus in Bile” (TUBE) Trial is the creation of a laboratory parameter for the early detection of hepatic injury after liver transplant.

Methods: TUBE is a single-blind prospective monocentric trial,in which liver recipients who had Kehr’s tube inserted into the biliary tract were enrolled.In the first 10 post-operative days (POD),a bile sample was collected together with a bloodsample.The blood and biliary values of Tacrolimus were correlated to create the”blood-bile ratio of Tacrolimus”(BBRT).The primary outcome was the assessment of the predictive ability of BBRT in the evaluation of liver rejectioninjury,diagnosed through laboratory or pathological analysis.The relationship between BBRT and liver injury was examined through a Wilcoxon-Mann-Whitney test.A ROC curve was developed to estimate the BBRT threshold with the best sensitivity/specificity ratio.

Results: Among the 35 patients enrolled,12(34%) presented with acute rejection liver injury,diagnosed by standard methods between the 5thand 7thPOD.Transaminases,total bilirubin and blood tacrolimus levels did not differ significantly in the two study patient groups,unlike eosinophils within the rejection period.The mean BBRT value presented a significant difference between the two study groups already in the 4thPOD(p=0.026)(Figure 1).The ROC curve confirmed the statistical significance of BBRT(p=0.018).The sensitivity and specificity achieved with a BBRT cut-off value of 4.1 was 75% and 74%,respectively.

Conclusions: The early diagnosis of acute rejection liver injury allows an improvement in the overall transplant outcome.The TUBE trial is the first study evaluating the relationship between blood and biliary concentrations of a marker with hepatic excretion in liver transplant patients.This research field can be deepened by considering other aspects,such as liver enzyme polymorphism or blood flow alterations to the graft.Todate,BBRT can be considered an additional laboratory marker for detecting liver rejection damage after liver transplantation.

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Celiac Disease Awareness among Physicians in Kazakhstan: First Country-Wide Study

Abstract

Background. Celiac disease (CD) is a common genetically predisposed autoimmune condition affecting gut and other organs. Due to frequent atypical forms it is hugely under diagnosed or diagnosed late, leading to complications. Disease awareness is one of the key components of early cases identification. This study aimed to assess awareness about CD among primary care physicians, who are the front-liners in suspecting the diagnosis, and other medical specialists, which could help identifying pitfalls in timely diagnosis and efficient treatment of the condition.

Methods and Findings. The questionnaire for this country-wide cross-sectional survey-based study was created based on the latest international clinical guidelines on CD and included consent form, 5 general questions (inquiring age, gender, work experience, specialty, place of work and country location) and 10 specific questions concerning CD (etiology, clinical manifestation, associated conditions and complications, methods of diagnosis and treatment). Overall 232 respondents from 13 country provinces and two republican cities (former and current capitals) were recruited into this study. Of them, 110 (47.4%) were primary care physicians (general practitioners, internists and pediatricians), 10 (4.3%) gastroenterologists and 112 (48.3%) physicians with narrow specialization in other areas. A scoring system was used to classify the level of awareness of participants into 3 categories: poor, fair, and good. Analysis of responses revealed poor awareness on different aspects of CD in 59.4% of physicians, which was associated with the type and level of medical institution (respondents from republican/province/district/rural/village hospitals had less knowledge than those from university clinics, research centers and city hospitals, p=0.004), gender (female respondents had higher scores, p=0.006) and age (respondents aged over 50s demonstrated the lowest awareness on atypical forms of CD, although general awareness on CD was the highest, p=0.02). The most common “myths” about CD existing among physicians were the following: “symptoms of CD are always obvious in children and adults” (92.5% and 88.4% of respondents, respectively); “genetic mutation HLA DQ2/DQ8 causes development of CD in all carriers of the mutation” (51.3%); “CD is a disease of children only” (12.5%); “CD is triggered by dairy products” (8.6%). Genotyping of HLA DQ genes has been chosen as a test used in case of CD suspicion by every third respondent and was advocated as a “golden standard” confirmatory test by every fifth respondent. Quarter of respondents (25%) revealed their incorrect treatment strategies: gluten-free diet for 1 month, a dairy

free diet, H. pylori eradication therapy, or responded that did not know how to treat. Overall 93.5% of respondents expressed intention to learn more about CD, while the rest 6.5% thought that they knew enough, although assessment of their responses showed poor knowledge.

Conclusions. This study revealed poor level of awareness among physicians in Kazakhstan and identified common misconceptions about CD, which potentially could lead to incorrect application of diagnostic tests, delays in diagnosis and inefficient treatment. Educational programs are needed to be developed and implemented in order to increase awareness and unravel misconceptions; curriculum of medical schools needs to be enhanced.

