1867th Conference

Breast Pathology and
MedChem & Rational Drugs 2018

6th World Congress and Expo on

Breast Pathology and Cancer Diagnosis

&

20th International Conference on

Medicinal Chemistry and Rational Drugs

July 25-26, 2018 | Vancouver, Canada

Keynote Forum

Day 1

Andrea Nicolini, J Clin Exp Pathol 2018, Volume 8
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Andrea Nicolini

University of Pisa, Italy

Hormone-immunotherapy in endocrine dependent metastatic breast cancer patients

Hormone therapy is advised for ER+ metastatic breast cancer patients due to its efficacy concomitant with low toxicity however, in most patients the occurrence of resistance is a not well yet understood hurdle to overcome. In these patients, during clinical benefit (CB) from conventional anti-estrogens, the addition of cycles of sequential immunotherapy could prolong the benefit and delay the arising of acquired hormone resistance. In order to validate this hypothesis, in 1992 we started an open exploratory clinical trial. Forty-two of these patients in CB during first line anti-estrogen salvage therapy also received beta-interferon (INF-beta) 3,000,000 IU i.m./day 3 days/week, weeks 1-4 and successively recombinant interleukin-2 (IL-2) 3,000,000 IU s.c./day 3 days/week, weeks 5-8 until progression. The immunotherapy cycle lasted 10 weeks and the patient continued anti-estrogen alone during weeks 9-10, the 11th week being the first week of the successive cycle. At each control visit, routine laboratory examinations and serum measurement of a CEA-TPA-CA15.3 tumor marker (TM) panel were carried out, and an immunological assessment was made (total lymphocytes, CD4+, CD8+, NK cells, T-reg, IL-6, IL-10, IL-12, TNFa,TGFbeta1 and IFN-gamma.) The addition of INF-beta-IL-2 sequence significantly prolonged clinical benefit and overall survival from conventional antiestrogens. During CB as opposed to progression, a significant immune stimulation was observed. During CB also a significant CEA, TPA, CA15.3 decrease occurred 24–72 h after interleukin-2 administration. At the progression a significant increase for CEA and for all 3 markers (standardized values) was found 24–72 h after interleukin-2 administration. In patients who survived less than 5 years, the Treg cell increase occurred at a significantly shorter time interval than in those who survived longer than 5 years (20 vs 45.5 months, respectively; P = 0.001). To further confirm these promising results a multicenter prospective phase II trial is going to be launched by the Cancer Center Institute of Tuscany in Italy.

Biography

Andrea Nicolini graduated (summa cum laude) at School of Medicine, University of Pisa in 1974. He received postgraduate diplomas at University of Pisa in Internal Medicine (1980), Pneumology (1984), and Nuclear Medicine (1986). His research interests include breast and gastrointestinal cancer and their metastases, tumour markers, post-operative follow-up, physiopathology, immunology and immunotherapy of cancer, and thyroid tumours.

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B Moon Kim, J Clin Exp Pathol 2018, Volume 8
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B Moon Kim

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Extremely potent, pan-genotypic Hepatitis C virus NS5A inhibitors based on novel core structures

Hepatitis C virus (HCV) infection often leads to serious liver diseases such as cirrhosis followed eventually by hepatocellular carcinoma. Several HCV RNA gene products (NS2, NS3, NS4A, NS4B, NS5A and NS5B) involved in the reproduction of HCV have been instensively studied for new therapeutic target identification. Recently, combinations of direct acting antivirals (DAA) including HCV NS3/4A protease inhibitors such as boceprevir, telaprevir, paritaprevir, and grazoprevir, polymerase inhibitors such as sofosbuvir and dasabuvir, and NS5A inhibitors such as daclatasvir, ledipasvir, ombitasvir, elbasvir and velpatasvir have shown successful arrest of the infection. However, even with the new DAA's, resistance to the drugs in patients infected with various strains of HCV has emerged. Therefore development of effective anti-HCV drug candidates possessing pan-genotype activities is still needed. Herein we report the discovery of a series of extremely potent HCV NS5A inhibitors based on a few new core skeletons. From these efforts, we have identified a series of NS5A inhibitors that exhibit highly potent anti-HCV activities particularly against several genetic variants and some mutant strains. Several interesting compounds were further evaluated with other studies and are shown to be nontoxic and anticipated to be effective HCV drug candidates.

