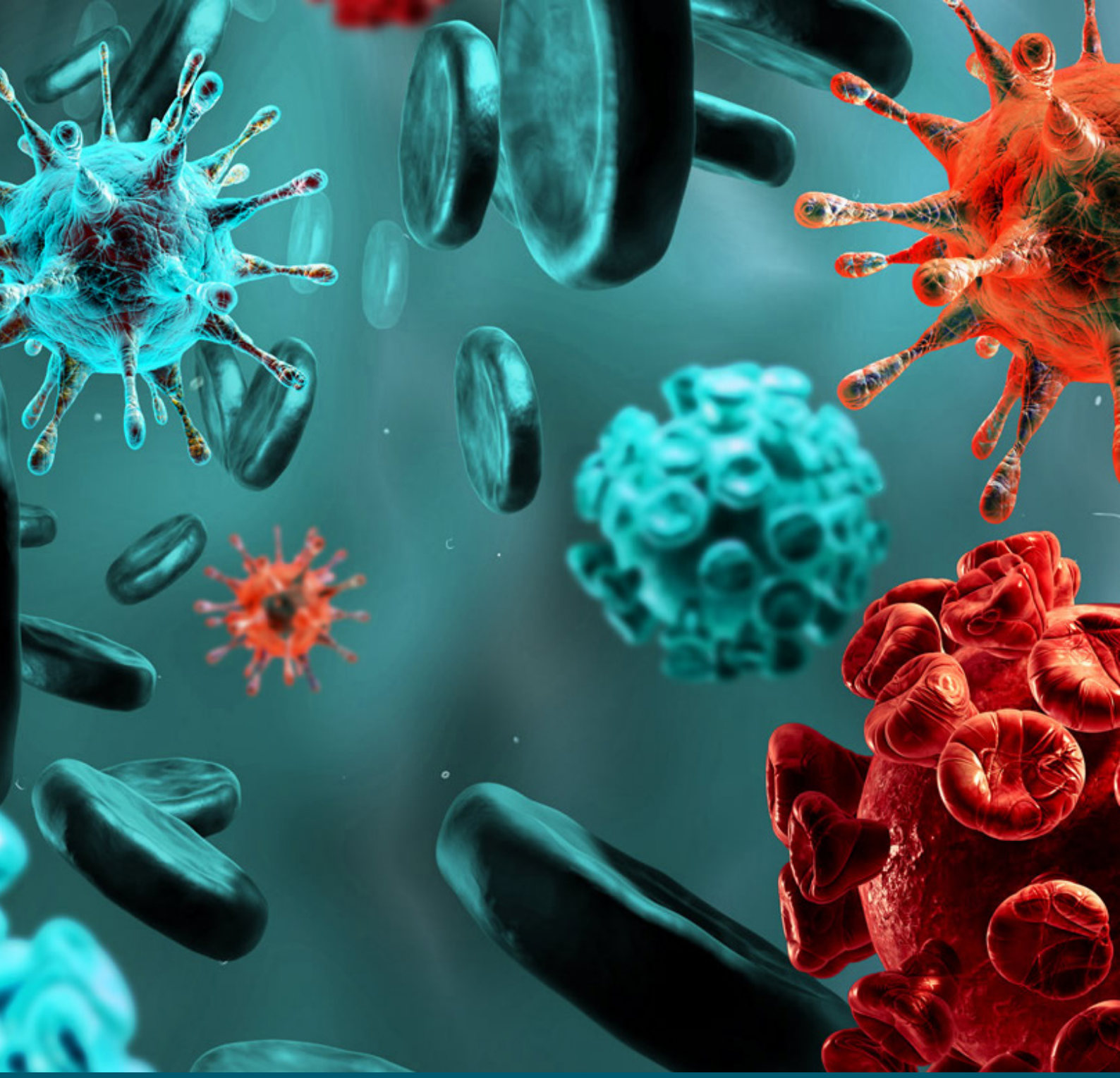

Abstract Book

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Plenary Abstract

Susu M. Zughaier

gonorrhea, Neisseria gonorrhoeae, vaccine, microneedles, microparticles, serum bactericidal assay, protective immunity

Gonococcal microparticle vaccine in dissolving microneedles induced immunity and enhanced bacterial clearance in infected mice

Abstract

There is an alarming rise in the number of gonorrhea cases worldwide. Neisseria gonorrhoeae, the bacteria that causes gonorrhea infection, has gradually developed antimicrobial resistance over the years. To date, there is no licensed vaccine for gonorrhea. This study investigates the in vivo immunogenicity of a whole-cell inactivated gonococci in a microparticle formulation (Gc-MP) along with adjuvant microparticles (Alhydrogel®-Alum MP and AddaVax™ MP) delivered transdermally using dissolving microneedles (MN). The proposed vaccine formulation (Gc-MP+ Alum MP+ AddaVax™ MP) was assessed for induction of humoral, cellular, and protective immune responses in vivo. Our results show the induction of significant gonococcal-specific serum IgG, IgG1, IgG2a, and vaginal mucosal IgA antibodies in mice immunized with Gc-MP+ Alum MP+ AddaVax™ MP and Gc-MP when compared to the control groups receiving blank MN or no treatment. The serum bactericidal assay revealed that the antibodies generated in mice after immunization with Gc-MP+ Alum MP+ AddaVax™ MP were bactericidal towards live Neisseria gonorrhoeae. Gc-MP+ Alum MP+ AddaVax™ MP and Gc-MP-immunized mice showed enhanced clearance rate of gonococcal bacterial infection post challenge. In contrast, the control groups did not begin to clear the infection until day 10. In addition, the mice which received Gc-MP+ Alum MP+ AddaVax™ MP showed enhanced expression of cellular immunity markers CD4 and CD8 on the surface of T cells in the spleen and lymph nodes. Taken together, the data shows that microneedle immunization with whole-cell inactivated gonococci MP in mice induced humoral, cellular, and protective immunity against gonococcal infection.

