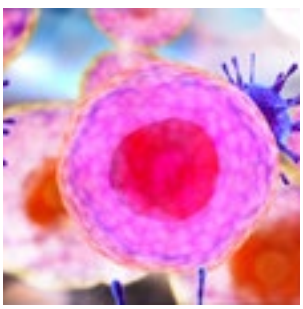
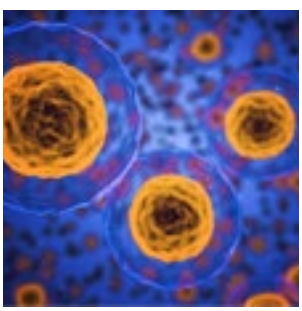
Keynote Forum
June 13, 2022

Cancer Summit 2022




18th International Conference on

CANCER AND CANCER THERAPY

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Stephen J Beebe

Anthony Nanajian, Brittney Ruedlinger, Kamal Asadipour and Siqi Guo

Old Dominion University, USA

Nanopulse stimulation can reverse immunosuppression and activate immunity memory in two orthotopic cancer models

Nanopulse Stimulation (NPS) is a pulsed power technology that delivers non-thermal, high-power, nanosecond duration pulses to cells and tumors. Innate and adaptive immunity are scheduled NPS responses. In orthotopic models of rat N1-S1 liver and mouse 4T1-Luc breast cancers, NPS induces an in situ vaccination such that animals are immune to challenge injections post-treatment. Significant for tumor elimination and immunity, NPS causes electric field intrusion into intracellular domains, with mitochondria as primary sensors. In both cancer models, NPS resolves the immunosuppressive tumor microenvironment (TME). In the 4T1-Luc model, TGFβ+ and 4-1BB+ activated T-regulatory cells (Tregs), myeloid-derived suppressor cells (MDSC), and tumor-associated macrophages (TAMs) are selectively eliminated with concomitant M-1 macrophage polarization and Tregs shifting from an activated to a naïve identity. With increases in resident memory T cells, the effector T cell / Treg ratio increases, demonstrating mechanisms for adaptive immunity. The rat liver model also showed specific increases in two activated natural killers (NK) cell phenotypes, one of which returned during the challenge-response.

In contrast, in the ectopic B16f10 melanoma model, NPS was less effective in eliminating tumors and inducing vaccine effects. NPS began to dismantle the B16f10 TME and initiate an immune response with increases in various activated, effector, and memory T cells, NKs, and M1 macrophages. However, the initial decreases in immunosuppressive cells are followed by the combined effects of persistent T regulatory cells and M2 TAMs along with various expression markers, including exhaustion signatures that potentiated the suppressive TME

We are now directed to resolve this return of immunosuppression to the TME. We have combined NPS with gene electron delivery (GET) of an IL-12-plasmid. This approach did not induce a better vaccine effect. Our ongoing approach is to inject carbon nanotube (CNTs) functionalized with anti-PD-L1. CNT alone deceased NPS conditions by 3-fold *in vitro.*

Recent Publications

1. Stephen J Beebe, et.al, (2022): Photodynamic Therapy of Inorganic Complexes for the Treatment of Cancer. Photochemistry and Photobiology 98 (1), 17-41
2. Stephen J Beebe (2021): Effects of usEPs on Plasma Membranes—Pores, Channels, and Repair. Ultrashort Electric Pulse Effects in Biology and Medicine, 33-75
3. Stephen J Beebe (2021): Effects of usEPs on DNA, Nuclear, and Subnuclear Compartments. Ultrashort Electric Pulse Effects in Biology and Medicine, 159-174

Biography

Stephen J Beebe received his BS degree in Zoology, Ohio University, Athens (1970), and Ph.D. in Medical Sciences (Pharmacology), Toledo University School of Medicine (1982). He was a Post-Doctoral Fellow / Associate, Department of Molecular Physiology and Biophysics, Vanderbilt (1982-1987), and a Fulbright and Marshal Scholar at the National Hospital and Institute for Medical Biochemistry, Oslo, Norway (1987-1989). At the Eastern Virginia Medical School (1989-2007), he was an Assistant Professor, Jones Institute for Reproductive Medicine, Department of Obstetrics and Gynecology (1989-1994), and an Associate Professor in the Departments of Pediatric and Physiological Sciences (1994-2007). He is now a Professor in the Frank Reidy Research Center for Bioelectrics, Old Dominion Univ., Norfolk, VA (2007-present).