Biography

B Moon Kim has completed his PhD and postdoctoral studies at M.I.T. After 5 year experience at Merck Research Laboratories in USA, he took a faculty position at the Chemistry Department of Seoul Naitonal University Korea. He was Chemistry Department Chair and Director of the BK21 Chemistry & Molecular Engineering Division at SNU. He has published more than 120 papers and 25 patents and has been serving as an editorial board member of Bioorganic Medicinal Chemistry and Bioorgnaic & Medicinal Chemistry Letters and an editor-in-chief of Bulletin of the Korean Chemical Society.

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Biomarkers in cancer immunotherapy

Immunotherapy has gained increasing consent in different types of advanced and/or metastatic cancer. More recently, checkpoint inhibitors have been extensively studied and in some cases they have been approved by regulatory authorities for cancer therapy. However, only a minority of patients exhibits a durable response to immunotherapy, while toxicity and costs of these treatments are not insignificant. In this view, biomarkers predicting response, resistance and toxicity should be important for a better selection of patients. PD-L1 expression, TIL identification and characterisation, mutation load, microsatellite instability, MDSCs, IDO, IFN-gamma/Jak pathway mutations are some of these markers. Due to the complexity of immune response, the identification of reliable markers is difficult and research is in progress.

Biography

Paola Ferrari graduated in Medicine and Surgery at Pisa University in 1995 (full marks), specialized in Internal Medicine in 2000, PhD in Medical Physiopathology and Pharmacology. She works as medical oncologist at Unit of Oncology 1, Department of Oncology, New Technologies and Transplantations, University of Pisa. Clinical activity: Follow-up and therapy of cancer patients, mainly breast cancer patients. Principal fields of research: Breast and gastrointestinal cancer follow-up and therapy, breast cancer biomarkers and prognostic factors, cancer immunology, circulating tumor cells, cancer stem cells. Paola Ferrari is author/co-author of about 50 articles in peer reviewed journals. She regularly serves as reviewer for international oncology journals.

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Day 2

Yoshitsugu Akiyama, J Clin Exp Pathol 2018, Volume 8
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Yoshitsugu Akiyama

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Colorimetric screening of DNA-functionalized gold nanoparticles with drug-nucleic acid interactions

Gold nanoparticles modified with high surface-density of DNA (DNA–AuNPs) have been widely used in highly sensitive bioassays. Until now, we developed a colorimetric single-nucleotide polymorphism (SNP) genotyping method and detected dynamic structural changes in DNA-AuNP assemblies with beads on string-like structure based on a unique phenomenon of non-crosslinking aggregation of double-stranded DNA-functionalized AuNPs (dsDNA–AuNPs). For example, dsDNA–AuNP having a full-match sequence can undergo aggregation in highly ionic aqueous solutions, showing a drastic color change owing to a band shift of the surface plasmon resonance. On the contrary, dsDNA–AuNP having a mismatch sequence can remain dispersed under the same conditions. Recently, we have also demonstrated the extremely higher colloidal stability of ds DNA–AuNP having a single-base protrusion as compared with that of dsDNA–AuNP having a mismatch sequence. This behavior allowed us to perform more reliable SNP genotyping of the human related-cytochrome P450 2C19 gene that plays a role in the metabolism of pharmaceutical agents. Notably, drastic color change can be induced by single-base differences in the dsDNA located on outermost surfaces of AuNP in highly ionic aqueous solutions. In this study, we attempted to assess colorimetric drug efficacy of small molecules to facilitate selection of DNA-associated drugs that have a mechanism related to an antitumor activity. The rapid color difference derived from high colloidal stability can allow visual screening of potent antitumor agents.

Biography

Yoshitsugu Akiyama has completed his PhD at the age of 28 years from University of Tokyo. He started postdoctoral studies from University of Virginia and The Biodesign Institute at Arizona State University in US (2004–2009) and was promoted to Research Assistant Professor with Prof. Sidney M. Hecht in 2009. Then he joined NOF Corporation, followed by RIKEN as a Senior Research Scientist in Japan (2010–2015). He is now an Assistant Professor in the Faculty of Industrial Science and Technology at Tokyo Universtiy of Science. He has been serving as an editorial board member of *Journal of Drug Toxicology and Pharmacology*.

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Mark Priebe

Quality Star LLC, USA

Quality assurance tools to help reduce the diagnostic interpretive error in breast cancer surgical pathology

Objective: To review the frequency and related impact of interpretive errors in anatomic pathology and how quality assurance (QA) programs measure in their ability to help reduce diagnostic interpretive error in surgical pathology.