Biography

Dr. Susu Zughaier is an Associate Professor of Microbiology and Immunology and chair of Infectious Diseases research Network at Qatar University College of Medicine. Trained as a clinical microbiologist at University College London; MSc and PhD in Microbiology and Immunology from Cardiff University, UK. Postdoctoral training at Harvard Medical School in Boston, USA and was Assistant Professorof Microbiology and Immunology, Emory University School of Medicine in Atlanta, USA. Herresearch interests are focused on host-pathogen interactions, vaccine development and nanotechnology for rapid detection of bacterial infections. Her translational research is focused on vitamin D immune modulatory effects and she implements artificial intelligence in medical applications in her research. Dr Zughaier published more than 80 scientific research papers and awarded two patents on her discoveries. She has been listed among the top 2% of highly cited authors with impact in their field in 2020 Stanford study. She is an active member of various international societies and serves as Associate Editor, Editorial board member and ad-hoc reviewer for multiple international journals.

Keynote Abstract

Xue-Zhong Yu

Departments of Microbiology & Immunology and Medicine, the Cancer Center, Medical College of Wisconsin, USA

Sphingolipid Metabolism Regulates T-cell Responses in Cellular Immunotherapy

Abstract

Allogeneic hematopoietic cell transplantation (allo-HCT) is an effective immunotherapy for various hematologic malignances, predominantly through potent graft-versus-leukemia (GVL) effect. However, the mortality after allo-HCT is because of relapse of primary malignancy and followed by graft-vs-host-disease (GVHD) as a major cause of transplant-related mortality. Hence, strategies to limit GVHD while preserving the GVL effect are highly desirable. Ceramide and sphingosine-1-phosphate (S1P) are two bioactive sphingolipids, which are involved in the biogenetic processes of different immune cells. In the current work, we studied the impacts of CerS6/C16-ceramide and S1P/S1PR pathways in T-cell activation, differentiation and migration using pre-clinical murine models of allo-HCT. With genetic or pharmacologic approaches, we found that both CerS6/C16-ceramide and S1P/S1PR1 pathways are required for optimal T-cell activation, effector T-cell differentiation, and migration to GVHD target organs. Blocking either pathway significantly reduces GVHD development. However, either pathway alone is dispensable for T-cell-mediated GVL effect. Interestingly, CD4 T cells are much more dependent on C16-ceramide or S1PR1 signaling than CD8 T cells. In clinical study, we observed that only C16-Ceramide, dhSph-1P and Sph-1P among all the sphingolipids display a positive correlation with gut, liver and overall but not skin GVHD development. These results suggest that C16-ceramide and S1P metabolism may contribute to GVHD pathogenesis in human. In summary, the current study provides rationale and means for targeting CerS6 or S1PR to control GVHD and leukemia relapse, which would enhance the efficacy of allo-HCT as an immunotherapy for hematologic malignancies in the clinic.

Biography

Dr. Xue-Zhong Yu is a professor in the departments of Microbiology & Immunology and Medicine, and an endowed research scholar and an associate director in the Cancer Center at Medical College of Wisconsin. Dr. Yu received his MD and MS degrees in China and did his post-doctoral fellowship at Fred Hutchinson Cancer Research Center. His research focuses on elucidating mechanisms of T-cell immunity and tolerance in allogeneic and anti-tumor responses. His Lab has two interconnected lines of basic and translational research: 1) Allogeneic HeDr. Xue-Zhong Yu is a professor in the departments of Microbiology & Immunology and Medicine, and an endowed research scholar and an associate director in the Cancer Center at Medical College of Wisconsin. Dr. Yu received his MD and MS degrees in China and did his post-doctoral fellowship at Fred Hutchinson Cancer Research Center. His research focuses on elucidating mechanisms of T-cell immunity and tolerance in allogeneic and anti-tumor responses. His Lab has two interconnected lines of basic and translational research: 1) Allogeneic Hematopoietic Cell Transplantation (allo-HCT) for treatment of hematologic malignancy; 2) Adoptive T-cell Therapy (ACT) for treatment of solid tumor.Dr. Xue-Zhong Yu is a professor

in the departments of Microbiology & Immunology and Medicine, and an endowed research scholar and an associate director in the Cancer Center at Medical College of Wisconsin. Dr. Yu received his MD and MS degrees in China and did his post-doctoral fellowship at Fred Hutchinson Cancer Research Center. His research focuses on elucidating mechanisms of T-cell immunity and tolerance in allogeneic and anti-tumor responses. His Lab has two interconnected lines of basic and translational research: 1) Allogeneic Hematopoietic Cell Transplantation (allo-HCT) for treatment of hematologic malignancy; 2) Adoptive T-cell Therapy (ACT) for treatment of solid tumor.matopoietic Cell Transplantation (allo-HCT) for treatment of hematologic malignancy; 2) Adoptive T-cell Therapy (ACT) for treatment of solid tumor.

Invited Abstracts

Ajay Kumar

King Fahad Super speciality Hospital, Saudi Arabia

Diagnostic Stewardship in Tuberculosis

Abstract

Tropical diseases increase healthcare burden globally. Tuberculosis is one of the diseasescausing increase morbidity and mortalitybecause of various patient and pathogen factors. The patient's chief demographic factors areilliteracy, non-agricultural civilized populationin downtown societies, poverty, and poor patient follow-ups. The genomic mutation of Mycobacterium tuberculosis, delay in diagnostic methods and expensive, less sensitive 2nd line drugs are chief pathogen factorscauses of defaulters. The non-classical clinical presentationof the Mycobacteriumand shortage of radiological interpretation worsen the outcome of elimination strategies.

Most of the time extra pulmonary, latent, and multidrug resistant tuberculosis are failure todiagnose because wrong specimen collection and faulty specimen process protocols. Itleads to clinical dilemma. The specific public health diagnostic methods need to follow and promote awareness among the clinicians. The correct diagnosis of Mycobacterium tuberculosis in various pulmonary/extra-pulmonary disease with the drug susceptibility detection is the prime way to make Tuberculosis free world by 2050 in the most vulnerable population. The evidence-baseddiagnosis and direct observation-based drug treatment are the backbone of TB elimination. This should be implemented at the primary care level of80% world 20 countries of tuberculosis disease.

Biography

Dr. Ajay Kumar, M.D., Clinical Microbiology, M.Sc. Infectious Diseases is working as a specialist, Clinical Microbiologist at the Kingdom of Saudi Arabia for the last 8 years. I have about nine years of ICU clinical experience as a resident and senior resident at Indraprastha Apollo Hospitals New Delhi, a JCI-accredited hospital, and eleven years as a Clinical Microbiologist in various hospitals in India and Saudi Arabia. I have completed my M.Sc., I.D. (University of London) 2017-22 batch.

