UPSTATE CANCER CENTER

2024 ANNUAL RETREAT

APRIL 26 · 8 A.M.–6 P.M.

CNY BIOTECH ACCELERATOR
841 EAST FAYETTE STREET, SYRACUSE
Shuttle Transportation Will Be Available

AGENDA

- Introductory remarks by University and Cancer Center leadership
- Progress reports from research programs and committees
- Recognition of the Upstate Foundation for supporting the Cancer Center Research Program
- Morning Scientific Session – Focus on Basic and Translational Research
- Baldwin Distinguished Lecture, Suzanne Conzen, M.D., University of Texas Southwestern Medical Center: Context-dependent role of glucocorticoid receptor in breast cancer subtypes
- Presentation of Beth Baldwin Oncology Nursing Award
- Lunch break and poster viewing
- Afternoon Scientific Session I – Presentations by 2023 Pilot Grant Awardees
- Afternoon Scientific Session II – Focus on Clinical and Public Health Research
- Announcement of 2024 Pilot Grant Awards
- Closing remarks
- Poster session and reception

To register, visit redcap.link/2024_CCRetreat_registration or use this QR code:

UPSTATE CANCER CENTER

Upstate Cancer Center
2024 Annual Retreat

April 26, 2024, 8am-6pm,

CNY Biotech Accelerator, 820 E. Fayette St., Syracuse NY 13210

Agenda

8:00 - 9:00 Opening Session

Welcoming Remarks (8-8:35) – Introductions by Dr. van der Meer

- 8:00 - Thomas van der Meer, M.D., FACS Upstate Cancer Center Interim Director
- 8:05 - Mantosh Dewan, M.D., President, Upstate Medical University
- 8:10 - David Amberg, Ph.D., Vice President for Research
- 8:20 - Recognition of Upstate Foundation for Support of Cancer Center Research Programs, remarks by Eileen Pezzi, MPA, Vice President for Development, Upstate Medical University and Executive Director of The Upstate Foundation, Inc.


Thomas van der Meer, M.D.


Mantosh Dewan, M.D.


David Amberg, Ph.D.


Eileen Pezzi, MPA

Research Program Reports 8:40-9:00 – *Introductions by Dr. Kotula*

- 8:40 - Research director, Leszek Kotula, M.D., Ph.D.
- 8:45 - Cancer Genetics and Cell Biology – Mariano S. Viapiano, Ph.D., Program Director
- 8:50 - Cancer Prevention, Survivorship, and Population Health – Christopher Morley, Ph.D, MA
- 8:55 - Communications Committee - Jason Horton, Ph.D., Communications Committee Chair


Leszek Kotula, M.D., Ph.D.


Mariano Viapiano, Ph.D.


Christopher Morley, Ph.D, MA


Jason Horton, Ph.D.

9:00 - 10:30 Morning Scientific Session – *Moderated by Dr. Viapiano*
Oral presentations selected from abstracts focused on Basic and Translational Science topics. 12min+3min discussion.

- 9:00 – Podium 1: "*Unraveling MLL1-fusion Leukemia: Epigenetic Revelations from an iPS Cell Point Mutation*" Michael Cosgrove, Ph.D.
- 9:15 – Podium 2: "*mTOR Activation and Blockade in Checkpoint Inhibitor-Induced Autoimmune Diseases (CIAD)*" Andras Perl, M.D., Ph.D.
- 9:30 – Podium 3: "*Reshaping Current Practices in Pathology using Computational Tools and Artificial Intelligence*" Tamara Jamaspishvili, M.D., Ph.D.
- 9:45 – Podium 4: "*Immunomodulatory Telodendrimer Nanomedicine in Treating Ovarian Cancer*" Juntao Luo, Ph.D.
- 10:00 – Podium 5: "*Targeting Hypoxia-Inducible Factor-2 Alpha in Kidney Cancer*" Jennifer Heritz, Ph.D, candidate.
- 10:15 – Podium 6: "*Development of ABI1 as biomarker to monitor prostate cancer ADT- and enzalutamide-resistance.*" Leszek Kotula, M.D., Ph.D.

