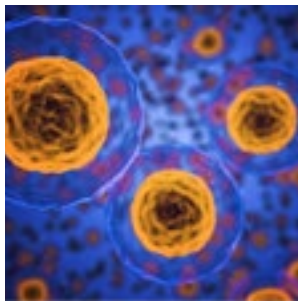
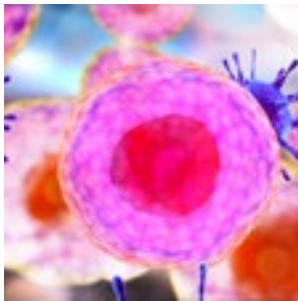

Scientific Tracks & Sessions

June 13, 2022

Cancer Summit 2022



18th International Conference on
CANCER AND CANCER THERAPY
June 13-14, 2022 | Webinar

Cancer Research and Therapy | Cancer Nanotechnology | Surgical Cancer | Cervical & Brain Cancer



Chair
Stephen J Beebe
Old Dominion University | USA

Title: New therapeutic approaches in the treatment of triple-negative breast cancer

Krisztina Kovacs | University of Pecs Medical School | Hungary

Title: MWCNTs based nanocomposites for the removal of oil and organic dyes from water

Thamer Adnan Abdullah | University of Pannonia | Hungary

Title: Effect of co-culturing both placenta-derived mesenchymal stem cells and HepG2 cells in cancer cell (HepG2) migration, damage through apoptosis, cell cycle arrest

F A Dain Md Opo | King Abdulaziz University | Saudi Arabia

Genome Expression | Gastric and Breast Cancer | Gastrointestinal Cancer



Chair
Bulent Ozpolat
The University of Texas- MD Anderson Cancer Center | USA

Title: The growing role of personalized and precision medicine (PPM): finding the right balance between precision medicine and personalized care to drive personalized & precision oncology (PPO) adoption and to get cancer cured

Sergey Suchkov | Institute for Global Health of MGUPP | Russia

Title: Radiotherapy during lumpectomy (TARGIT-IORT): the least disruptive treatment for breast cancer patients, which can improve their length and quality of life

Jayant S Vaidya | University College of London | UK

Title: An immuno-genomic atlas for cancer immunotherapy response

Qi Liu | Vanderbilt University Medical Center | USA

Title: Targeting the thromboxane A2 pathway suppresses Barrett's esophagus and esophageal adenocarcinoma development

Tianshun Zhang | University of Minnesota | USA

Title: Measles virus in classic Hodgkin lymphoma and additional cancers - A long lasting saga

Daniel Benharroch | Soroka University Medical Center | Israel

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New therapeutic approaches in the treatment of triple-negative breast cancer

Krisztina Kovacs

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The treatment of triple-negative breast cancer (TNBC) has several limitations, mostly because of treatment resistance, and till nowadays women with TNBC have poor prognoses. In these studies, we examined the different responses of triple-negative breast cancer line MDA-MB-231 and hormone receptor-positive breast cancer (HR+BC) line MCF7. We used a combined treatment including olaparib, a poly-(ADP ribose) polymerase (PARP) inhibitor, oxaliplatin, a third-generation platinum compound, and LY294002, an Akt pathway inhibitor. We applied the drugs in a single, therapeutically relevant concentration individually and in all possible combinations. Additionally, we tested as mono-therapy novel mitochondria-trageted compounds, and MitoCP, a positive control. We assessed cell viability, type of cell death, reactive oxygen species production, cell-cycle phases, colony formation, and invasive growth. In the case of PARP inhibitor treatment, in agreement with the literature, MDA-MB-231 cells were more treatment-resistant than the MCF7 cells. However, and in contrast with the findings of others, we detected no synergistic effect between olaparib and oxaliplatin, and we found that the Akt pathway inhibitor augmented the cytostatic properties of the platinum compound and/or prevented the cytoprotective effects of PARP inhibition. Our results suggest that, at therapeutically relevant concentrations, the cytotoxicity of the platinum compound dominated over that of the PARP inhibitor and the PI3K inhibitor, even though a regression-based model could have indicated an overall synergy at lower and/or higher concentrations. In contrast

to the combination therapy, we could not detect increased resistance by the TNBC line over the HR+BC line against the mitochondria-trageted compounds. Additionally, these substances were effective at sub-micromolar concentrations in the aforementioned *in vitro* tests. Taken together, these results indicate their potential of the novel mitochondria-trageted compounds in the treatment of TNBC.

Recent Publications

1. Krisztina Kovacs, et.al (2022): Effects of pituitary adenylate cyclase activating polypeptide (PACAP) in corneal epithelial regeneration and signal transduction in rats. *International Journal of Peptide Research and Therapeutics*. 28(3).
2. Krisztina Kovacs, et.al (2021): The Protective Effects of Endogenous PACAP in Oxygen-Induced Retinopathy. *Journal of Molecular Neuroscience*. 71 (12). 1-12
3. Krisztina Kovacs, et.al (2021): Cytostatic Effect of a Novel Mitochondria-Targeted Pyrroline Nitroxide in Human Breast Cancer Lines. *International Journal of Molecular Sciences*. 22 (16). 9016.