Anis Rageh Al-Maleki

Department of Medical Microbiology, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia

Metabolic Reprogramming, Polymorphism of Virulence Genes and Biofilm Associated with in vitro Induced Resistance to Clarithromycin in Helicobacter pylori

Helicobacter pylori (H.pylori) is a gram-negative bacterium that thrives in stomach mucus and epithelial mucosa, causing gastric ulcers which may develop into gastric cancer. One of the most prevalent causes of treatment failure is the emergence of antibiotic-resistant of H. pylori infection. The goal of this work is to employ whole-genome sequencing (WGS) technology and metabolomics approach via liquid chromatography mass spectrometry (LCMS) to identify genomic alterations related with the development of antibiotic resistance in H. Pyloriand explore the metabolites associated with the development of Clarithromycin-resistance in H. pylori.

The clarithromycin-sensitive H. pylori strains were induced to become resistant against clarithromycin. To induce resistance, the strains were exposed to gradual increased concentration of clarithromycin in vitro for 3days on a chocolate agar (CA). The identity between resistant strains and their corresponding parental sensitive strains before induction were verified by random amplification of polymorphic DNA polymerase chain reaction (RAPD-PCR). WGS for bacterial DNA was performed, using Illumina platform. Bacterial metabolites were isolated using the Bligh and Dyer technique and analysed using liquid chromatography-mass spectrometry (LCMS). Sensitive (S), breakpoint (B), and induced resistant(R) are three separate categories.

Among the B and R strains, mutations in cag1, cag4, fliR, obgE, tlpA, and vacA were detected, which are known virulence genes that may help in bacterial survival, indicating that those mutations may be associated with the emergence of resistant H. pylori. Moreover, point mutations A2143G in 23S rRNA were discovered in S, B and R strains. Furthermore, using one-way ANOVA, a total of 982 molecular features were identified to be significantly different (p-value < 0.005) between S, B, and R strains. Additionally, 292 molecular features matched the metabolites in the Agilent METLIN database based on accurate mass, isotope ratios, abundances and spacing. In contrast to sensitive strains, induced-resistant strains generated more metabolites (585 features). Further investigation was carried out in order to find metabolites that varied substantially (p-value <0.05) between S, B, and Rstrains. Our data imply that D-Mannitol, L-Leucine,Sphinganine, Dulcitol, Indoleacrylic acid and Pyridoxine, which correlate with bacterial survival, may constitute a potential antibiotic mechanism.

Therefore, we hypothesise that in these strains, alternative mechanisms unrelated to the 23S rRNA gene sequence may play a role in the development of Clarithromycin resistance. Understanding the underlying metabolic variations between Clarithromycin-sensitive H. pylori strains and Clarithromycin-resistance H. pylori strains may be a promising technique for developing novel antibiotic candidates.

Acknowledgement: The work is supported financially by the Ministry of Higher Education Malaysia (MOHE) via Fundamental Research Grant Scheme (FRGS/1/2020/SKK0/UM/02/20), Project No. (FP105-2020).

Biography:

Dr. Anis Rageh Al Maleki is a senior lecturer in the Department of Medical Microbiology, Faculty of Medicine at the University of Malaya (UM), Malaysia. He received his Ph.D. in Medical Microbiology from UM, and a postdoctoral fellowship at the Faculty of Medicine and Faculty of Dentistry, University of Malaya, Malaysia. His research focuses on the genomics, transcriptomics, proteomics, metabolomics next generation sequencing of Helicobacter pylori, Burkholderia spp, Candida spp, and oral microbiota. He has published several research articles and served as an Editorial member in the Asian Council of Science Editors.

Belma Nural

Eskisehir Osmangazi University, Turkey

Molecular Microbial Techniques in Extremophiles: Insight of Acidophiles

Microorganisms are one of vital elements belong to countries. It is possible to classify the microorganisms based on the properties especially according to showing behavior at extreme conditions. Extremophiles are survived in habitats where no humans are available. The habitats differentiate from temperature, pH, salinity, pressure. Thermophiles, acidophiles, halophiles and barophiles are the most studied microorganisms.

The culture dependent and culture independent techniques are used for the diversity studies of these microorganisms. Culture dependent techniques consist of classical microbiological methods include isolation procedures, the identification of isolates and their culturing processes. On the other hand, culture independent techniques interest only genetic material of microorganisms. Therefore, in these techniques can be given us knowledge about environmental diversity. The culture independent techniques are grouped on using of PCR techniques of total environmental DNAs. The key gene for these studies is 16S rRNA coding gene which is evolving chronometer molecules for prokaryotic microorganisms. DGGE, TGGE, 16S clone library construction, Real Time Expression, metagenomics, FISH, ARDRA are the most used techniques. The protocols are available on the literatures and can be integrated to diversity studies.

In this presentation, the techniques and their literature examples were discussed and shared. Microorganisms with different properties were identified and some of isolated. Their biotechnological potentials were presented. Variety extreme conditions were evaluated on these studies.

Biography:

Dr.Belma NURAL YAMAN graduated from Bioengineering at Yıldız Technical University in 2012 and completed a Ph.D. at Eskisehir Osmangazi University in 2019 She has been working for 8 years as a research assistant at Eskisehir Osmangazi University. Her research area includes molecular microbiology, metagenomics approach, recombinant enzyme production, extremophile microorganisms, their metabolites, and biotechnological application. She has 15 papers in an international and national refereed journal, 5 book chapters in an international publisher, and 18 presentations at national and international congresses. She has worked as a researcher, manager, and supervisor on 15 projects.

Binhua (Julie) Ling

Texas Biomedical Research Institute

HIV/SIV reservoirs and viral rebound

Abstract

Current combination antiretroviral therapy (ART) greatly improves quality and life expectancy of HIV-1 infected people. However, there is still no cure for HIV infection. HIV persists in tissues even viral replication is undetectable in peripheral blood by the standard clinical assay when individuals are on suppressive ART. The central nervous system, the gut, and other lymphoid tissues are major anatomical reservoirs. To determine the source of viral rebound upon antiretroviral interruption is critical for development of novel strategies to cure of HIV-1 infection. Our recent studies suggest that lymphoid tissues contribute to early viral rebound after analytical antiretroviral interruption.