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Bulent Ozpolat

The University of Texas- MD Anderson Cancer Center, USA

Development of novel targeted therapeutics for breast cancer

Breast cancer is the most common cancer in women and the second leading cause of cancer-related deaths. Triple-negative breast cancer (TNBC) is a highly aggressive, metastatic, and the deadliest and most incurable type of breast cancer. Significant heterogeneity with 6 genetically-defined subtypes has prevented the development of targeted therapeutics for TNBC. Chemotherapy remains a mainstay treatment, however, only 30% of the patients achieve remission and most patients develop resistance and relapse. To develop highly effective targeted therapeutics and prolong patient survival novel molecular targets needed to be identified. After a decade of research, our studies identified an oncogenic atypical kinase, Elongation Factor-2 kinase (EF2K), as a major oncogenic driver in TNBC and validated it as a novel therapeutic target in triple-negative breast cancer. To specifically target, we developed tumor-targeting RNA-based (siRNA and microRNA) nanotherapeutics. We demonstrated that single lipid or albumin-based nanoparticles can effectively deliver EF2K-specific siRNA and microRNAs into TNBC tumors in mice, inhibit the EF2K gene, and suppresses tumor growth with no toxic or side effects in mice, suggesting that this technology may be used in clinical translation to patients for Phase 1 clinical trials. We also developed small molecule EF2K-inhibitors (patented) with significant efficacy. Overall, the talk will focus on the current state of targeted therapies and the development of successful novel RNA-based nanotherapeutics which is considered a novel era of targeted therapeutics in the treatment of human cancers and diseases.

Recent Publications

1. Bulent Ozpolat, et.al (2022): Translational Modeling Identifies Synergy between Nanoparticle-Delivered miRNA-22 and Standard-of-Care Drugs in Triple-Negative Breast Cancer. Pharmaceutical Research. 39(3). 1-18.
2. Bulent Ozpolat, et.al (2022). Simvastatin-loaded liposome nanoparticles treatment for uterine leiomyoma in a patient-derived xenograft mouse model: a pilot study. Journal of Obstetrics and Gynaecology. 1-5.
3. Bulent Ozpolat, et.al (2022). RNAi-based therapeutics and tumor targeted delivery in cancer. Advanced Drug Delivery Reviews. 182. 114113

Biography

Bulent Ozpolat has expertise in Immunology, Cancer Biology, Genetics, Gene therapy, Experimental Therapeutics, Nanotechnology, nanocarriers, and the development of highly targeted therapeutics for cancer. After getting his M.D. degree from Dokuz Eylul University, he received his Ph.D. degree in Immunology from The University of Texas- MD Anderson Cancer Center Houston, TX, USA, and completed post-doctoral training at MD Anderson Cancer. He has been serving as a faculty for more than 15 years at MD Anderson Cancer Center, which is ranked one top of cancer centers for 15 years in the US. He has 5 patents for the development of targeted therapeutics and published more than 137 publications (H-index 39) (90 research papers, 20 book chapters, and 24 review articles) in peer-reviewed high-impact journals.

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Ferenc Gallyas

University of Pecs Medical School, Hungary

Repurposing an anti-arrhythmic agent for cancer therapy

Desethylamiodarone (DEA) is a major metabolite of the widely used antiarrhythmic drug amiodarone. DEA accumulates in tissues up to a thousand times its therapeutic plasma concentration and has detrimental direct mitochondrial effects, as demonstrated previously using isolated mitochondria. Based on these properties, we proposed that the compound has potential use in cancer therapy and provided experimental evidence for its cytostatic and metastasis-limiting properties in human bladder, cervix, and melanoma cell lines *in vitro* and *in vivo*.