Biography

Krisztina Kovacs is a Professor in the Department of Biochemistry and Medical Chemistry at the University of Pecs Medical School, Hungary. Her major research works are the biological effects of benzofuran derivatives, BGP-15 derivatives, effects of PARP inhibitors, and pulmonary hypertension model system. She has participated in various conferences and published many articles in reputed journalsn.

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MWCNTs based nanocomposites for the removal of oil and organic dyes from water

Thamer Adnan Abdullah, Tatjana Juzsakova, Ali D Salman and Sebestyén Viktor

University of Pannonia, Hungary

Although the global economy continues to expand rapidly because of the exploitation and production of crude oil, its transportation and derivatives potentially remain a serious threat to the environment. Among many other challenges, oil spills remain major ecological and environmental concerns. Oil spills release volatile organic compounds (VOCs) and heavy hydrocarbons into the aquatic environment causing severe damage to the ecosystem. The intensive development of the pharmaceutical, agricultural and chemical industries has resulted in the release of a diverse range of chemical compounds such as antibiotics, plastics, pesticides, and dyes into aquatic environments. These industries serve as major contributors towards the contamination of aquatic environments since manifold chemicals are discharged directly and very frequently into the environment.

This study aims to develop effective, flexible, sustainable, and environmentally friendly adsorbent-based multi-walled carbon nanotube (MWCNTs) composites by adding polymers and metal oxides which make MWCNTs cost-effective and increase their removal efficiency of hydrocarbons and dyes from water.

Recent Publications

1. Thamer Adnan Abdullah, et.al, (2022) V2O5, CeO2 and Their MWCNTs Nanocomposites Modified for the Removal of Kerosene from Water. *Nanomaterials*. 2022; 12(2):189.

2. Thamer Adnan Abdullah, et.al, (2022). Polyethylene over magnetite-multiwalled carbon nanotubes for kerosene removal from water. *Chemosphere*, 287, 132310.
3. Thamer Adnan Abdullah, et.al, (2021). V2O5 Nanoparticles for Dyes Removal from Water. *16(2)*, 102-111.
4. Thamer Adnan Abdullah, et.al, (2021). "Polystyrene-Fe3O4-MWCNTs Nanocomposites for Toluene Removal from Water" *Materials* 14, no. 19: 5503.
5. Thamer Adnan Abdullah, et.al, (2021). Preparation and characterization of MnO2-based nanoparticles at different annealing temperatures and their application in dye removal from water. *International Journal of Environmental Science and Technology*, 18(6), 1499-1512.

Biography

Thamer Adnan Abdullah completed his Master of Chemical Engineering from Guru Gobind Singh Indraprastha University New Delhi in 2008. He is working as an assistant lecturer at the University of Technology, Baghdad, in the Applied Science Department, Chemistry Branch Group. Currently, he is doing his PhD and he is a researcher in the Sustainability Solutions Research Lab, Faculty of Engineering, University of Pannonia, Veszprem, Hungary. He has several articles published in ScienceDirect reputed journals and has participated in many international conferences in the field of environmental chemistry and nano-research.

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Effect of Co-culturing both placenta-derived mesenchymal stem cells and HepG2 cells in cancer cell (HepG2) migration, damage through apoptosis, cell cycle arrest

F A Dain Md Opo¹, Mohammed Moulay¹, Ghadeer Alrefaei^{1,2}, Nouf Hamid Alsubhi¹ and Saleh Alkarim¹

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Human placental-derived mesenchymal stem cells (hPMSCs) are a promising candidate to inhibit the proliferation of hepatocellular carcinoma (HCC) cell lines such as HepG2. However, the effects of hPMSCs and their conditioned media on HepG2 are still elusive. Therefore, this study aimed to investigate the effects of hPMSCs and their conditioned media on HepG2 and elucidate the underlying mechanism of action. The percentage of cell death (early apoptosis, late apoptosis) was observed by fluorescence-activated cell sorting and MTT assay. The DIO and DID color were used to detect interaction and cell death of both cells through cell fusion. Co-treatment of HepG2 cells with hPMSCs or hPMSCs-conditioned medium (hPMSCs-CM) inhibited HepG2 proliferation and induced their apoptosis. Morphological changes were also observed in the case of 30%, 50%, and 70% co-culture of both cells together *in vitro*. Treatment with hPMSCs or hPMSCs-CM induced HepG2 cell death through apoptosis as detected by flow cytometry, caspase 9 immunofluorescence, qPCR (detection of Bax, Bcl-2, and B catenin genes), by western blot, immunophenotyping (detection of caspase 9, caspase 3 protein). The hPMSCs and hPMSCs-CM could induce HepG2 cell cycle arrest. HepG2 cell growth was arrested in the G0/G1 phase following treatment with hPMSCs or hPMSCs-CM. These treatments also inhibited the migration of HepG2 cells with maximum effect when using the highest ratio/concentration of hPMSCs (70%) and hPMSCs-CM (90%). Our results suggested that hPMSCs and hPMSCs-CM will be promising candidates to treat liver cancer.