Design: From an extensive number of published studies, the rate of major discrepancies identified for cancer patients referred to another institution occur from 4.6% to 14.7%, depending on type of tissue. However published data indicates the current intra-lab QA programs ability to detect these discrepancies is only 0.8% to 1.7%. To help understand the cause of this gap, four formal quality assurance case review programs both inter and intra-lab were reviewed for their ability to satisfy a set of selected design attributes known to help identify interpretive error. Peer reviewed literature was researched to support claims for each program percent compliance to the attributes, strengths, drawbacks, and best demonstrated practices were identified.

Results: No program met the selected attribute listing 100%, compliance ranged from 29% (met 2 of 7) to 86% (met 6 of 7) for each program.

Conclusion: Laboratories should be aware of the limitations of each QA program and take into consideration their case and pathologist mix and current on-site concerns, select a program with attributes that best match their QA needs. In general, programs that are standardized, include external review by subspecialist and are performed close to the final sign-out date may offer the greatest amount of error discovery and potential to positively influence patient outcomes and continuous improvement. Although this study focused on discordance in cancer related surgical pathology, case review can also be an effective tool in discovery of all histology/cytology diagnostic and clerical discrepancies.

Biography

Mark Priebe is a subject matter expert in the utilization of whole slide digital imaging for quality assurance of surgical pathology for cancer. Mark has presented on quality in surgical pathology via podium and posters at multiple scientific meetings and was the Co-Chair for Pathology 16 (Chicago) and Keynote at 5th International Meeting on Breast Pathology and Cancer Diagnosis 2018 (Miami), Mark received his undergraduate degree in Medical Technology from Marquette University, Milwaukee, and advance certification by the ASCP in Immunohematology from the Medical College of Wisconsin, Mark is the co-developer of QualityStar quality consortium of Omaha Nebraska. QualityStar is an external peer review quality assurance program for Surgical Pathology, approved by the American Board of Pathology for Part II (SAM) and IV (QA) MOC and multiple other certification/accreditation agencies. The Mission of QualityStar is to support the reduction of major diagnostic discordance in surgical pathology by 5% (7 to 2%) impacting the lifes of over 80,000 patients annually in North America.

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B Moon Kim

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Development of potent autoinducer-2 quorum-sensing inhibitors equipped with novel bicyclic brominated furanones against bacterial biofilm formation

Biofilm formation is one of the critical factors affecting bacterial survival in association with bacterial virulence factors. It is effectively regulated through a process called quorum sensing, which is an intra- and interspecies bacterial communication system. According to changes in cell deinsity and species complexity, complex biological responses are triggered through the quorum sensing. Chronic inflammation of the periodontium is one of the most common inflammatory diseases, which is in part caused by subgingival biofilm formation from periodontopathogens. Particularly, the early and late colonizers in periodontal biofilms are linked together by Fusobacterium nucleatum, which is thus regarded as a major co-aggregation bridge organism in forming aqnd growing subgingival biofilms. We have previously shown that autoinducer-2 (AI-2) of F. Nucleatum, the intergeneric quorum-sensing signal molecule, can be a possible target for the inhibition of periodontal biofilm formation, since it plays a key role in intra- and interspecies interactions of periodontopathogens. Recently, inhibition of biofilm formation via AI-2 by novel brominated furanones originated from marine natural products such as those from macroalga Delisea pulchra has been reported, and further studies toward the goal of increasing the inhibition effect have been conducted. Herein, we describe the synthesis and quorum sensing inhibitory activities of new bromofuranone analogs in relation with biofilm formation by periodontopathogens such as *F. nucleatum, Porphyromonas gingivalis,* and Tannerella forsythia.

Biography

B Moon Kim has completed his PhD and postdoctoral studies at M.I.T. After 5 year experience at Merck Research Laboratories in USA, he took a faculty position at the Chemistry Department of Seoul Naitonal University in Seoul, Korea. He was Chemistry Department Chair and Director of the BK21 Chemistry & Molecular Engineering Division at SNU. He has published more than 120 papers and 25 patents and has been serving as an editorial board member of Bioorganic Medicinal Chemistry and Bioorgnaic & Medicinal Chemistry Letters and an editor-in-chief of Bulletin of the Korean Chemical Society.

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