Biography:

Dr. Ling is a Professor at the Texas Biomedical Research Institute in San Antonio, Texas. She received her Ph.D. degree from Peking University Health Science Center in Beijing, China. Dr. Ling's laboratory is interested in using nonhuman primate models to study the persistence of HIV in tissues and organs to develop novel drug delivery and therapeutic strategies for HIV reduction or eradication. Her team also aims to understand what controls or spreads the virus in a host with or without therapeutic intervention. Additional interests include the relationships between HIV/SIV and aging, and HIV/SIV and the microbiome. Ling's current research is supported by NIH. She has a broad background in molecular virology, immunology, and many years of experience and expertise in nonhuman primate models in HIV/SIV pathogenesis and cure studies.

Dr Darren Chen Pei WONG1,2,† and Professor Jeak Ling Ding
Co-senior authors

Department of Biological Sciences, National University of Singapore, Singapore 117543 Mechano biology

Institute Singapore, National University of Singapore, Singapore 117411

Integrative Sciences and Engineering Programme, National University of Singapore, Singapore 119077

Elucidating the multifaceted roles of intracellular contractility for NK anti-cancer cytotoxicity

Abstract

Mechano transduction allows cells to sense and transduce mechanical forces into functional biochemical signals. Immune cells in homeostasis and pathophysiology constantly experience mechanical forces. Understanding how mechanical forces affect natural killer (NK) cell transcriptional programming and cytotoxicity adds insights into a subtle level of immune regulation for cancer immunotherapy. In this talk, I will share recent findings on how NK cells harness intracellular contractility when induced by cancer cells and how NK cellpattern recognition receptors enhance its innate killer function.

Biography:

Dr Wong, Darren is a senior research fellow with the Department of Biological Sciences, National University of Singapore. He received his B.Sc (Hons) from the National University of Singapore and was awarded his PhD in mechanobiology by the Mechanobiology Institute Singapore, NUS. His research focuses on the mechanobiology of innate immune natural killer cells, cardiac ageing and the translational potential of harnessing cellular contractility in treating cancer. He is the recipient of numerous awards, including the prestigious NUS-National Research Foundation Singapore (NRF) industrial sponsorship.

Elnaz Elahirad

Department of Pathology, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

Mycology Research Center, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

TLRs expression in canine mammary gland neoplasm's: a pathological and molecular study

Abstract

TLRs are a class of PRRs that play a vital role in innate immunity. TLRs are expressed on immune cells and mammary epithelial cells. They can promote tumor growth, angiogenesis, invasion, and viability signaling. The current study aimed to test the correlation between histological types and grades of neoplasm's and TLRs gene expression levels. Twenty-one tissue samples of canine mammary neoplasms were stained with H&E. Then, it evaluated histologic type and grade according to the methods of Goldschmidt et al. and Pena, respectively. We established real-time PCR quantification assays to measure the mRNA abundances of TLRs in normal and neoplastic mammary glands. Profile pattern of TLR 1, 2, 3, 4, 5, 6, and 9 genes expression in canine mammary glands performed in 21 samples of mammary gland neoplasms and three non-neoplastic mammary gland samples from normal dogs.TLR 3, 4, and 9 mRNA overexpression were detected. In addition,ubulopapillary carcinoma grade II, SCC grade III, and carcinoma mixed type grade II demonstrated the highest relative TLR-3, and 9 mRNA expression levels. Complex carcinoma grade I, ductal carcinoma grade II, and anaplastic carcinoma grade II showed the highest relative TLR4 mRNA expression level. Although histopathological characteristics of tumors, including histologic type, grade, and inflammation, influenced TLRs mRNA expression level, such correlation was insignificant (P>0.05).

Biography:

Elnaz Elahirad, Veterinary pathology She started studying for his DVM degree at the University of Tehran, faculty of veterinary medicine, in September 2007 and received the degree upon working on "Histopathological classification and immunohistochemical evaluation of MMP-9 in canine mammary gland neoplasms". The abstract of the study was accepted by the 2nd Joint European Congress of the ESVP, ESTP, and ECVP, Cutting edge Pathology August 27â€"30, 2014, Berlin, Germany. In September 2013, he started postgraduate education as a resident of veterinary pathology in the Department of Pathology, faculty of veterinary medicine, University of Tehran, Tehran, Iran. On February 19, 2020, he graduated as a top student upon working on the subject "Histopathological, histochemical evaluation and gene expression level assessment of TLR3, 4, and 9 in canine mammary gland neoplasms".

Hassan Elsayed

National Research Centre, Egypt

Harnessing Peptide and Nanoparticle Technology for developing innovative vaccination strategy against COVID-19.

Abstract

Despite the presence of highly efficient mRNA vaccines and other vaccines against SARS-COV-2 with proved safety, a B- and T-cell multi-epitope prophylactic vaccine that can generate effective humoral and cellular immunity against the disease is needed. Herein, we used an immunoinformatics approach to develop a multi-epitope subunit vaccine incorporating CD4+T-cells and CD8+T-cell epitopes of COVID-19 spike proteins. The selected epitopes were synthesized and coupled to nanoparticle vehicles. Experimental animals including rats and mice were immunized with different peptides to explore the immunogenicity and safety of our innovative vaccine applying biochemical and histopathological examination of immunized compared to non- immunized animals. Examined tissues including lungs, brains, hearts, kidneys, livers, spleens, tests and bone marrows investigated at 2 weeks and 2 months after vaccination, revealed no histo-pathological changes in the different tested organs. Interestingly, immunized animals exhibited strong immune responses against various vaccine antigens. Also, the vaccine epitopes used in our animal experiments were able to recognize protective/specific immunoglobulins in COVID-19 patients. In addition, no reactivity towards the tested peptides was identified in our healthy volunteers. Overall, the results indicate that the selected epitopes were able to recognize antibody responses related to natural SARS-CoV-2 infection in studied patient. This study describes a potential innovative multi-epitope and peptide-based vaccine that induces immune responses with no histopathological changes in experimental animals.

Keywords:

COVID-19 vaccine- Immune responses-Immuno-informatics- Nanoparticles- Histopathological changes.

Acknowledgment: This project was funded by Academy of Scientific Research and Technology (ASRT) Ideation Fund 7380.

Biography:

Elnaz Elahirad, Veterinary pathology She started studying for his DVM degree at the University of Tehran, faculty of veterinary medicine, in September 2007 and received the degree upon working on “Histopathological classification and immunohistochemical evaluation of MMP-9 in canine mammary gland neoplasms”. The abstract of the study was accepted by the 2nd Joint European Congress of the ESVP, ESTP, and ECVP, Cutting edge Pathology August 27â€“30, 2014, Berlin, Germany. In September 2013, he started postgraduate education as a resident of veterinary pathology in the Department of Pathology, faculty of veterinary medicine, University of Tehran, Tehran, Iran. On February 19, 2020, he graduated as a top student upon working on the subject “Histopathological, histochemical evaluation and gene expression level assessment of TLR3, 4, and 9 in canine mammary gland neoplasms”..