Recent Publications

1. F A Dain Md Opo, et.al, (2022): Comprehensive Studies of Different Cancer Diseases among Less-Developed Countries. Health-care (Basel) ;10(3):424
2. F A Dain Md Opo, et.al, (2021): Cytotoxicity Study of Cadmium-Selenium Quantum Dots (CdSe QDs) for Destroying the Human HepG2 Liver Cancer Cell. J Biomed Nanotechnol;17(11):2153-2164
3. F A Dain Md Opo, et.al, (2021): Structure based pharmacophore modeling, virtual screening, molecular docking and ADMET approaches for identification of natural anti-cancer agents targeting XIAP protein. Sci Rep ;11(1):4049.

Biography

F A Dain Md Opo is a Ph.D. Graduate at King Abdul-Aziz University in 2019. He is a member of the global collaborative research team based on the Novel Global Community Educational Foundation (NGCEF), Australia. Currently working in the cancer stem cell unit, King Fahd Medical Research Center from 2019. His research field includes stem cell biology, cancer biology, molecular biology techniques, animal handling (*in-vivo*), type 2 diabetes, cancer informatics, and Nano product modification for efficient drug delivery against cancer. His publication was included in several renowned journals (more than eight) from the beginning of his research career in 2014. He currently works on two projects, Stem cells effect against several cancers and the discovery of new natural compounds through EGFR targeting. His research interests are Stem cells, Cancer informatics, Cancer biology, Nano-products, and Cancer stem cell.

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The growing role of personalized and precision medicine (PPM): finding the right balance between precision medicine and personalized care to drive personalized & precision oncol-ogy (PPO) adoption and to get cancer cured

Sergey Suchkov

Institute for Global Health of MGUPP, Russia

A new systems approach to diseased states and wellness result in a new branch in the healthcare services, namely, personalized and precision medicine (PPM). To achieve the implementation of PM concept, it is necessary to create a fundamentally new strategy based upon the subclinical recognition of biomarkers (biopredictors) of hidden abnormalities long before the disease clinically manifests itself.

It would be extremely useful to integrate data harvesting from different databanks for applications such as prediction and personalization of further treatment to thus provide more tailored measures for the patients resulting in improved patient outcomes, reduced adverse events, and more cost-effective use of health care resources.

Individualizing patient treatment is a core objective of the medical field. Meanwhile, the inherent variability of cancer illustrating the molecular differences between tumors, securing the linkages of those differences to an effective drug and resulting in immense patient benefits, lends itself to the growing field of PPM.

Personalized cancer treatment in particular stands to highly benefit from PPM therapies, since extensive variability between tumors presents a need to target each case in a personalized manner.

At this point, personalized cancer therapy is considered to be a treatment strategy centered on the ability to predict which patients are more likely to respond to specific cancer therapies. This approach is founded upon the idea that cancer biomarkers are associated with patient prognosis and tumor response to therapy. And personalized tumor molecular profiles (tumor biomarkers can be OMICS-profiles that predict therapy response.), tumor disease site and other patient characteristics are then potentially used for determining optimum individualized therapy options.

We are entering an era of rapidly evolving transformation

in translational cancer research as it relates to PPM-related practice, and a shifting paradigm of standardized health care in which de-tailed molecular information regarding a patient's cancer is being used for individualized treatments. PPO describes a diverse set of strategies in cancer medicine tailored to the unique biology of a patient's disease. And strategies range from the use of targeted and/or smart therapies to the use of data from genomic profiling to select treatments independent of cancer type, and hence go beyond traditional organ-based oncology. Patients, healthcare systems, and economies all stand to benefit.

Meanwhile, a lack of medical guidelines has been identified by the majority of responders as the predominant barrier for adoption, indicating a need for the development of best practices and guidelines to support the implementation of PPM

Implementation of PPM and PPO, in particular, require a lot before the current model "physician-patient" could be gradually displaced by a new model "medical advisor-healthy person-at-risk". This is the reason for developing global scientific, clinical, social, and educational projects in the area of PPM to elicit the content of the new branch

Biography

Sergey Suchkov was born in the City of Astrakhan, Russia. In 1980, graduated from Astrakhan State Medical University and was awarded with MD. In 1985, maintained his PhD at the I.M. Sechenov Moscow Medical Academy and Inst of Med Enzymology. In 2001, and then his Doctor Degree at the Nat Inst of Immunology in Russia. From 1989 through 1995, was being a head of the Lab of Clin Immunology, Helmholtz Eye Research Inst in Moscow. From 1995 through 2004 - a Chair of the Dept for Clin Immunology, Moscow Clin Research Institute (MONIKI). In 1993-1996, was a Secretary-in-Chief of the Editorial Board, *Biomedical Science*, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK. Dr Suchkov is a member of the Editorial Boards of "Open Journal of Immunology", EPMA J., American J. of Cardiovascular Research and "Personalized Medicine Universe".