Keywords
celiac disease, physicians' awareness, survey, country-wide

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Said Dermime
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Persistent anti-NY-ESO-1-specific T cells and expression of differential biomarkers in a patient with metastatic gastric cancer benefiting from combined radio immunotherapy treatment

Abstract

Combined radio immunotherapy is currently being investigated to treat patients with cancer. Anti-programmed cell death-1 (PD-1) immunotherapy offers the prospect of long-term disease control in solid tumors. Radiotherapy has the ability to promote immunogenic cell death leading to the release of tumor antigens, increasing infiltration and activation of T cells. New York esophageal squamous cell carcinoma-1 (NY-ESO-1) is a cancer-testis antigen expressed in 20% of advanced gastric cancers and known to induce humoral and cellular immune responses in patients with cancer. We report on the dynamic immune response to the NY-ESO-1 antigen and important immune-related biomarkers in a patient with metastatic gastric cancer treated with radiotherapy combined with anti-PD-1 pembrolizumab antibody.Our patient was an 81-year-old man diagnosed with locally advanced unresectable mismatch repair-deficient gastric cancer having progressed to a metastatic state under a second line of systemic treatment consisting of an anti-PD-1 pembrolizumab antibody. The patient was subsequently treated with local radiotherapy administered concomitantly with anti-PD-1, with a complete response on follow-up radiologic assessment. Disease control was sustained with no further therapy for a period of 12 months before relapse. We have identified an NY-ESO-1-specific interferon-γ (IFN-γ) secretion from the patients' T cells that was significantly increased at response (****$p<0.0001$). A novel promiscuous immunogenic NY-ESO-1 peptide P39 (P153-167) restricted to the four patient's HLA-DQ and HLA-DP alleles was identified. Interestingly, this peptide contained the known NY-ESO-1-derived HLA-A2-02:01(P157-165) immunogenic epitope. We have also identified a CD107+ cytotoxic T cell subset within a specific CD8+/HLA-A2-NY-ESO-1 T cell population that was low at disease progression, markedly increased at disease resolution and significantly decreased again at disease re-progression. Finally, we identified two groups of cytokines/chemokines. Group 1 contains five cytokines (IFN-γ, tumor necrosis factor-α, interleukin-2 (IL-2), IL-5 and IL-6) that were present at disease progression, significantly downregulated at disease resolution and dramatically upregulated again at disease re-progression. Group 2 contains four biomarkers (perforin, soluble FAS, macrophage inflammatory protein-3α and C-X-C motif chemokine 11/Interferon-inducible T Cell Alpha Chemoattractant that were present at disease progression, significantly upregulated at disease resolution and dramatically downregulated again at disease re-progression. Combined radioimmunotherapy can enhance specific T cell responses to the NY-ESO-1 antigen that correlates with beneficial clinical outcome of the patient.

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Per M. Hellström
Uppsala University, Sweden

Motility Disorders Relieved by GLP-1 Analogue ROSE-010: Effects Based on Translational Research

Abstract

The first observation of glucagon-like peptide-1 (GLP-1) in diabetic subjects in 1996 revealed a pronounced inhibition of gastric emptying bringing down postprandial blood glucose excursions to almost normal levels. This initiated research in depth on the motility inhibitory actions of GLP-1 primarily of the stomach, where the inhibitory actions on gastric emptying have profound effects not only in diabetes type 2, but also on morbid obesity. Novel GLP-1 receptor agonists with prolonged actions show immense reductions of body weight in the range of 15% as compared to placebo controls. Differently from this, short-acting GLP-1 receptor agonists have found their way into motility disorders where their short actions are preferred for relief of attacks of disordered motility commonly encountered as dyspeptic conditions or irritable bowel syndrome.

The short-acting GLP-1 receptor agonist ROSE-010 has been studied in exploratory studies for management of irritable bowel syndrome (IBS), be it diarrheal, constipation or mixed forms of IBS. The clinical effects of ROSE-010 have been studied with luminal pressure measurements, transit studies and symptom recordings, while parallel translational research has been carried out to reveal basic mechanisms of action using immunohistochemistry for GLP-1 and the GLP-1 receptor as well as tetrodotoxin for nerve conduction blockade and L-nitro-mono-methyl-arginine for inhibition of nitric oxide synthase.