Guojun Wu

Karmanos Cancer Institute, Department of Oncology

Wayne State University School of Medicine

The EMT Program and Tumor Immune Microenvironment

Abstract

The epithelial-to-mesenchymal transition (EMT) is critical for developing many tissues and organs in the developing embryo by involving numerous embryonic events. Accumulated experimental evidence has suggested that EMT is pathologically activated in cancer cells, leading to an increased propensity for chemotherapeutic resistance, tumor recurrence, and distal metastatic progression. In recent years, the effect of EMT in regulating immune response and promoting resistance to anti-tumor immunity has been discovered. However, the mechanism remains unclear. To explore the underlying mechanism of EMT in regulating immune response, we first investigated the correlation between EMT transcription factor expression and immune cell abundance in breast cancer. We found that stromal-corrected expression of a master EMT regulator ZEB1 and its regulated gene signatures showed a significant inverse correlation with immune cell abundance in breast tumors. We further identified RBMS3, an RNA binding protein and one of the ZEB1 gene signatures, as a common downstream gene of different EMT programs. RbMS3 promotes EMT in human mammary epithelial cells and TNBC cells, contributing to TNBC cell motility and tumor metastatic progression. The underlying mechanism is that RbMS3 could stabilize many essential target genes, including PRRX1 and many immune-modulating genes, which further change the tumor immune microenvironment. Future directions include the development of a novel approach to target the RBMS3/PRRX1 axis to inhibit EMT and modulate tumor immune microenvironment for TNBC patients.

Biography:

Dr. Guojun Wu received his Ph.D. in Genetics in 1998 from the Fudan University, Shanghai, P. R. China. He completed a postdoctoral fellowship at the Mayo Clinic, Rochester, MN, and Johns Hopkins University School of Medicine, Baltimore, MD. He is now a tenured associate professor in the Department of Oncology. As a cancer biologist, Dr. Wu has an active research portfolio focused primarily on genetic and epigenetic alterations in human breast cancer initiation, progression, and metastasis. He has more than 60 peer-reviewed publications in journals which include Nature Communications, Nature Medicine, JNCI, PNAS, Cancer Research, and Oncogene. His research was supported by NIH/NCI, Susan Komen, and multiple internal grants from Karmanos and University. Dr. Wu is also actively teaching nine courses in the cancer biology program and across the medical school. He has mentored or served as a committee member for multiple medical students and Ph.D. or MD/Ph.D. students in their cancer research projects.

Dr. Kwan T Chow

Assistant Professor, City University of Hong Kong, Hong Kong

Elucidating osteoclast-breast tumor hybrids cell fusion mechanisms for bone metastatic disease progression

Abstract

Tumor hybrid cells in cancer biology have garnered greater attention with the discovery of circulating hybrid cells (CHC). CHCs are identified as the predominant cell type in circulating tumor cells (CTC) and they co-express leukocyte and tumor markers. Current studies indicate that tumor hybrids play an important role in tumor progression as they acquire genetic and phenotypic characteristics from parental cells and reportedly have enhanced motility and invasiveness, increased stem cell characteristics, and elevated resistance to chemo- and radiotherapies. It has been proposed that cellular fusion leads to the formation of these hybrids. Amongst leukocyte fusion partners, macrophages (osteoclast precursors) are identified as a frequent fusion partner with tumors. However, mechanisms and pathways that lead to fusion between macrophages and tumors are highly underexplored. To address this, we investigated macrophage fusion pathways that could be involved in regulating macrophage fusion with breast tumor. Here we report the finding of a novel hybrid cell type that is formed by in-vitro cellular fusion between osteoclast precursors/mature osteoclasts and breast tumor (hereby known as osteoclast hybrid) in the presence of osteoclastogenic cytokines. Fusion was observed at all stages of osteoclast differentiation with individual macrophages fusing with tumor cells, interfusion between osteoclast hybrids, and individual tumor cells fusing into mature osteoclast hybrids. Tumor nuclei in osteoclast hybrids were found to be transcriptionally active, which may infer that osteoclast hybrids are transcriptionally different compared to regular osteoclasts. Future directions will emphasize on understanding the mechanisms that lead to osteoclast hybrid formation and their potential roles in bone metastatic disease progression. These experiments will involve single cell sequencing on osteoclast hybrids and to evidence the formation of osteoclast hybrids in animal models.

Keywords:
breast cancer, osteoclast, cell fusion, circulating hybrid cells, circulating tumor cells, bone metastasis

Biography:

Dr Chow received her PhD from the University of California, Berkeley (USA) studying gene regulation during B lymphocyte development and malignant transformation. With a Croucher Foundation Fellowship and an NIH F32 National Research Service Award, Dr. Chow conducted postdoctoral research at the University of Washington (USA) studying innate immune signaling and gene networks that regulate the anti-viral immune response. She also conducted research in cancer genomics at the Broad Institute and Dana-Farber Cancer Institute of Harvard and MIT (USA). Dr. Chow started her own lab at the City University of Hong Kong in 2018. Currently, the Chow lab focuses on investigating what constitutes a protective immune response against cancer in order to design effective cancer immunotherapy. The lab combines concepts and techniques from biochemistry, molecular and cell biology, cancer biology, immunology, virology, genomics, cell and animal models, and systems biology to dissect the molecular pathways and gene regulatory networks that modulate the anti-cancer immune response. The ultimate goal of the lab is to develop vaccines and targeted therapies that harness the natural ability of our immune system to fight cancer. Dr. Chow received a Croucher Innovation Award in 2019 for her work in developing cancer immunotherapy.