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Radiotherapy during lumpectomy (TARGIT-IORT): The least disruptive treatment for breast cancer patients, which can improve their length and quality of life

Jayant S Vaidya, Max Bulsara, Michael Baum and Jeffrey S

University College of London, UK

Breast cancer patients with early disease have traditionally had just two options lumpectomy (breast conservation), which invariably has to be followed by whole breast radiotherapy, or a mastectomy.

Unfortunately, for some patients, there hasn't really been a choice since postoperative radiotherapy requires repeated daily hospital visits for up to six weeks. Furthermore, whole breast radiotherapy is invariably accompanied by scattered irradiation of nearby vital organs (e.g. heart, lung) which can lead to heart attacks and cancer formation

We invented a new way to give radiotherapy during the lumpectomy operation and tested in a large international randomised TARGIT-A trial. Reported risk-adapted targeted intraoperative radiotherapy (TARGIT-IORT) during lumpectomy for breast cancer to be as effective as whole-breast external beam radiotherapy (EBRT).

Methods: 2298 women ≥ 45 years, invasive ductal carcinoma ≤ 3.5 cm, cN0–N1 were randomised in 32 centres in 10 countries in the United Kingdom, Europe, Australia, the United States, and Canada, to the EBRT arm, which consisted of a standard daily fractionated course (three to six weeks) of whole breast radiotherapy, or the TARGIT-IORT arm. TARGIT-IORT was given immediately after lumpectomy under the same anaesthetic and was the only radiotherapy for most patients (around 80%). TARGIT-IORT was supplemented by EBRT when postoperative histopathology found unsuspected higher risk factors (around 20% of patients). We also performed subgroup analyses

Results: With long term follow-up (median 8.6 years, maximum 18.90 years) no statistically significant difference was found for local recurrence-free survival (hazard ratio 1.13, 95% confidence interval 0.91 to 1.41, $P=0.28$), mastectomy-free survival (0.96, 0.78 to 1.19, $P=0.74$), distant disease-free survival (0.88, 0.69 to 1.12, $P=0.30$), overall survival (0.82, 0.63 to 1.05, $P=0.13$), and breast cancer mortality (1.12, 0.78 to 1.60, $P=0.54$).

Mortality from other causes was significantly lower (0.59, 0.40 to 0.86, $P=0.005$).

Local recurrence-free survival was no different between TARGIT-IORT and EBRT, in every tumour subgroup. Unlike in the EBRT arm, local recurrence in the TARGIT-IORT arm was not a predictor of a higher risk of distant relapse or death. Our new predictive tool for recommending supplemental EBRT after TARGIT-IORT is at <https://targetit.org.uk/addrtr>.

Overall survival at 12-years was significantly improved from 84.9% to 89.3% (mortality reduced by 28% in relative terms, 4.5% in absolute terms) in the large number ($n=1797$) of patients who had grade 1 or grade 2 cancers.

Conclusion: For patients with early breast cancer, risk adapted immediate single dose TARGIT-IORT during lumpectomy is an effective alternative to EBRT, with comparable long-term efficacy for cancer.

Recent Publications

1. Vaidya JS, Vaidya UJ, Baum M, Bulsara M, Joseph D, Tobias JS, et al. Global adoption of single-shot targeted intraoperative radiotherapy (TARGIT-IORT) to improve breast cancer treatment – better for patients, better for health care systems. UCL preprint 2021. <https://discovery.ucl.ac.uk/id/eprint/10121050/>
2. Vaidya JS, Bulsara M, Sperk E, Massarut S, Douek M, Alvarado M, et al. TARGIT-IORT during lumpectomy for breast cancer - better for patients than other PBI approaches. *Int j of radiation oncol, biol, physics* 2021. [https://www.redjournal.org/article/S0360-3016\(21\)00199-1/pdf](https://www.redjournal.org/article/S0360-3016(21)00199-1/pdf)
3. Vaidya JS, Bulsara M, Baum M, Wenz F, Massarut S, Pigorsch S, et al. New clinical and biological insights from the international TARGIT-A randomised trial of targeted intraoperative radiotherapy during lumpectomy for breast cancer. *British journal of cancer* 2021;125(3):380-89. <https://www.nature.com/articles/s41416-021-01440-8.pdf>

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Biography

Vaidya is a Professor of Surgery and Oncology at University College London specialising in the diagnosis and treatment of diseases of the breast. Professor Jayant Vaidya conducts ground-breaking research in breast cancer surgery, radiotherapy and oncology. He is a world-renowned

control, lower non-breast cancer mortality and significantly improved overall survival in those with grade 1 or 2 cancers who form the majority of cases. This is in addition to the obvious benefit of finishing the radiotherapy during the lumpectomy operation, greatly reducing hospital visits, reduced pain and improved cosmetic outcome and quality of life.