We demonstrated that DEA induced cell death, caused cell cycle arrest in the G0/G1 phase, and reduced colony formation at physiologically relevant concentrations *in vitro* in all said cell lines. Mechanistically, DEA shifted the Bax/Bcl-2 ratio to initiate apoptosis, promoted AIF nuclear translocation, activated PARP-1 cleavage and caspase-3 activation and reduced activation of the major cytoprotective kinases, ERK and Akt. All these effects are consistent with DEA's cytostatic properties. In a rodent experimental lung metastasis model, DEA attenuated *in vivo* metastasizing properties of B16-F10 human melanoma cells.

When revisiting DEA's mitochondrial effects in a metastasizing human melanoma line, it is found that it did not affect cellular oxygen radical formation. However, it did decrease the mitochondrial transmembrane potential, induced mitochondrial fragmentation, caused outer mitochondrial membrane permeabilization, and evoked a cyclosporine A–independent mitochondrial permeability transition. Energetically, DEA decreased maximal respiration, ATP production, coupling efficiency, glycolysis, and non-mitochondrial oxygen consumption. These mitochondrial effects likely contributed to the drug's cytostatic and anti-metastasizing properties.

We propose repurposing of DEA based on these data augmented by the fact that amiodarone is the most frequently prescribed antiarrhythmic drug and has been in therapy since 1961. Accordingly, safety concerns could be resolved more easily for DEA than for a novel pharmacological agent.

Recent Publications

1. Ferenc Gallyas, et.al (2022). Involvement of Mitochondrial Mechanisms and Cyclooxygenase-2 Activation in the Effect of Desethylamiodarone on 4T1 Triple-Negative Breast Cancer Line. International Journal of Molecular Sciences. 23. 1544.
2. Ferenc Gallyas, et.al (2021). Cyclophilin D-dependent mitochondrial permeability transition amplifies inflammatory reprogramming in endotoxemia. FEBS open bio 11 (3), 684-704
3. Ferenc Gallyas, et.al (2021). Mitochondrial protective effects of PARP-inhibition in hypertension-induced myocardial remodeling and in stressed cardiomyocytes. Life Sciences 268, 118936.

Biography

Ferec Gallyas has completed his M.sc in Chemistry in 1985. He worked for the Pharmacology Research Centre of Chemical Factory G. Richter Ltd. (Budapest, Hungary) as a researcher for 3 years before joining the University of Pecs Medical School (Pecs, Hungary), where he is a Full Professor and Head of the Department of Biochemistry and Medical Chemistry. He obtained his PhD in 1995 and DSc in 2008. He has co-authored more than 100 scientific publications, which have received more than 3500 citations, his publication H-index is 32, and he has been an invited speaker at several prestigious conferences. He is a member of seven Hungarian and three international scientific societies, Section Editor for PLoS One, editorial board member of Cancers and PeerJ, and is a reviewer for major journals and scientific foundations.

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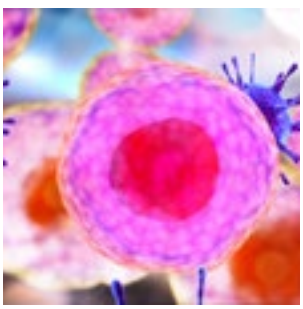


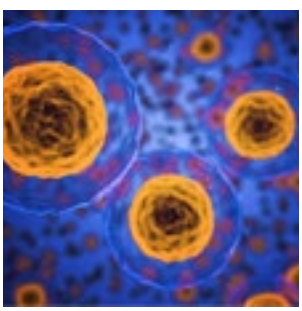


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Nitin Telang

Palindrome Liaisons Consultants, USA

Efficacy of Chinese herbs for secondary prevention/therapy of breast cancer: Preclinical leads