Lanying Du

Institute for Biomedical Sciences, Georgia State University, Atlanta, GA

Effective vaccines with protective efficacy against SARS-CoV-2 variants

Abstract

Effective vaccines are needed to prevent multiple SARS-CoV-2 variant strains. Here, mRNA and subunit vaccines are designed and tested for their broadly neutralizing activity and/or protection against SARS-CoV-2 infection. First dose of an mRNA vaccine encoding the spike protein of Omicron BA.1 (BA1-S-mRNA) and two boosts of a mRNA vaccine encoding the original receptor-binding domain (RBD-mRNA)of SARS-CoV-2 induced potent neutralizing antibodies (nAbs) against several pseudo typed Omicron sub variants (e.g., BA.1,-BA.2, and BA.5), Alpha, Beta, Gamma, and Delta variants, as well as live Omicron BA.1 and Delta variants. By contrast, first-dose of RBD-mRNA plus two-boosts of BA1-S-mRNA, three-doses of RBD-mRNA or BA1-S-mRNA, or their combinations, failed to elicit high-titer Abs against all these viruses. In addition, compared with a SARS-CoV-2 wild-type spike (WT-S) protein, a cocktail of WT-S and Omicron-BA1-S proteins, or WT-S prime-BA1-S boost, elicited higher nAbs against several pseudo typed Omicron sub variants, such as BA.1, BA.2, and BA.5. It also induced higher or significantly higher nAbs than the WT-S-prime-BA1-S boost, WT-S alone, or BA1-S alone against tpseudo typed Alpha, Beta, Gamma, and Delta variants. Moreover, the WT-S-prime-BA1-S boost and WT-S/BA1-S cocktail vaccinations completely protected mice against lethal challenge of a Delta variant with negligible weight loss. Overall, these vaccines demonstrate effective in eliciting broadly and potent nAbs and/or protective efficacy against SARS-CoV-2 variants, which will provide useful guidance for development of efficacious vaccines to prevent current and future variants.

Biography

Dr. Du is a professor in the Institute for Biomedical Sciences at Georgia State University. Her research mainly focuses on the rational design and development of effective and safe vaccines and therapeutic agents to prevent and treat infection caused by corona viruses, flaviviruses, and other pathogenic viruses.

Linda Chia-Hui Yu

Graduate Institute of Physiology, National Taiwan University College of Medicine, Taipei, Taiwan

Impact of Invasive Pathobionts and Microbiota Dysbiosis on Intestinal Innate Immunity and Cancer Progression

Abstract

Patients with inflammatory bowel diseases (IBDs) are at higher risk for developing colorectal cancers (CRC) at later stages. Accumulating evidence indicated that immune hyperactivation and gut microbiota are involved in chronic inflammation and cancer development. Intestinal commensal bacteria are normally not in direct contact with epithelium due to the presence of a mucus barrier. However, abundance of mucosa-associated bacteria has been reported in patients with IBD and CRC. High amounts of mucosa-associated Escherichia coliand Bacteroides fragiliswere identified inclinical biopsy specimens of CRC and familial adenomatous polyposis. Human Crohn's isolated adherent-invasive E. coliexhibited strong colitogenic ability in transgenic mouse models.Our previous work showed that dysregulated epithelial innate signaling led to CRC growth in experimental mouse models (Kuo et al., Cell Death Diff 2015, Cancer Res2016). Moreover, the presence of intraepithelial bacteria was observed during the course of colitis and cancer development (Pai et al., J Crohns Colitis 2021, Yu et al., Cell Mol Gastro Hepatol 2022). We recently identified virulence-expressing invasive E. coli in the dysbiotic microbiota that promoted inflammation and increased tumor load through counteracting epithelial antimicrobial innate defense in the inoculated recipient mice. A gradual increase of bacterial virulence factors associated with heightened innate immune profiles and free radical-associated enzyme gene expression was also observed in human CRC specimens from stage I to IV (Yu et al., Cell Mol Gastro Hepatol 2022). The findings provided evidence of a core mechanism of aberrant host innate immunity and microbiota dysbiosis in intestinal tumorigenesis. Funding: MoST 110-2320-B-002-011-MY3, NHRI-EX111-11108BI, NHRI-EX112-11108BI, NHRI-EX113-11108BI

Biography

Linda Chia-Hui Yu is a Professor at the Graduate Institute of Physiology, National Taiwan University College of Medicine in Taiwan. She received her Ph.D. degree from McMaster University and postdoctoral training at the University of Calgary in Canada. Dr. Yu laboratory investigates pathophysiological mechanisms of intestinal epithelial biology and mucosal immunology. Her research interest is focused on host-microbe interaction for the regulation of epithelial barrier and intestinal tumorigenesis. She has received numerous competitive

research grants from the Ministry of Science and Technology and the National Health Research Institute in Taiwan. She currently serves as a Council member of the Federation of Asian and Oceanian Physiological Societies (FAOPS) (2019-2023), Chair of Commission V secretion and absorption in the International Union of Physiological Sciences (IUPS) (2022-2025), Councillor of Chinese Physiological Society (CPS) in Taiwan(2022-2024).

Dr. SelmaZ.D'Silva

Transplant Immunology & Immunogenetics Lab ACTREC, Tata Memorial Centre, Kharghar Navi Mumbai-410210, India

Nk cells and their implication in Hematopoeitic stemcell transplantation

Abstract

Hematopoietic stem cell transplantation (HSCT) is a choice of treatment for patients who suffer from various hematological malignancies. Even after finding a full HLA matched donor, the success of HSCT is marred by conditions such as relapse, graft vs. host disease (GvHD) and transplant related mortality (TRM). Recently, non HLA genes such as Killer Immunoglobulin like (KIR) genes have been implicated in predicting HSCT outcomes. KIR genes are present on Natural killer (NK) cells and modulate the cytotoxic capability of NK cells towards recognition of self and non self cells. The NK cytotoxic activity depends on the recognition of different KIR receptors by their specific MHC-Class I ligands. There are 4 different theories reported in literature describing NK cytotoxicity: KIR ligand model, missing KIR ligand model, KIR gene- gene model, and KIR receptor-ligand model. Knowledge of the presence or absence of activating/inhibitory KIR receptors and their corresponding ligands both in the graft vs host and host vs graft direction can predict transplant outcomes such as graft vs leukemia effect (GvL) or graft rejection. Since the frequency of KIR genes differs between populations, studies on frequency estimation of these genes within a population gives the clinician an opportunity to select a haplomatched HLA donor with best predicted transplant outcomes.