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An immuno-genomic atlas for cancer immunotherapy response

Qi Liu, Jing Yang and Yu Shyr

Vanderbilt University Medical Center, USA

An increasing number of studies on cancer immunotherapy have generated a huge amount of omics data and provided an unprecedented opportunity to identify response-related genomic signatures. However, those valuable datasets are not easily accessible to the research community. We established Cancer-Immu a comprehensive portal that connects large-scale multidimensional omics data with immunotherapy responses. Currently, Cancer-Immu has collected 3,652 patients for 16 cancer types, which provides a great resource for the discovery and validation of novel signatures predictive of response. Meta-analysis of 3,652 patients and single-cell RNA-seq highlights the importance of circuits between macrophage and T cells in immunotherapy sensitivity.

Recent Publications

1. Qi Liu, et.al, (2022): Interaction of lncRNA MIR100HG with hnRN-

PA2B1 facilitates m6A-dependent stabilization of TCF7L2 mRNA and colorectal cancer progression. *Molecular Cancer* 21 (1), 1-18

2. Qi Liu, et.al, (2022): Dysregulated Ligand-receptor interactions from single cell transcriptomics. *Bioinformatics*, 1–6.
3. Qi Liu, et.al, (2022): VAP-A and its binding partner CERT drive biogenesis of RNA-containing extracellular vesicles at ER membrane contact sites. *Developmental Cell* 57 (8), 974-994.

Biography

Qi Liu is an Associate Professor and Director of the Omics Coordinating Center at Vanderbilt University Medical Center for Quantitative Sciences, USA. She completed her PhD from Shanghai Jiaotong University, China in 2003. She has over 150 publications that have been cited over 7000 times, and her publication H-index is 36 and has been serving as an editorial board member of reputed Journals.

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Targeting the thromboxane A2 pathway suppresses Barrett's esophagus and esophageal adenocarcinoma development

Tianshun Zhang

University of Minnesota, USA

Esophageal adenocarcinoma (EAC) is a major cause of cancer-associated morbidity and mortality worldwide. Barrett's esophagus (BE), a complication of gastroesophageal reflux disease (GERD), predisposes patients to EAC. The discovery of potential drug targets is urgently needed for improved BE and EAC patient outcomes. Our previous study showed that cyclooxygenase-2 (COX2) and thromboxane A synthase (TBXAS) are highly expressed in BE and EAC patients accompanied by a pronounced elevation of circulating thromboxane A2 (TXA2) levels. Aspirin suppressed BE and EAC growth by targeting the TXA2 pathway. Additionally, biopsies from 49 patients (with similar baseline characteristics) showed that aspirin substantially decreased serum TXA2 levels, resulting in reduced inflammation. Our results showed that TXAS and TXA2 are correlated with the progression of BE and EAC. This study establishes the importance of the COX1/2-driven TXA2 pathway in BE and EAC pathophysiology and lays the groundwork for introducing a TXA2- targeting strategy for EAC prevention and early detection. Aspirin targets the TXA2 pathway and suppresses BE and EAC development. These findings drove us to study the role of TBXA2R (the receptor of TXA2) in the development of BE and EAC. We found that TBXA2R is highly expressed in BE and EAC patient biopsy samples. Knocking down the expression of TBXA2R markedly suppressed BE and EAC cell growth. Our goal is to establish

the TXA2 pathway as a novel target for preventing BE and EAC development. A novel TBXA2R inhibitor is a potential agent for the prevention and treatment of BE and EAC.

Recent Publications

1. Tianshun Zhang, et.al, (2021). Gastric tumorigenesis induced by combining *Helicobacter pylori* infection and chronic alcohol through IL-10 inhibition. *Carcinogenesis*. 43(2).
2. Tianshun Zhang, et.al, (2021). Prostaglandin Pathways: Opportunities for Cancer Prevention and Therapy. *Cancer Research*. 82. canres.2297.2021.
3. Tianshun Zhang, et.al, (2021). 229 Local and Systemic anti-inflammatory effects of Fatty acids in Barrett's esophagus patients: results from a randomized double-blind placebo-controlled trial. *Gastroenterology*. 160(6). S-48-S-49.

Biography

Tianshun Zhang received his PhD in Applied Chemistry in Bioscience from Kobe University, Japan. He currently works as a Senior Scientist at The Hormel Institute-University of Minnesota, USA. He focuses on identifying the mechanisms of cancer development or novel drug discovery for cancer prevention and treatment. He published his research in many prestigious journals including *Cancer Research*, *Theranostic*, and *EbioMedicine*, and is serving as guest editor of reputed Journals.