After showing promising inhibitory actions of GLP-1 on gastric emptying and disordered motility of the small bowel, ROSE-010 has in a large double-blind study been shown to relieve abdominal pain in IBS in a sign ificantdose-dependent manner, maximally by 50%. Females show greater pain relief than males; age and BMI did not affect the treatment response. The relief of IBS pain was greatest in constipation-dominant IBS (IBS-C) and mixed IBS (IBS-M) relative diarrhea-dominant and unspecified IBS. ROSE-010 was also able to promote colon transit and simultaneously relieve symptoms in IBS-C,speaking for favorable effects of ROSE-010 due to motility effects in the gut. Pre-clinical translational studies is supporting an inhibitory role of GLP-1 and ROSE-010 on gastric emptying and small bowel motility. The mechanism for the inhibitory effect is based on immunohistologicalfindings of GLP-1 and its receptor in the myenteric plexus speaking of GLP-1 as a neurotransmitter, along with nerve-mediated and nitric oxide-dependent relaxing effects of GLP-1 and ROSE-010 on gastrointestinal smooth muscle.

Against a background of preclinical translational data of GLP-1 and ROSE-010 indicating GLP-1 to be a neurotransmitter in addition to its hormonal actions with GLP-1 receptors that can be stimulated with ROSE-010 to inhibit motility which seems to be of benefit in patients, preferentially females with IBS-C and IBS-M. We look forward to upcoming studies using short-acting GLP-1 receptor agonists such as ROSE-010 for the treatment of gastrointestinal motility disorders.

Keywords
Gut hormones, Irritable bowel syndrome, Motility, Neuropeptides, Pain.

Biography
Educated as PhD and assoc prof in physiology and pharmacology at Karolinska Institute, Stockholm, with position as professor of gastroenterology in 2001, later moving on to full professor for the chair of gastroenterology at Uppsala University, Uppsala, in 2009. Research activities on gastrointestinal peptide hormones and inflammatory reactions including nitric oxide, cytokines and chemokines.

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Clarisse Dromain
University Hospital Vaud Lausanne

Tumor Response to Immunotherapy: A New Challenge for Imaging

Abstract

A wide range of cancer immunotherapy approaches have been developed including non-specific immune-stimulant such as cytokines (Interferon, IL2),cancer vaccines (peptide or dendritic-cell-based vaccines), adoptive T-cell therapy (TILs, CAR, TRC) and immune checkpoint inhibitors (anti CTLA-4, anti PD1 and anti PDL1). The most commonly used and intensively studied are the immune checkpoint inhibitors (ICIs).Their mechanism of action signifies a true shift in oncology where instead of targeting the tumor cells, ICIs target the immune system in order to break the cancer tolerance and stimulate the anti-tumor immune response. These new drugs have, since 2011, received marketing authorization for melanoma, lung, bladder, renal, and head and neck cancer with remarkable and long-lasting treatment response.The novel mechanism of action of these drugs, with immune and T-cell activation, lead to unusual patterns of response withpresence of flare phenomenon or pseudo-progression more pronounced and more frequent than previously described responses. Pseudo-progression, that has been described in about 3-10% of patients treated using ICIs, corresponds to increase of tumor burden and/or appearance of new lesions due to Infiltration of the tumor by activated T-cells before the disease responds to treatment. To overcome the limitation of RECIST criteria to assess this specific changes in tumour burden, new criteria so-calledirRC, irRECIST and iRECISTwere proposed.The major modification the need of a 4-week CT re-assessment to confirm progression.

Learning objectives:

To describe the different pattern of disease response to immunotherapy.

To learn the current response criteria of i-RECIST.

To describe the spectrum of imaging manifestations of immune-related adverse events.

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Identification of early biomarkers of non-alcoholic fatty liver disease - could they be used for targeted treatment?

Abstract
Results from our laboratory and others have shown that specific gut microbes contribute to the non-alcoholic fatty liver disease (NAFLD). However, despite the importance of gut-liver axis via portal vein, studies describing the role of microbial metabolites in NAFLD are surprisingly scarce. We aimed to increase the understanding on the metabolites in the context of fatty liver.

By using untargeted liquid chromatography/high resolution mass spectrometry, we have compared the plasma and fecal metabolomes of humans with high (>5%) and low (<5%) liver fat content. By using 16S rRNA gene sequencing, we compared the gut microbiota composition and diversity between the groups. We also studied differences in several clinical variables between the groups.

Here we present evidence that together with many clinical variables, specific metabolites (and microbes) might serve as early biomarkers of liver disease even before NAFLD has been diagnosed. Based on the existing literature, we present hypotheses of how the metabolites could be considered, when developing possible personalized treatments for NAFLD in the future.

Keywords
gut microbiota, metabolomics, fatty liver, biomarkers.