Biography

Dr. Selma Zenia Dâ Silva has been working with India's largest tertiary cancer care hospital Tata Memorial (Mumbai) since 2016. She has been involved in Transplant diagnostics mainly HLA typing, KIR genotyping, and antibody screening for identifying donors for hematopoietic stem cell transplantation for various hematological malignancies. Her research involves identifying the role of KIRs, cytokine, and chemokine receptors in hematopoietic stem cell transplant outcomes, which will help in the identification of patients at high risk of developing complications post-transplant. An ongoing project aims at validating NK cell-mediated cytotoxicity which will translate into NK cell Immunotherapy to improve transplant outcomes. More recently she has been involved in deciphering the role of MIC A and B genes and their associations with transplant outcomes. These projects have been funded by the Terry Fox cancer association; industry sponsored (GenDx) as well as intramural funds. Her research work (>50 peer-reviewed articles and 3 chapters) has been published in various national and international journals

Shikha Singla
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Association between biological immunotherapy for psoriasis and time to incident inflammatory arthritis: a retrospective cohort study

Abstract

Background:

Targeted biological immunotherapy's have been highly effective in controlling skin disease in patients with psoriasis, but whether therapy delays progression to inflammatory arthritis is unclear. The aim of this study was to compare the time to incident inflammatory arthritis among patients newly receiving biological therapies for psoriasis.

Methods:

In this retrospective cohort study, we obtained data on a national sample of patients in the USA from the electronic health records database of the US-based TriNetX network. We included adult patients (aged ≥18 years) with two diagnostic codes for psoriasis (>30 days apart; International Classification of Diseases [ICD] codes) who had been newly prescribed a biologic (inhibitors of tumor necrosis factor [TNF], interleukin [IL]-17, IL-23, or IL-12/23, first prescribed on or after the date of receiving a first psoriasis diagnosis code). The time to incident inflammatory arthritis, defined by first occurrence of a diagnostic code for psoriatic arthritis or other inflammatory arthritis after initiation of biological therapy, was graphed with use of the Kaplan-Meier estimate. Time-dependent risk for inflammatory arthritis was calculated with weighted Cox proportional hazards regression with anti-TNF exposure as the reference, adjusted for demographic and clinical co variables. Sensitivity analyses were used to evaluate incident cases of psoriasis, increased exclusion periods for prevalent cases of inflammatory arthritis, drug switching, and more stringent disease and outcome definitions.

Findings:

Between Jan 1, 2014, and June 1, 2022, we identified 15 501 patients with psoriasis (mean age 50•2 years [SD 15•0]; 8399 [54•2%] women and 7102 [45•8%] men; 11 175 [72•1%] White). 976 (6•3%) of the 15 501 patients developed inflammatory arthritis, with a cumulative incidence of 2•6 cases per 100 person-years. In multivariable regression analyses, the risk of developing inflammatory arthritis was significantly lower in patients prescribed IL-12/23 inhibitors (adjusted HR 0•58, 95% CI 0•43–0•76) or IL-23 inhibitors (0•41, 0•17–0•95) than in patients prescribed TNF inhibitors. We found no significant difference for IL-17 inhibitors (0•86, 0•54–1•38) compared with TNF inhibitors. For IL-12/23 inhibitors, the results persisted in all sensitiv-

ity analyses. For IL-23 inhibitors, the results persisted in three of six sensitivity analyses, when a higher diagnostic threshold for incident arthritis was used and when excluding patients who developed arthritis within 3 or 6 months after first biologic prescription.

Interpretation:

In this large cohort study of patients with psoriasis, treatment with IL-12/23 inhibitors or IL-23 inhibitors was associated with reduced risk of progression to inflammatory arthritis compared with TNF inhibitors. Prospective observational cohorts with disease activity measures and pooled analyses of previous randomized trials are required to confirm these findings.

Stefan T Orszulik

Formerly:Process Improvement Engineer at De La Rue Currency, Overton UK

The Quality of Antimicrobial Susceptibility Test Discs and Implications for Patient Outcomes

Abstract

Most discs are made to one of three main standards (FDA, WHO, DIN); these all describe an assay method for assessing the quality of discs using a linear method. Theory predicts a curved relationship, and this is backed up in many cases in practice. In such cases, the assays are invalid. Even the example given in the WHO manual has an error of 13% in the assay due to curvature in the calibration line. Organizations such as EUCAST (European Committee on Antimicrobial Susceptibility Testing) use manufactured discs to create quality zone sizes and break points without checking quantitatively the quality of the discs. Using a wide range of different conditions, quality zone ranges are calculated by applying ±2σ to the data thereby accommodating 95% of all possible variation in zone sizes. The adoption of such very broad zone ranges, generated using potentially flawed discs, is unsafe. There has been no comprehensive study into the quality of discs using validated, quantitative methods despite the many decades of use. Therefore, the true quality of discs used to create quality zone ranges and break points is not known. If quality zone ranges and breakpoints were based on properly validated discs, it is not known what difference that would make to clinical outcomes and antimicrobial resistance. There has been no comprehensive study into the effectiveness of AST discs in terms of patient outcomes. In Summary, disc assays, quality zone sizes, and break points are based on bad science, and the clinical effectiveness of the system of AST discs is not known. All statements and analyses presented in this review are based on peer-reviewed articles.

Biography

Stefan T Orszulik, Quality Specialist Stefan Orszulik graduated from Royal Holloway College, University of London, with a B.Sc. and Ph.D. in Chemistry. This was followed by a postdoctoral fellowship at the University of Strathclyde under the supervision of Prof. Colin Suckling, researching the reaction mechanisms of enzymes. There then followed a career in industry, specializing in medical devices, qualityimprovement using 6 sigma techniques, experimental design, and multivariate analysis.

Dr Orszulik's publications include books on lubricants, the impact of the oil industry on the environment, and research papers inorganic chemistry, medical devices, statistics, and mathematical modeling.

Tian Wang,

Department of Microbiology & Immunology, 2Sealy Institute for Vaccine Sciences, University of Texas Medical Branch, Galveston, TX, 77555, USA.