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Measles virus in classic Hodgkin lymphoma and additional cancers - A long lasting Saga

Daniel Benharroch

Soroka University Medical Center, Israel

The suggestion of a relationship between the measles virus and classic Hodgkin lymphoma was first presented by our laboratory in 2003. Four years later, our hypothesis was refuted conjointly by two European groups. However, reevaluation of the rebutting arguments allowed us to carry on with our line of research. By that time, we submitted evidence of associations between the measles virus and several further solid tumors, including lung and breast cancers. Modulation of apoptosis was later proposed as a possible mechanism in the oncogenesis of classic Hodgkin lymphoma. Measles virotherapy has been knowingly excluded from our discussion. Additional evidence has been compiled in the form of Western blots of lung cancers, and of a tissue micro-array in four categories of cancer. The possible role of atypical measles syndrome in cancer, which although a rare condition, is still prevalent, is discussed in the context of immune waning. Since measles virus and EBV expression were displayed in various combinations, we raise the possibility that their net consequences on tumor cell apoptosis in classic Hodgkin lymphoma, might originate from opposing effects from the two viruses.

Recent Publications

1. Daniel Benharroch, et.al, (2021): Transformation of low-grade follicular lymphoma with partial marginal zone differentiation: Two cases. Hematol Rep.13(3):8896.
2. Daniel Benharroch, et.al, (2021): A. Multiple Myeloma with Foamy Mott Cells. Case Rep Hematol. 2021:7391895.
3. Daniel Benharroch, et.al, (2020): Indirect formaldehyde exposure and the appearance of respiratory symptoms. Respir Med Case Rep.31:101166.

Biography

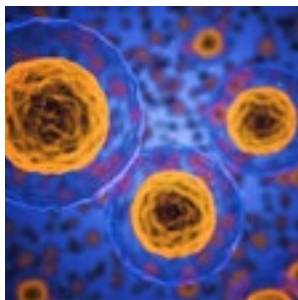
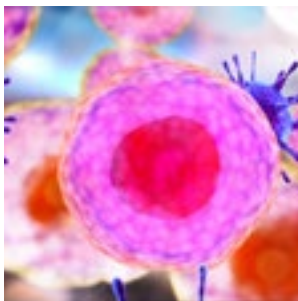
Daniel Benharroch is a Retired professor and an Independent Physician in the Department of Pathology, Soroka University Medical Center. He also served as a Faculty of Health Sciences, Ben Gurion University of the Negev, Israel. He has well experienced in his field and published many articles..

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Scientific Tracks & Sessions

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Cancer Summit 2022



18th International Conference on
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Stem Cell and Cancer Therapy | Cancer Treatment | Breast Cancer



Chair

Raghavan Rajagopalan

Daya Drug Discoveries | USA

Title: DDD-028: A potent, neuroprotective, non-opioid medication for the treatment of chemotherapy induced peripheral neuropathy (CIPN)

Raghavan Rajagopalan | Daya Drug Discoveries | USA

Title: Genetic and epigenetic remodeling of the tumor microenvironment to boost antitumor immunity

Jianmei Wu Leavenworth | University of Alabama at Birmingham | USA

Title: Immunoglobulin Light-Chain Partners: Key to high yields of recombinant monoclonal antibodies in transient transfection systems?

Ruth M Ruprecht | University of Louisiana | USA

Title: Personal therapeutic cancer vaccine: Autologous dendritic cells and antigens from autologous self-renewing cancer cells

Robert O Dillman | AIVITA Biomedical, Inc. | USA

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DDD-028: A potent, neuroprotective, non-opioid medication for the treatment of chemotherapy induced peripheral neuropathy (CIPN)

Raghavan Rajagopalan¹, Parthasarathi Rajagopalan¹, Lorenzo Di Cesare Mannelli², Laura Micheli², Alessandra Pacini², Donatello Carrino², Carla Ghelardini² and Ghelardini²

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²University of Florence, Italy

Chemotherapy induced peripheral neuropathy (CIPN) is a painful and major dose-limiting side effect of cancer treatment that can interrupt or lead to discontinuation of therapy. Current CIPN medications, including *oxycodone* and *duloxetine*, relieve pain but have no effect on underlying CNS tissue damage. Disease modifying medications to treat CIPN as well as other neuropathies remains a critical unmet need, and our extensive work on pentacyclic *pyridoindole* scaffolds resulted in the identification of DDD-028 (1) for the treatment of CIPN. DDD-028 displays potent analgesic activity CIPN and other well-accepted models of neuropathy. DDD-028 displays no activity at any of the key off-target receptors, including opioid, cannabinoid, NMDA, or dopamine receptors. Chronic administration of paclitaxel along with DDD-028 over an 18-day period demonstrated that DDD-028 is exerting a prophylactic effect against CIPN. Plasma neurofilament assay and intraepidermal nerve fiber (iENF) density demonstrated that DDD-028 is neuroprotective. Histopathological analysis of tissues from the spinal cord and the key areas of the brain involved in pain sensation indicates that DDD-028 is preventing astrocyte proliferation and damage. DDD-028 is well tolerated in all of the tests and does not induce sedation in any

of the animals tested.