Biography
I currently hold an Academy of Finland Research Fellowship, which is comparable to tenure track position, at the Faculty of Sport and Health Sciences, University of Jyväskylä, Finland. I am also

Docent (Adjunct professor) in Bacteriology at the Faculty of Medicine, University of Turku, Finland. My research team focuses on studying host-gut microbiota interactions related to health and disease. Our approach has been in detecting gut microbiota-related phenomena in human cohorts and then to prove the biological significance and the underlying mechanisms of the phenomena using cellular and animal models. By this way, we have found ways to treat metabolic diseases, such as non-alcoholic fatty liver disease, by using or targeting specific gut microbes.

Ramon Mangues Bafalluy
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CXCR4-targeted nanoparticlesablate colon cancer stem cellsto blocktumor growth and metastases

Abstract

Selective elimination of cancer stem cells (CSCs) promises to block tumor growth and metastatic dissemination, as well as recurrence after chemotherapy. It is known that CXCR4 overexpression associates with chemotherapy resistance, metastases and poor prognosis in CRC patients. We have developed nanomedicines, in the form of drug-nanoconjugates or protein-only cytotoxic nanoparticles, that selectively target CXCR4+ CSCs in CXCR4-overexpressing colorectal cancer (CRC) models. In these models, a high percent of intravenously the administered dose is uptaken in tumor tissue, reaching low uptake in normal organs. Moreover, repeated intravenous administration of T22-GFP-H6-FdU nanoconjugates achieve metastasis prevention as well as antimetastatic effect in established metastatic foci, without systemic toxicity. Moreover, administration of the T22-PE24-H6, a protein-only nanoparticle that incorporates a bacterial exotoxin, induces a high number of apoptotic bodies in subcutaneous (SC) tumors, whereas its repated dosage in SC CRC models reverts 5-FU, oxaliplatin and apoptosis resistance, inducing instead pyroptotic cell death and tumor growth control. Finally, subcutaneous administration of bacterial inclusion bodies, a depot form that achieves sustained release of T22-PE24-H6 soluble nanoparticles, inhibits metastatic dissemination in all clinically relevant metastatic sites, again in the absence of toxicity in non-tumor organs. Taken together, our results validate CXCR4+ CSCs as targets for CRC therapy, and validates nanoparticles for targeted drug delivery as promising approaches to the control cancers that overexpress CXCR4.

Biography

Ramon Mangues currently works at the Research Institute of the Hospital Sant Pau in Barcelona as a Research Professor. He obtained his Pharm.D. and PhD at Navarra University and University Clinic of Navarra, Spain. He performed 5 years work in a Postdoctoral position and 5 more years as Research Assistant at New York University Medical Center. He is currently serving at the Board of Directors of the National Network for Nanomedicine (CIBER-BBN) and the Committee of the Board of Trustees at IIB-Sant Pau, Barcelona.

He published 140 papers in reputed journals and is inventor in 9 patents, 4 of them licensed to the Biotech Nanoligent, a spin-off of IIB-Sant Pau that he co-founded. He currently runs competitive projects, as PI or Partner, that are funded by the European Union, Spanish Government, and Private Investors all oriented towards Clinical Translation and Industrial Transfer of nanomedicine products that achieve targeted drug delivery. He also serves at National and International Committees for Project Evaluation in the area of Cancer and Biotechnolgy, including the French Cancer Institute and the Spanish State Agency for Research.

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Zoran Todorovic
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Significance of Lipidomics in Multiorgan Inflammation and Injury

Abstract

Lipidomics is a new field of research that deals with the metabolism of small molecules with a mass < 1500. In recent years, the crucial role of lipids in the pathogenesis and therapy of ischemic-reperfusion (IR) injury has become increasingly apparent. For example, IR injury can trigger oxidative stress leading to harmful changes in membrane lipids, with the detrimental accumulation of fatty acids leading to lipototoxicity. The changes are manifested not only on the organ where the IR injury occurred but also on the distant organs (organ crosstalk). Our studies used experimental models of IR injury to the liver and kidneys, as well as two models of sepsis (faecal- and endotoxin-induced). Lipid analysis provides additional insight into the pathogenesis of IR disorders in such models and reveals new targets for drug action. The therapeutic approach to reperfusion lipototoxicity involves reducing fatty acid overload, i.e., their transport to adipose tissue, and/or inhibiting the harmful effects of fatty acids on cell damage and death. The latter option involves using PPAR agonists and drugs that modulate the transport of fatty acids via carnitine into the mitochondrial interior or the redirection of long-chain fatty acids to peroxisomes (e.g., meldonium). Lipids are otherwise a heterogeneous group of molecules, and their signaling molecules do not precipitate but form "on-demand" in the cell. On the other hand, exosomes transmit lipid signals between cells, and the profile of such changes can be monitored by lipidomics. Changes in the lipid profile are organ-specific and may indicate new targets for drug action.