Rationale: Progression of advanced stage metastatic breast cancer represents a major cause of mortality in women. The American Cancer Society has projected 281,550 new cases of female breast cancer and 43,600 cancer-related deaths in 2022. Conventional chemo-endocrine therapy or small molecule-based targeted therapy constitute mainstream treatment options. These treatment strategies are associated with systemic toxicity and spontaneous/acquired therapy resistance. These limitations promote the progression of therapy-resistant breast cancer. Chinese herbs, mostly nutritional in nature, function as anti-estrogens, anti-inflammatory, and immune-modulatory agents. The herbs represent major constituents of herbal formulations that are used in traditional Chinese medicine for estrogen-related issues for breast cancer in women. Because of their low systemic toxicity and documented efficacy in patients, Chinese herbs may represent testable alternatives against therapy-resistant breast cancer.

Cellular Models: Human mammary carcinoma-derived MCF-7 cells and MDA-MB-231 cells represented models for clinical Luminal A and triple-negative breast cancer subtypes, respectively. Status of cell cycle progression, cellular apoptosis, estrogen metabolism, retinoblastoma protein (RB), phosphoinositide 3-kinase (PI3K), protein kinase B (PKB), and RAS signaling pathways represent quantitative endpoints for mechanistic leads for the efficacy of herbal extracts.

Research Outcome: The breast carcinoma-derived cellular models exhibit hyper-proliferation, downregulated cellular apoptosis, increased cancer risk, altered estrogen metabolism, and upregulated signaling pathways. Mechanistically distinct herbs at their respective maximum cytostatic concentrations downregulate the status of endpoint biomarkers.

Conclusions: The data provides evidence for mechanistic leads of growth inhibitory efficacy of nutritional herbs on clinically relevant models for breast cancer. This outcome validates an experimental approach to identify and prioritize efficacious herbs as testable alternatives for the treatment of therapy-resistant advanced-stage breast cancer.

Recent Publications

1. Nitin Telang (2022): The Divergent Effects of Ovarian Steroid Hormones of the MCF-7 Model for Luminal A Breast Cancer: Mechanistic Leads for Therapy. International Journal of Molecular Sciences 23 (9), 4800
2. 2. Nitin Telang (2022): Drug-Resistant Stem Cells: Novel Approach for Colon Cancer Therapy. International Journal of Molecular Sciences 23 (5), 2519
3. 3. Nitin Telang, et.al, (2022): Anti-proliferative and pro-apoptotic effects of Dipsacus asperoides in a cellular model for triple-negative breast cancer. Archives of Breast Cancer, 66-75

Biography

Nitin Telang is the Director of the Cancer Prevention Research Program at Palindrome Liaisons Consultants, New Jersey. He earned his Ph.D. degree in India (1974) and obtained post-doctoral training at the University of Nebraska, American Health Foundation, New York, and Memorial Sloan-Kettering Cancer Center, New York (1976-1985). He has served as a faculty member at Memorial Sloan-Kettering Cancer Center, Weill-Cornell Medical College, and Strang Cancer Prevention Center, New York (1986-2007). He has published peer-reviewed papers in the areas of carcinogenesis, cancer prevention, and cancer stem cell biology. He has served on Grant Review Study Sections for the National Cancer Institute (NCI) and the US Department of Defense (DOD). He is on the editorial boards for Oncology Reports, International Journal of Oncology, and World Academy of Sciences Journal. His research has been funded by grants from NCI and DOD. He has received NCI FIRST Award, DOD IDEA Award, and AN Marquis Lifetime Achievement Award.