Recent Publications

1. Raghavan Rajagopalan (2021): Pain Relieving and Neuroprotective Effects of Non-opioid Compound, DDD-028, in the Rat Model of Paclitaxel-Induced Neuropathy. *Neurotherapeutics*. 18(7).
2. Raghavan Rajagopalan (2013). The synthesis and comparative receptor binding affinities of novel, isomeric pyridoindolobenzazepine scaffolds: *Bioorg Med Chem Letter*; 24(2):576-9

Biography

Raghavan Rajagopalan has over 35 years of experience in diagnostic and therapeutic drug discovery and developmental research. He has considerable medicinal chemistry expertise in oncology, nephrology, and pain, focusing on radiotherapy and phototherapy. He has made a pioneering contribution to Type 1 phototherapy of tumors. He was principally responsible for IND and NDA applications for 4 drug candidates, of which one is in the market and the other is undergoing Phase 2 clinical trials. In addition to his research work, he is a Registered Patent Agent with the United States Patent & Trademark Office. He has over 100 patents and 30 publications, of which four are pioneering works in oncology, pain, and nephrology.

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Genetic and epigenetic remodeling of the tumor microenvironment to boost anti-tumor immunity

Jianmei Wu Leavenworth

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The tumor microenvironment is highly immunosuppressive, often attributing to the activity of subsets of suppressor cells that inhibit anti-tumor effector T-cells. Effective approaches to cancer immunotherapy, such as checkpoint inhibitors, depend on reviving the immunosuppression while boosting the effector cell activity. We have recently defined a new mechanism by which the genetic deletion of a transcription factor in immunosuppressive regulatory T-cells reprograms these cells into effector cells, which cooperate with both cellular and humoral anti-tumor components to control tumor growth. We have also discovered that the ablation of an epigenetic modifier in tumor cells reshapes the tumor microenvironment and enhances anti-tumor immunity, depending on the collaborative action of natural killer cells and CD4+ T-cells. Insights from these studies will facilitate the identification of new therapeutic targets, and provide critical strategies to develop novel cancer immunotherapies.

Recent Publications

1. Jianmei Wu Leavenworth, et.al, (2022). Immune Activity and Response Differences of Oncolytic Viral Therapy in Recurrent Glioblastoma: Gene Expression Analyses of a Phase IB Study. *Clinical cancer research: an official journal of the American Association for Cancer Research*. 28. 498-506.

2. Jianmei Wu Leavenworth, et.al, (2022). Editorial: Immune Cell Lineage Reprogramming in Cancer. *Frontiers in Immunology*. 12.838464
3. Jianmei Wu Leavenworth, et.al, (2021). Remodeling of the tumor microenvironment via disrupting Blimp1+ effector Treg activity augments response to anti-PD-1 blockade. *Molecular Cancer*. 20(1).

Biography

Jianmei Wu Leavenworth is an Associate Professor in the Department of Neurosurgery at the University of Alabama at Birmingham. Previously, she was at the Dana-Farber Cancer Institute and Harvard Medical School serving as a postdoctoral fellow and then as an instructor. Her research has been published in many prestigious journals, including *Nature Cancer*, *Molecular Cancer*, *Nature Immunology*, *Cell Reports*, *Proceedings of the National Academy of Sciences of the United States of America*, and *Journal of Clinical Investigation*. She has also been serving as a reviewer and editor for many reputed journals.

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Immunoglobulin Light-Chain Partners: Key to high yields of recombinant monoclonal antibodies in transient transfection systems?

Ruth M Ruprecht
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In the 1990s, the first monoclonal antibodies (mAbs) were Food and Drug Administration (FDA) approved as cancer therapies. Since then, this field has expanded rapidly. The initially approved mAbs are IgGs. Clinical trials have been performed with IgM mAbs. Recombinant mAb technology cannot only generate IgG mAbs, but also mAbs of other immunoglobulins (Ig) classes, including recombinant IgM and dimeric IgAs (dIgAs). Our group has systematically examined the potential of recombinant mAbs of different Ig classes to block mucosal transmission of simian-immunodeficiency virus (SHIV) in nonhuman primates and used it as a model system for blocking mucosal human immunodeficiency (HIV-1) transmission in humans.

Generation of polymeric recombinant mAbs can present technical challenges. When constructing isogenic recombinant IgM/IgG pairs, we discovered that mu (μ) heavy chains strongly prefer partnering with lambda (λ) light chains for optimal IgM expression in a transient cotransfection system. When μ chains were paired with kappa (κ) light chains, IgM yields were low but increased by logs – up to 20,000 X – by using λ chains instead. Switching light chains did not alter epitope specificity. For dIgA2, optimal expression involved pairing with λ chains, whereas light chain preference varied for other Ig classes. In summary, the production of recombinant IgM can be markedly increased by using λ chains, an important aspect of clinical studies.