Tao Zuo
Sun Yat-Sen University, China

Roles of Gut Virome and Mycobiome in Fecal Microbiota Transplantation

Abstract

Enormous efforts have been devoted to the gut bacterial microbiome in human health and disease. By contrast, the 'dark matters' of the gut microbiome, including virome and mycobiome are significantly less studied. Fecal Microbiota Transplantation (FMT), as onemicrobiome rectification-based therapeutic approach, has garnered substantial clinical and translational research interest. The efficacy of FMT has long been ascribed to the transfer and role of bacteria in treating disease. Since our seminal studies showing the importance of gut virome/phageome and mycobiome in FMT treating Clostridioidesdifficile infection (CDI), there have been a series of studies investigating the effect of transfers of gut phages/viruses and fungi on a number of diseases treated by FMT, in both humans and animals. It is timely to summarize all clinical as well as basic research evidence to enhance the community's understanding of the roles of gut phages/viruses and fungi in FMT, and to drive the field forward.

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Surgical Strategies in Children with Short Bowel Syndrome

Abstract

Short bowel syndrome (SBS) is defined as a condition of malabsorption that is due to reduction of functional intestinal mass necessary for adequate digestion and absorption for nutrient, fluid and growth requirements. SBS typically follows resection of 50% or more of the small intestine and is associated with diarrhea, steatorrhea, dehydration, electrolyte disturbances, malabsorption and progressive malnutrition. The significant increase in overall survival of patients with SBS over the last decade has mainly been due to improved overall care, new total parenteral nutrition (TPN) formulas, and improved surgical techniques. The final goal of surgical treatment in these patients should be to facilitate bowel adaptation with a consequent reduction in TPN-dependence and to achieve finally enteral autonomy, and minimizing complications. The first line surgical treatment following an extensive small bowel resection include central line insertion for TPN and stoma formation. The two most commonly applied techniques are those labeled as intestinal lengthening procedures. These include the LILT (longitudinal Intestinal Lengthening) described by Bianchi and the more recently STEP (Serial Transverse Enteroplasty) described by Kim. These "lengthening" procedures correct bacterial overgrowth by correcting the dilatation and dysmotility, leading to improved absorption and a decreased need for bowel transplantation. LILT procedure is excellent as it doubles the length of the remaining bowel while respecting the anatomical criteria of bowel vascularization. This technique creates an optimal intestinal lumen and does not prevent any future bowel reconstructive surgeries if needed. Additional bowel length (68%) can be achieved through the STEP procedure. Other techniques include: single or multiple anti-peristaltic (reversed) segments and colonic interposition, antiperistaltic intestinal segment and Intestinal valves and sphincters (to delay transit and increase mucosal contact time and enhance bowel absorption); the Iowa segment (as described by Kimura); longitudinal colonic lengthening with or without a sigmoid J-pouch (as described by Devesa). Intestinal transplantation is indicated in recurrent septical infections or if nearly all of the small bowel is missing. In the current presentation, we aimed to review the available knowledge in order to delineate steps of management for autologous gastrointestinal reconstruction in general and lengthening procedures in children with SBS.

Keywords

short bowel syndrome; surgery; lengthening procedures; STEP; LILT

Helmut Weiss

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Advanced Single Port Surgery in Hepatology

Abstract

Background: Laparoscopic hepatectomy has proven beneficial. The single port approach is technically challenging, but offers possible further benefits for the patient. In this presentation procedural strategies in single port minor (SPMIN) versus single port major (SPMAJ) hepatectomies are demonstrated.

Methods: A matched-pairs analysis of 50 SPMAJ and SPMIN was performed. Age, weight, BMI, and liver cirrhosis served as matching parameters. Differences in procedural steps were documented. Intraoperative parameters served as the primary endpoint. Secondary endpoints were complications and pathohistological outcome.

Results: All resections could be completed without converting to open surgery. The incision was changed from the umbilicus towards a right subcostal site only in 11 patients with SPMAJ. Time for hepatectomywas 112min and 161min for SPMIN and SPMAJ, respectively, p=0.016. Hemostasis was achieved in all SPMIN by use of pre-coagulation but failed in 28% of SPMAJ (p=0.010). Blood loss >50ml (in mean 202ml) occurred only with SPMAJ (p=0.022). One intestinal laceration (SPMAJ) accounted for the only intraoperative complication; 90-day mortality was zero. Postoperative complications occurred in 20.6% and 4% of patients for SPMAJ and SPMIN, respectively. During a median oncologic follow-up at 61 and 63 months (SPMAJ and SPMIN, respectively) no local tumor recurrence was observed.