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Osman Adiguzel

Firat University, Turkey

Shape Reversibility and Functional Characterization of Shape Memory Alloys

A series of alloy system take place in a class of advanced functional materials with the stimulus-response to external effect. Shape memory alloys take place in this class by exhibiting a peculiar property called the shape memory effect. This phenomenon is characterized by the recoverability of two certain shapes of material in a reversible way under different conditions. These alloys are used as shape memory devices in many fields from medicine, metallurgy, building industry. The choice of material is very essential to developing main materials and structures These alloys have dual characteristics called thermoelasticity and superelasticity in a memory manner. The shape memory effect is initiated by cooling and deformation and performed thermally in a temperature interval on heating and cooling after the first cooling and stressing processes, and this behavior is called thermoelasticity. Superelasticity is performed by stressing and releasing material at a constant temperature in the parent phase region. For the Superelasticity, materials are stressed in the elasticity limit in the parent phase region and, shape recovery is performed instantly and simultaneously upon releasing the applied stress, by recovering the original shape. Superelasticity exhibits elastic material behavior but stressing and releasing paths are different at the stress-strain profile, and the hysteresis loop refers to the energy dissipation. These phenomena are governed by structural transformations, basically called martensitic transformations. The shape memory effect is governed by thermal, and stress-induced martensitic transformations and performed thermally, on heating and cooling. Thermal induced martensitic transformation occurs on cooling with cooperative movements of atoms by means of lattice invariant shears in two opposite directions, <110 > -type directions on the {110} - type planes of austenite matrix along with lattice twinning and ordered parent phase structures turn into the twinned martensite structures. The twinned structures turn into the detwinned structures by means of stress-induced martensitic transformation, by stressing material in the martensitic condition. Superelasticity is also the result of stress-induced martensitic transformation and ordered parent phase structures turn into the detwinned martensite structure with stressing. Copper-based alloys exhibit this property in the metastable β-phase region, which has bcc-based structures at a high-temperature parent phase field. Lattice invariant shear and twinning are not uniform in these alloys and give rise to the formation of complex layered structures, depending on the stacking sequences on the close-packed planes of the ordered parent phase lattice. The layered structures can be described by different unit cells as 3R, 9R, or 18R depending on the stacking sequences on the close-packed planes of the ordered lattice. In the present contribution, x-ray diffraction and transmission electron microscopy (TEM) studies were carried out on two copper-based CuAlMn and CuZnAl alloys. X-ray diffraction profiles and electron diffraction patterns exhibit superlattice reflections. X-ray diffractograms took in a long-time interval show that diffraction angles and intensities of diffraction peaks change with the aging duration at room temperature. This result refers to the rearrangement of atoms in a diffusive manner.

Recent Publications

1. Osman Adiguzel, et al (2021). Lattice Reactions Governing Thermoelasticity and Superelasticity in Shape Memory Alloys. Phys Sci & Biophys J 2021, 5(1): 000170
2. Osman Adiguzel (2020). Factors and Lattice Reactions Governing Phase Transformations in Beta Phase Alloys. In: Bonča, J., Kruchinin, S. (eds) Advanced Nanomaterials for Detection of CBRN, 101-109.
3. Osman Adiguzel (2020). Thermally and Stress Induced Phase Transformations and Reversibility in Shape Memory Alloys. In: Sidorenko, A., Hahn, H. (eds) Functional Nanostructures and Sensors for CBRN Defence and Environmental Safety and Security, 105-112.

4. Osman Adiguzel (2018). Thermoelasticity, Superelasticity and Nanoscale Aspects of Structural Transformations in Shape Memory Alloys. In: Struble, L., Tebaldi, G. (eds) Materials for Sustainable Infrastructure, 287–293.