10:30-11:00 Coffee Break/Poster viewing

11:00- 12:15 Carol M. Baldwin Distinguished Lecture *Introduction by Dr. Kotula*

- Suzanne Conzen, M.D. University of Texas Southwestern Medical Center.
  "*Context-dependent role of glucocorticoid receptor in breast cancer subtypes*"

The 2024 Endowed Lectureship is given in honor and memory of Elizabeth (O'Hara) Formoza. Elizabeth was from a large family, and with the love of her life Craig in 2005 raised four children Evie and Ella (2006), Jack (2008), and Emma (2011). Liz was diagnosed with breast cancer when Emma was just a few months old. After undergoing a double mastectomy and subsequent treatment, Liz beat her cancer and worked to keep herself healthy with diet exercise and mindfulness. Sadly, like so many, her cancer came back in 2016 and she bravely fight once again. She was treated at Upstate Cancer Center and the Dana-Farber Institute in Boston. She underwent treatment while raising four young children always trying to keep life as normal as possible for them with the help of a few amazing doctors, friends and family. What was most important to her was protecting her kids from worry and fear, which she did well also working a full-time job as a real estate agent and being a spectacular mother wife sister daughter and friend. In 2019, her doctors informed her that her chemotherapy was no longer working and that she should prepare for hospice care. She fought hard and lived life to the fullest with her family on the borrowed time her treatment gave her. We lost her in February 2020, but not before we could have a proper celebration of her phenomenal life. She was kind, loyal, honest, funny, generous, and fiercely loving. All of her best qualities can be seen in Craig family they created together. Thank you for honoring a life well lived.

Carol M. Baldwin Foundation Distinguished Lecturer

Suzanne D. Conzen, M.D.

The University of Texas Southwestern Medical Center

"Context-Dependent Role of Glucocorticoid Receptor in Breast Cancer Subtypes."

The Carol M. Baldwin Foundation and The Upstate Cancer Center are proud to welcome Dr. Conzen as to our retreat as our distinguished lecturer. She is a Professor in the Department of Internal Medicine and Chief of the Division of Hematology and Oncology, and Andrea L. Simmons Distinguished Chair in Cancer Research at UT. She specializes in the diagnosis and treatment of breast cancer. An established physician-scientist with multiple National Cancer Institute grants, Dr. Conzen's research focuses on the role of the glucocorticoid receptor in prostate, breast, and ovarian cancers. She will be speaking on her research focused on mechanisms of glucocorticoid receptor activity in breast, prostate, and ovarian cancer.

Dr. Conzen notes, "I am a physician-scientist and breast medical oncologist who leads an NIH-funded laboratory studying mechanisms of tumor initiation and progression. My laboratory identified glucocorticoid receptor (GR) signaling as a pathway involved in tumor progression. These findings have led to clinical trials examining antagonism of GR–mediated tumor cell survival pathways in breast, ovarian, pancreatic and prostate cancer."

At UTSW, Dr. Conzen established a program to integrate mentoring and training of basic and clinical blood disorder and cancer trainees. Her laboratory uses both animal modeling and molecular approaches to study GR signaling contributing to the development and progression of cancer. Current projects include (1) understanding how GR-mediated stress physiology (following androgen deprivation) drives prostate cancer and in breast cancer, produces divergent effects in ER+ versus ER- breast cancer through nuclear receptor crosstalk; (2) defining tumor cell intrinsic GR signaling pathways that mediate immune cell interactions; and (3) using ChIP-sequencing to determine how novel GR modulators alter chromatin association and subsequent gene expression in tissue-specific contexts.

Dr. Conzen's team was the first to bring GR antagonism to clinical trials, in collaboration with colleagues Drs. Nanda & Fleming (breast/ovarian) and Szmulewitz (prostate cancer). As a result of these discoveries, she has led several multidisciplinary projects, including two Challenge Awards from the Prostate Cancer Foundation, a Chicago Prostate Cancer SPORE Project and a P50 (Center for Interdisciplinary Health Disparities Research) Project.