Development of Vaccines and Nutraceuticals Against SARS-CoV-2 Infection

Abstract

The recent corona virus disease 2019 (COVID-19) pandemic had made a serious impact on global public health for more than three years. Neither licensed vaccines nor treatments are available for humans. Multiple COVID-19 vaccine platforms have been tested with collaborative efforts in our studies, including a multigenic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine based on an MVA vector expressing both viral nucleocapsid (N) and spike (S) proteins (MVA-S + N), a modified porous silicon microparticle (PS-M)-adjuvant toSARS-CoV-2 receptor-binding domain (RBD) vaccine, and an attenuated SARS-CoV-2 virus with modified viral transcriptional regulatory sequences and deletion of open-reading frames 3, 6, 7 and 8 (Δ3678) These candidate vaccines generated potent and/or durable SARS-CoV-2- specific humoral and type 1 helper T (Th) cell- mediated immune responsesin animalsand protected host from SARS-CoV-2 and variants challenge. The use of nutraceuticals could be an additive in attenuating COVID-19 complications. AHCC is an extract prepared from mycelia of the Basidiomycete family edible mushroom Lentinula edodes and are enriched in acetylated α-1,4-glucans. We found that dietary supplementation with AHCCto enhance host innate and adaptive T cell responses reduced host susceptibility to SARS-CoV-2 infection in mice. Overall, the candidate vaccines and nutraceuticalsare potentially important for prevention and control of COVID-19 morbidity and mortality following SARS-CoV-2 infection.

Biography

Dr. Wang is a Professor in the Department of Microbiology & Immunology at the University of Texas Medical Branch at Galveston. Dr. Wang's research focuses on understanding of the disease mechanisms of emerging and re-emerging RNA viruses, such as West Nile virus, Zika virus, Powassan virus, Chikungunya virus, and Sars-CoV-2, host immune responses to viruses and candidate vaccines, vaccine development, and antiviral agents.

Xingmin Sun

Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa, Florida, USA

Recombinant Fusion Protein Vaccine Containing Clostridioides difficile (FliC) and FliD Protects Mice against C. difficile Infection

Abstract

Bacterial flagella are involved in infection through their roles in host cell adhesion, cell invasion, auto-agglutination, colonization, the formation of biofilms, and the regulation and secretion of nonflagellar bacterial proteins that are involved in the virulence process. In this study, we constructed a fusion protein vaccine (FliCD) containing the Clostridioides difficile flagellar proteins FliC and FliD. The immunization of mice with FliCD induced potent IgG and IgA antibody responses against FliCD, protected mice against C. difficile infection (CDI), and decreased the C. difficile spore and toxin levels in the feces after infection. Additionally, the anti-liCD serum inhibited the binding of C. difficile vegetative cells to HCT8 cells. These results suggest that FliCD may represent an effective vaccine candidate against CDI.

Biography

Dr. Sun is an Associate Professor with tenure in the Department of Molecular Medicine, College of Medicine at the University Of South Florida (USF). He holds courtesy appointments in the Department of Internal Medicine, Department of Cell Biology, Microbiology & Molecular Biology, Department of Chemistry at USF, and USF Genomics. He received his Ph.D. in Natural Sciences from the University of Kiel, Germany, and his Master's Degree in Veterinary Microbiology and Immunology from the Nanjing Agricultural University, China. He received his postdoctoral training in Molecular Microbiology and Biochemistry at Brown University, USA. The research in his laboratory is focused on the pathogenesis of Clostridioides difficile and the development of novel therapeutics including vaccines to prevent/treat C. difficile infection (CDI). He was an NIH (National Institutes of Health) Career Development K01 Awardee. His laboratory has been continuously supported by the NIH. He has been actively serving NIH study section panels including chairing the NIH study section panel in 2020. He serves as an Associate Editor for "Molecular Medicine", Associate topic editor for "Frontiers in Microbiology", and editorial boards for "Infection and Immunity" and "Applied and Environmental Microbiology". He received Tufts Institute for Innovation Inaugural Award in 2014. In 2018, he was awarded the "Faculty Outstanding Research Achievement Award" at USF. In 2019, he was awarded "The Excellence in Innovation Award" at USF. He chaired the Research Committee of the College of Medicine at USF from 2019 to 2020. Currently, he serves as the President of the USF Chapter, National Academy of Inventors, USA.

Zahra Mozooni

Iran University of Medical Sciences, Tehran, Iran

The role of interferon-gamma and its receptors in gastrointestinal cancers

Abstract

Gastrointestinal malignancies are the most prevalent type of cancer around the world. Even though numerous studies have evaluated gastrointestinal malignancies, the actual underlying mechanism is still unknown. These tumors have a poor prognosis and are frequently discovered at an advanced stage. Globally, there is an increase in the incidence and mortality of gastrointestinal malignancies, including those of the stomach, esophagus, colon, liver, and pancreas. Growth factors and cytokines are signaling molecules that are part of the tumor microenvironment and play a significant role in the development and spread of malignancies. IFN-γ induce its effects by activation of intracellular molecular networks. The main pathway involved in IFN-γ signaling is the JAK/STAT pathway, which regulates the transcription of hundreds of genes and mediates various biological responses. IFN-γ receptor is composed of two IFN-γR1 chains and two IFN-γR2 chains. Binding to IFN-γ, causes the intracellular domains of IFN-γR2 to oligomerize and transphosphorylate with IFN-γR1 which activates downstream signaling components: JAK1 and JAK2. These activated JAKs phosphorylate the receptor, creating binding sites for STAT1. STAT1 is then phosphorylated by JAK, resulting in the formation of STAT1 homodimers (gamma activated factors or GAFs) that translocate to the nucleus and regulate gene expression. The balance between positive and negative regulation of this pathway is crucial for immune responses and tumorigenesis. In this paper, we evaluate the dynamic roles of IFN- γ and its receptors in gastrointestinal cancers and present evidence that inhibiting IFN- γ signaling may be an effective treatment strategy.

Biography

I am Zahra Mozooni, a researcher in the field of immune-oncology from Iran. I recently obtained my Master's degree from Semnan University, Iran. My current research focuses on biomarkers and their role in gastrointestinal cancer. I am collaborating with the Institute of Immunology and Infectious Diseases, Antimicrobial Resistance Research Center, Iran University of Medical Sciences, Tehran, Iran, on various research projects. I published this paper during my master's degree. In conclusion, my research has been focused on developing novel treatment and diagnostic approaches for cancer. My ambition is to pursue a Ph.D. in immuno-oncology or I am Zahra Mozooni, a researcher in the field of immuno-oncology from Iran. I recently obtained my Master's degree from Semnan University, Iran. My current research focuses on biomarkers and their role in gastro-

intestinal cancer. I am collaborating with the Institute of Immunology and Infectious Diseases, Antimicrobial Resistance Research Center, Iran University of Medical Sciences, Tehran, Iran, on various research projects. I published this paper during my master's degree. In conclusion, my research has been focused on developing novel treatment and diagnostic approaches for cancer. My ambition is to pursue a Ph.D. in immuno-oncology or Immunotherapies to further my knowledge and expertise in this field.

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