5. Osman Adiguzel (2018). Thermoelastic Phase Transformations and Microstructural Characterization of Shape Memory Alloys. In: Bonča, J., Kruchinin, S. (eds) Nanostructured Materials for the Detection of CBRN, 99-106

Biography

Osman Adiguzel graduated from the Department of Physics, Ankara University, Turkey in 1974 and received Ph.D.- degree from Dicle University, Diyarbakir-Turkey. He studied at Surrey University, Guildford, UK, as a post-doctoral research scientist from 1986 to 1987, and studied shape memory alloys. He worked as a research assistant, from 1975 to 1980, at Dicle University and shifted to Firat University, Elazig, Turkey in 1980. He became a professor in 1996, and he has been retired on November 28, 2019, due to the age limit of 67, following academic life of 45 years. He published over 80 papers in international and national journals; He joined over 120 conferences and symposia at the international and national level as a participant, invited speaker, or keynote speaker with contributions of oral or poster. He served as the program chair or conference chair/co-chair in some of these activities. In particular, he joined last six years (2014 - 2019) over 60 conferences as Keynote Speaker and Conference Co-Chair organized by different companies. He supervised 5 Ph.D.- theses and 3 M. Sc- theses in his academic life. Also, he joined over 70 online conferences in the same way in the pandemic period of 2020-2021. Dr. Adiguzel served his directorate of the Graduate School of Natural and Applied Sciences, Firat University, from 1999-to 2004. He received a certificate awarded to him and his experimental group in recognition of the significant contribution of 2 patterns to the Powder Diffraction File – Release 2000. The ICDD (International Centre for Diffraction Data) also appreciates the cooperation of his group and interest in the Powder Diffraction File.

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Zhengjun Zhang

University of Wisconsin, USA

Lift the veil of breast cancers using 4 or fewer critical genes

Known genes in the breast cancer study literature could not be confirmed whether they are vital to breast cancer formations due to lack of convincing accuracy, although they may be biologically directly related to breast cancer based on present biological knowledge. It is hoped vital genes can be identified with the highest possible accuracy, e.g., 100% accuracy and convincing causal patterns beyond what has been known in breast cancer. One hope is that finding gene-gene interaction signatures and functional effects may solve the puzzle. This research uses a recently developed competing linear factor analysis method in differentially expressed gene detection to advance the study of breast cancer formation. Surprisingly, three genes are detected to be differentially expressed in TNBC and non-TNBC (Her2, Luminal A, Luminal B) samples with 100% sensitivity and 100% specificity in one study of triple-negative breast cancers (TNBC, with 54675 genes and 265 samples). These three genes show a clear signature pattern of how TNBC patients can be grouped. For another TNBC study (with 54673 genes and 66 samples), four genes bring the same accuracy of 100% sensitivity and 100% specificity. Four genes are found to have the same accuracy of 100% sensitivity and 100% specificity in one breast cancer study (with 54675 genes and 121 samples), and the same four genes bring an accuracy of 100% sensitivity and 96.5% specificity in the fourth breast cancer study (with 60483 genes and 1217 samples.) These results show the four-gene-based classifiers are robust and accurate.

The detected genes naturally classify patients into subtypes, e.g., seven subtypes. these findings demonstrate the clearest gene-gene interaction patterns and functional effects with the smallest numbers of genes and the highest accuracy compared with findings reported in the literature. The four genes are considered to be essential for breast cancer studies and practice. They can provide focused, targeted researches and precision medicine for each subtype of breast cancer. new breast cancer disease types may be detected using the classified subtypes, and hence new effective therapies can be developed.

Recent Publications

1. Hongxuan Huang & Zhengjun Zhang (2019) Virtual Standard Currency for Approximating Foreign Exchange Rates, International Journal of Electronic Commerce, 23:1, 33-62,

2. Zhengjun Zhang&Kazuhiko Shinki, Extreme co-movements and extreme impacts in high frequency data in finance (2007) Journal of Banking & Finance, 1399–1415

Biography

Zhengjun Zhang writes about a variety of subjects, including fundamental dependence theory, extreme value theory and risk analysis, high-dimensional statistical learning using max-linear regression, zero-inflated protective barrier regression, variable selection based on tail limits, variable screening based on tail dependence and sure explained variability and nonlinear causal inference his collaborators, including my undergraduate/graduate students, and he introduced tail quotient correlation, generalized measures of correlation, competing factor copula, and max-linear computing regressions, amongst others.

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