- **12:00-12:15 Beth Baldwin Oncology Nursing Award** *Presented by Beth Baldwin and Dr. van der Meer* to *Lauren Calloway BSN, RN, ONC,* in recognition of her contributions to patient care and oncology nursing.

12:15-1:30 Lunch/Poster Viewing

1:30 - 3:00 – Afternoon Scientific Session – *Moderated by Stephen Graziano, M.D.*
Oral presentations selected from abstracts focused on Clinical, Public Health and Population Studies.

- 1:30 – Podium 7: "*State of Clinical Trials at Upstate*" Stephen Graziano, M.D.
- 1:45 – Podium 8: "*Predictors and patterns of complementary and integrative health therapy use among individuals with recent and non-recent cancer diagnoses: A national cross-sectional study*" Jamie Romeiser, MPH, Ph.D.
- 2:00 – Podium 9: "*Clinical-genomic Characterization Unveils More Aggressive Disease Features in Elderly Prostate Cancer Patients with Low-grade Disease*" Hanan Goldberg, M.D.
- 2:15 – Podium 10: "*Comparative survival after neoadjuvant vs adjuvant systemic therapy in resectable stage II and stage III non-small cell lung cancer: A retrospective study using the National Cancer Database*" Ghanshyam Ghelani, M.D.
- 2:30 – Podium 11: "*Investigating the Tumor Environment and Signalling Dependencies in Diffuse Midline Glioma: A Comprehensive Approach Leveraging Bulk Multiomics Deconvolution and Single-Cell Omics Validation*" Palak Patel, Ph.D.
- 2:45 – Podium 12: "*Study of Pathogenic Variants in CHEK2: Association with Breast Cancer Clinical Features and Family History of Cancers for the Optimization of Management and Surveillance*" Gloria Morris, M.D.

3:00-3:30 – Coffee Break/Poster Viewing

3:30-4:30: Cancer Center Pilot Grant Awards Moderated by Lesek Kotula, M.D., Ph.D.

- 3:30 – Podium 13: "*The role of NKG2D receptor and Ligands in Triple-Negative Breast Cancer (TNBC) relapse*" Mobin Karimi, Ph.D.
- 3:40– Podium 14: "*Phosphorylation of TRAP1 by the tyrosine kinase c-Abl drives pro-survival signaling in renal cell carcinoma*" Mark Woodford, Ph.D.
- 3:50 – Podium 15: "The neuroendocrine factor VGF provides paracrine support for glioma growth and is a circulating marker of tumor burden" Mariano Viapiano, Ph.D.
- 4:00 – Podium 16: "*Establishment of a microfluidic platform to model physiology of human tumors and normal tissues*" Jason Horton
- 4:10 - Podium 17 "*Development and Analysis of a Single-Center, Retrospective Research Cohort of Intermediate, High-Very High Risk, and Metastatic Prostate Cancer"* Jonathan Bearden
- 4:20 - Young Clinical Investigator Award Presentation "*A Meta-Analysis Analyzing The Efficacy Of Trastuzumab-Deruxtecan (T-Dxd) On Central Nervous System (CNS) Disease In Metastatic Breast Cancer (Mbc) Patients."* Prashant Ashok Kumar, M.D.; introduced by Alina Basnet, M.D.

4:30: Closing Remarks by Lesek Kotula, M.D., Ph.D.

4:30-6:00 Poster Presentations and Reception
Wine & Cheese reception and Poster presentations selected from submitted abstracts.

Abstracts

1. Does Race Impact Survival Outcome In Premenopausal Hormone Positive (HR+) Breast Cancer (BC) Patients With A Low Genomic Risk. A National Cancer Database (NCDB) Analysis.

Ashok Kumar, Prashanth; Huang, Danning ; Wang, Dongliang; Sivapiragasam, Abirami.