Conclusions: SPMAJ requires advanced surgical strategies when compared to SPMIN. However,in selected patients the low complication rate and the favorable oncologic outcome justify the performance of SPMIN and SPMAJ in expert centers.

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Transplant Oncology: Treating Cancer by Liver Transplantation in HCC and Beyond

Abstract

Transplant oncology is an emerging concept of cancer treatment with a promising prospective outcome. The application of oncology, transplant medicine, and surgery to improve patients' survival and quality of life is the core of transplant oncology. Hepatobiliary malignancies have been treated by liver transplantation (LT) with significantly improved outcomes. In addition, as the liver is the most common site of metastasis for colorectal cancer (CRC), patients with CRC who have stable unresectable liver metastases are good candidates for LT, and initial studies have shown improved survival compared to palliative systemic therapy. The indications of LT for hepatobiliary malignancies have been slowly expanded over the years in a stepwise manner, however, they have only been shown to improve patient survival in the setting of limited systemic therapy options. This review illustrates the concept and history of transplant oncology as an evolving field for the management of hepatocellular carcinoma, intrahepatic biliary cancer and liver-only metastasis of non-hepatobiliary carcinoma. The utility of immunotherapy in the transplant setting will be discussed as well as the feasibility of using circulating tumor DNA for surveillance post-transplantation.

Keywords

Transplant Oncology; Liver Transplantation; Cholangiocarcinoma; Neuroendocrine Tumor; Liver Metastases; Hepatocellular Carcinoma; Circulating tumor DNA; Colorectal cancers; Immunotherapy.

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Different Important Aspects of Liver Cirrhosis

Abstract

Background: Liver cirrhosis (LC) is a common disease with varied primary causes, different complications resulting in high morbidity and mortality.

Objective: our purpose was to investigate different and important aspects of liver cirrhosis including clinical characteristics, complications and mortality of elderly patients, different ethnic groups and focusing on spontaneous bacterial peritonitis (SBP) as a complication.

Methods: A retrospective study enrolled all patients diagnosed with liver cirrhosis in Soroka University Medical Center (SUMC), a Tertiary Medical Center. Patient records were reviewed for demographics, clinical data, complications and mortality. Bedouin patients were compared with Jew's patients, elderly patients were compared with younger patients and clinical, microbiological and risk factors of patients with SBP were reviewed.

Results: We included 1,046 patients, 39% of the patients were older than age of 65 years, fatty liver and cryptogenic liver were more common than among younger cirrhotic patients, higher rate of non-HCC cancer and mortality of elderly patients. 95 (9%) patients of our cohort were of Bedouin origin, fatty liver, cryptogenic and hepatitis B were more common among Bedouin patients, while hepatitis C and alcoholic liver disease were more common among patients of Jewish origin. 173 patients developed SBP, and scetic fluid culture growth was found only 47.4% of them. E.coli is the most common bacteria grew in the scetic fluid. In the Cox regression model, the SBP, male gender, prolonged INR at diagnosis and HCC were found to be risk factors for mortality of cirrhotic patients. The long-term all-cause mortality of our cohort was 60% and 90% in the SBP patients.

Conclusion: aspects such as ethnicity, age and SBP have different clinical characteristics of liver cirrhosis such as different clinical characteristics and influence the complications rate and mortality.

Keywords

Liver cirrhosis, elderly, complications, mortality, SBP, Bedouin.

Biography

Senior physician at the Institute for Gastroenterology and Hepatology, Soroka University Medical Center.

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Multivisceral Resection for Gastric Cancer

Abstract

Introduction

Multivisceral resections (MVR) in gastric cancer are potentially curable in selected patients in whom clear resection margins are possible. However, there is still insufficient data on their feasibility and safetyabout short- and long-term outcomes.

Aim

The study's main objective is to compare the survival, complications, clinical, pathoanatomical, and surgical characteristics of MVR in standard gastric resections (SGR).

Material and Methods

A monocentric retrospective study in patients with histologically verified adenocarcinoma of the stomach, covering the period from 2004 to 2020. Of the 336 operable cases, 101 patients underwent MVR. The remaining 235 underwent SGR, of which 173 patients were in stage T3/T4. To compare survival, a representative control group of 101 patients with palliative procedures (PP) was used – bypass anastomosis or exploration. Mantel-Cox, Breslow, Tarone-Ware analyses, confidence interval (95% CI), $\chi 2$-test, standard deviation (SD), and t-statistics were used to compare the data. The statistical information processing was performed using IBM® SPSS Statistics ™ Ver.26, and a p-value less than 0.05 is considered significant.