Recent Publications

1. Ruth M Ruprecht, et.al, (2022). Antibody light chains: key to increased monoclonal antibody yields in Expi293 cells?. *Antibodies*; 11(2):37.
2. Ruth M Ruprecht, et.al, (2021). Cooperation between systemic IgG1 and mucosal dimeric IgA2 monoclonal anti-HIV Env antibodies: passive immunization protects Indian rhesus macaques against mucosal SHIV challenges. *Frontiers Immunology*; 12:705592.
3. Ruth M Ruprecht, Siqi Gong, (2020). Immunoglobulin M: an ancient antiviral weapon – rediscovered. *Front Immunol*; 11:1943

Biography

Ruth Ruprecht completed her PhD at Columbia University, USA, and her MD at the University of Miami School of Medicine, USA; she is board-certified in Internal Medicine and Medical Oncology. She served as a tenured Professor of Medicine at the Dana-Farber Cancer Institute and Harvard Medical School and is currently a Senior Professor of Research at the University of Louisiana at Lafayette, USA. She has published more than 200 peer-reviewed papers (cited more than 13,000 times); her publication H-index is 57. She is the inventor of several patents, including a cancer vaccine approach. She has been serving as a Member of Scientific Advisory Boards, as an Associate Editor/Editorial Board Member of highly regarded Journals, and as a Consultant for WHO and pharmaceutical companies. She has received a number of honors, including being named Honorary Professor of the Institute of Medical Biology at the Chinese Academy of Medical Science at Peking Union Medical College, Kunming, PRC

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Personal therapeutic cancer vaccine: Autologous dendritic cells and antigens from autologous self-renewing cancer cells

Robert O Dillman

AIVITA Biomedical, Inc., USA

AIVITA Biotechnology has a platform technology for patient-specific therapeutic anti-cancer vaccines. Each vaccine is unique in that the tumor antigens are derived from self-renewing autologous tumor cells (cancer stem cells and progenitor cells) to address challenges and limitations that result from tumor initiating cells and interpatient tumor heterogeneity, which limit the efficacy of existing therapies. Each vaccine product is “personal” rather than “personalized.” Short-term autologous tumor cell lines are now established reliably from fresh tumor samples, and dendritic cells are reliably differentiated from peripheral blood mononuclear cells (PBMC). Personal DC-ATA (dendritic cells-autologous tumor antigens) can now be manufactured and released within three weeks of collection of tumor and PBMC. Each dose is admixed with granulocyte-macrophage colony-stimulating factor (GM-CSF) prior to injection. For now, ideal patients are those with cancers for which surgery continues to be a major component of treatment for advanced diseases, such as hepatocellular cancer, renal cell cancer, metastatic melanoma, ovarian cancer, glioblastoma (GBM), soft tissue sarcomas, and cancers that metastasize to skin, liver, lung, and brain. To date, 186 patients have received 1200 subcutaneous injections of personal DC-ATA. Key observations include confirmation of feasibility for collection of tumor and PBMC and shipping of vaccine doses to distant sites in multicenter trials; safety in various clinical settings including concurrently with other anti-cancer therapies and in the setting of hepatitis-B viral infection; delayed objective complete tumor regression in some patients with measurable disease at the time of treatment, prolonged progression-free survival compared to historical controls in GBM, and prolonged overall survival in melanoma compared to historical controls and to an autologous tumor cell vaccine in a randomized trial. This presenta-

tion will review the evolution of these personal therapeutic cancer vaccines and the results from various clinical trials.

Recent Publications

1. Robert O Dillman, et.al, (2020): Insights from immuno-oncology: the Society for Immunotherapy of Cancer Statement on access to IL-6-targeting therapies for COVID-19, *J Immunother Cancer*; 8(1).
2. Robert O Dillman, et.al, (2020): Cytokine network analysis of immune responses before and after autologous dendritic cell and tumor cell vaccine immunotherapies in a randomized trial, *J Transl Med*; 18(1):176
3. Robert O Dillman, et.al, (2020): Genomic, proteomic, and immunologic associations with a durable complete remission of measurable metastatic melanoma induced by a patient-specific dendritic cell vaccine, *Hum Vaccin Immunother*; 16(4):742-755

Biography

Robert O Dillman, M.D. is Chief Medical Officer, AIVITA Biomedical Inc., Irvine, CA., and Clinical Professor of Medicine, University of California Irvine. Since 2000 his research has focused on patient-specific therapeutic cancer vaccines consisting of autologous dendritic cells loaded with tumor antigens from cultures of self-renewing autologous tumor initiating cells. He did pioneering work in biotherapy including human clinical trials with monoclonal antibodies and autologous cellular immunotherapies. For over 20 years he directed a bench-to bedside translational cell biology laboratory specializing in patient-specific cell-based therapies. He was a principal investigator for Cancer and Leukemia Group B, Cancer Biotherapy Research Group Chairman, and a founding member and former president at the Society for Immunotherapy of Cancer (SITC). He has authored over 300 publications. He trained in Internal medicine at Baylor, and hematology/oncology at the University of California San Diego, with board certification in the above specializations. He earned M.D. from Baylor College of Medicine, and a B.A. from Stanford University.

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