Results

We found that the MVR had a lower survival rate than the SGR but significantly higher than the PP ($p < 0.05$). The predominant gender in multivisceral resections was male (n = 73, 72.3%), with a mean age of 61 years. The perioperative 30-day mortality was 3.96% (n = 4), and the overall median survival was 28.1 months. The average postoperative stay is 13 days. The most frequently resected organs in theMVR were the spleen (n = 68, 67.3%), the pancreas (n = 33, 32.7%), the liver (n = 21, 20.8%) and the colon (n = 21, 20.8%). In 56.4% (n = 57) of the cases 2 organs were resected (stomach + 1), in 28.7% (n = 29) – 3 organs, in 13.9% (n = 14) – 4 organs, and in one case (0.99%) 5 organs were resected.No statistical significance was found for survival and complications relative to the number and type of resectedorgans ($p > 0.05$). The main complications of the MVR were bleeding (n = 10, 9.9%), intra-abdominal abscess (n = 8, 7.9%), anastomotic insufficiency (n = 6, 5.9%) and pancreatic fistula (n = 6, 5.9%). Compared to the classification of Clavien-Dindo, the significant postoperative complications (III + IV) in the MVR were 14.85% (n = 15) and in the SGR 6.4% (n = 11), and there was a significant difference ($p < 0.05$).In the analysis of survival against the involved lymph nodes (N- vs. N+), no significance was found ($p > 0.05$). When analyzing the M-status at the MVR (M0 vs. M1), no statistically significant difference was found in terms of survival ($p > 0.05$). Better long-term results were observed in patients who underwent R0-resection than those with R1 ($p < 0.05$). In the cases where reoperation was performed, lower survival was found compared to those whose hospital stay passed without revision ($p < 0.05$).

Conclusion

Multi-organ resections are characterized by poorer survival and a higher complication rate than standard gastric surgeries. On the other hand, they have better long-term results than palliative procedures. A significant and independent factor for better survival is the achievement of clear resection margins. Multivisceral resections are achievable when an experienced surgical team performs in high-volumecenters. However, no general conclusion can be drawn about their feasibility and safety at this stage.

Keywords

gastric adenocarcinoma; multivisceral resection.

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Fengzhi Li
Roswell Park Cancer Institute, USA

Validation of Targets as Biomarkers for Targeted Pancreatic Cancer Therapy

Abstract

The major problem in cancer chemotherapy is the cancer resistance to treatment. This is because cancer resistance to anticancer drug treatment is through multiple mechanisms of resistance. This includes, but may not be limited to, tumor high-heterogeneity with multiple genetic and epigenetic alterations (e.g., overexpression of anticancer cell death proteins, DNA repair regulators and efflux pump proteins; mutations of key oncogenes and/or tumor suppressor genes). Importantly, tumor cells that have these genetic alterations possess survival advantages and will be selected for survival during treatment of cancer patients. Therefore, overcoming treatment resistance is an unmet need for virtually all cancers. Our solution to resolve this key problem is to use one drug to overcome multiple treatment resistances to avoid unacceptable high toxicity resulted from such as multiple drug combination (e.g. FOLFIRINOX), while maintaining high efficacy. Our leading anticancer drug FL118 possesses such characteristics. In this keynote presentation, I will present how FL118 works to have such potential ability to resolve cancer multiple resistances.

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Francesco Scaglione
The University of Milan, Italy

Drug Interactions in Hepatitis C Virus Treatment: Do They Really Affect Treatment?

Abstract

The development of direct-acting antiviral (DAA) agents has revolutionized the treatment of hepatitis C infection

Chronic hepatitis C virus (HCV) infection has recently become a curable disease with antiviral therapy. The development of direct-acting antiviral (DAA) agents has revolutionized the treatment of hepatitis C infection.Ageing in the chronic hepatitis C population, along with added co-morbidities that require other medications, has increased the attention on drug interactions using DAA. Interactions between DAA and other drugs are frequent in clinical practice. However, the knowledge of drug interactions using DAA may permit maximizing antiviral efficacy and avoiding drug-related toxicities. The most frequent drug interactions modify drug metabolism by inducing or inhibiting the cytochrome P450, leading to abnormal drug exposures. HCV protease inhibitors, especially when co-formulated with ritonavir as pharmacoenhancer, and non-nucleoside HCV polymerase inhibitors interact with other medications. In contrast, NS5B nucleos (t) ide analog inhibitors (i.e., sofosbuvir) and some HCV NS5A inhibitors (i.e., ledipasvir), which do not or only marginally bind CYP450, are relatively free of significant pharmacokinetic interactions. However, exposure to HCV drugs may be influenced by induction/inhibition of drug transporters (i.e., P-glycoprotein) as well as by pharmacodynamic interference with other drugs used as antiviral or anticancer. In conclusion, with the broad range of choices for DAA-based therapy, drug interactions can be managed with dose adjustments or replacement with a non interactive drug. On the other hand the number of patients taking medicationswhere adjustments cannot be made to provide safe andeffective therapy for hepatitis C is few.

Ahmed Metwali

The University of Iowa, USA

Lymphocyte Recirculation in Inflammatory Bowel Disease

Abstract

We developed a mouse model of lung inflammation secondary to colitis to study mechanisms of the accelerated lung inflammation in response to challenge with bacterial endotoxin. Colitic mice developed accelerated lung inflammation compared to non-colitic mice with the same treatment. The cytokine pattern of the lung lymphocytes replicated that from the intestinal lamina propria lymphocytes (LPL). Pulmonary CD4+ lymphocytes from colitic mice displayed a proinflammatory cytokine profile as more IFN-γ+ and fewer IL-10+ cells were found. Lower expression of CTLA4 and FoxP3 regulatory markers and higher ICAM1 proinflammatory marker existed in colitic compared to lung lymphocytes from non-colitic mice with the same treatment. This is the first report demonstrating suppressed expression of α4β7 on non-regulatory LPL from colitic mice. This deranged expression highlighted the possibility of homing of these cells to other organs. The presence of gut-antigens binding, TLR4+, CD11c+ cells in the lungs of colitic mice favored the accelerated inflammatory response to bacterial endotoxin and raises the possibility of gut antigens carry-over with migratory dendritic cells from the intestine to the lungs. Taken together, these findings support our hypothesis that chronic intestinal inflammation exacerbates asthma.

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Biomarkers of stress and their relationship with physico-chemical characteristics of meat

Abstract

Oxidative stress is a large rise in the cellular reduction potential of the animal. The cells become damaged and their duty to perform is disturbed. It can influence the metabolism of cells in vital organs of the body such as heart, nerve tissues, lungs, muscles and brain. A variety of stress indicators that exhibit particularly the risk of contraction and the presence of disease are used. Potential markers of stress include thermal stress markers, such as heat shock proteins (HSPs), innate immune markers, such as Acute Phase Proteins (APPs), oxidative stress markers, and chemical secretions in the saliva and urine. In addition, stress biomarkers also play critical roles in the prognosis of stress-related diseases and disorders, and therapy guidance. Stress biomarkers can hypothetically react differently to pre-slaughter stress depending on the breed, farm management system, and the conditions that animals are kept in during transportation, and they may be useful to identify DFD meat at the pre-slaughter. This research therefore, focused on endocrine, metabolic changes and beef quality of slaughter exposed to pre-slaughter stress at the abattoir. Blood samples were collected during exsanguinations from the jugular vein of cattle at slaughter for the determination of plasma heat shock proteins, glucose and cortisol. Representative samples from the Muscularis thoracis et lumborum (LTL) were collected 48 hours after slaughter to measure meat quality. A negative correlation was observed between heat shock proteins 70 kDa (HSPA1A) and other parameters with the exception of conformation, lightness (L*), glucose (GLU) and cortisol (CORT). Warner Braztler Shear Force (WBSF) was negatively corrected with conformation, L*, redness (a*), yellowness (b*) HUE (HUE angle), HSPA1A, GLU and CORT positively correlated with fatness, ultimate pH (pHu) and meat temperature (Tm). There was a positive correlation observed between HUE, fatness, pHu, Tm, a*, b* and CORT. The first ten principal components (PC`s) which were pHu, L*, a*, b*, Tm, WBSF, fatness, conformation and Hsp contributed about 95 % of the total variance while the first and second PC`s contributed about 26 and 16.8 %, respectively there were significant effects of distance duration (P < 0.001), lairage duration (P < 0.001), stunnnig (P < 0.01) and animal class (P < 0.05) on the expression of plasma HSPA1A and levels of plasma GLU and CORT. Animals that travelled for < 400 had lower HSPA1A (0.05 ± 6.297) as compared to those that were transported for < 800 km (0.11 ± 3.778) and < 200 (0.13 ± 4.723). Animals that travelled for < 200km had higher (6.10 ± 6.297) and lower cortisol concentration (88.87 ± 6.297) while those that travelled for < 800 km had higher lower levels of glucose (5.50 ± 3.778) and increased concentration of cortisol (103.56 ± 3.778). Therefore, the initial and final transport duration, few hours of lairage duration and bulls had a negative impact on heat shock proteins, glucose and cortisol and on ultimate pH, which is widely used indicator of meat quality. Keywords: Breed, distance travelled, lairage duration, proteins, saturation index, stress biomarkers, stunning, ultimate pH.