SUNY Upstate Medical University, Division of Hematology/Oncology and Department of Biostatistics; Medical University of South Carolina, Department of Hematology-Medical Oncology

Background: It is hypothesized that in African American (AA) women, Oncotype DX Breast Recurrence Score (RS) has a lower prognostic accuracy. We evaluated this with a large population based national database. Methods: The 2021 NCDB PUF was used to include premenopausal female BC patients aged 18-50 years. Inclusion criteria were N0, M0 patients with any T stage, RS ≤ 15 or MP low risk, estrogen or progesterone receptor+ and HER2-. Patients were stratified by their recorded race (Caucasians vs AA). Univariate analysis was used to study the distribution. Kaplan-Meier (KM) and multivariate (MV) propensity score (PS) weighted Cox model were used to compare survival between the cohorts. Results: 27523 patients had an RS≤15 [Caucasian-25227(91.66%) AA-2296(8.34%)] and 4818 had MP low [Caucasian-4393(91.18%) AA-425(8.82%)]. >99% had regional lymph node surgery and >90% of the patients definitively did not get chemotherapy. >70% of the patients were T1. Majority did get hormonal therapy (HT) [RS≤15 Caucasian-92.97% AA-91.81%, MP low- Caucasian-92.42% AA-89.65%]. On analyzing grade, AA had more poorly differentiated tumors [RS≤15 Caucasian-6.18% AA-9.46% p=<0.001 MP low- Caucasian-9.1% AA-16.02% p=<0.001]. There were more AA patients with an income <$48000 [RS≤15 Caucasian-25.64% AA-51.15% p=<0.001 MP low- Caucasian-29.66% AA-52.57% p=<0.001]. KM survival estimates for RS≤15 at 5 years [Caucasian-99.3(99.2,99.5) %, AA-98.8(98.0,99.3) %] were similar and 10 years [Caucasian-97.5(97.0,97.9) %, AA-94.6(91.6,96.6)] showed a small difference. For MP low, the survival at 5 years [Caucasian- 99.0(98.6,99.3) %, AA-98.9(97.0,99.6) %] and 10 years [Caucasian- 97.0(95.9,97.8) %, AA-95.8(91.0,98.1) %] were almost equal. Adjusted Hazard Ratio estimate for Caucasian vs AA for RS≤15 did not reach significance overall [0.802 (95% CI 0.47-1.37)] nor when stratified by grade, histology, or T stage. Conclusions: Through our analysis, we show that there was no major difference in overall survival between Caucasians and AA among low genomic risk, premenopausal, hormone positive, N0 BC patients. There was a 2.9% difference between the racial groups at 10 years in the RS ≤ 15 group, but this was not seen in the adjusted analysis. The results show that genomic scores like RS and MP retain their prognostic utility even in the low-risk spectrum in both Caucasians and AAs. These results differ from other database studies.

2. A Meta-Analysis Analyzing The Efficacy Of Trastuzumab-Deruxtecan (T-Dxd) On Central Nervous System (CNS) Disease In Metastatic Breast Cancer (Mbc) Patients.

Ashok Kumar, Prashanth; Sandhu, Michael; Metapalli, Sravanthi Venkata ; Desai, Devashish; Suresh Kumar, Vishnu; Benjamin, Sam.

SUNY Upstate Medical University, Division of Hematology/Oncology and Departments of Internal Medicine and Gastroenterology

Background: CNS metastasis from BC portends a poor prognosis. While, T-DXd has demonstrated durable CNS activity, clinical trials with large cohorts are unavailable. We sought to analyze CNS activity of T-DXd through a meta-analysis. Methods: A systematic search with terms encompassing BC and T-DXd was conducted in PubMed, Embase, Scopus, and Cochrane/Central on November 23, 2023. There were no search restrictions on date, language, or type of study. A total of 2318 records were identified, and duplicates were removed using Mendeley 1.19.8. 1189 records that remained were imported into Rayyan, and the titles were screened independently by 2 reviewers. 47/75 full texts were relevant, of which 12 [7 clinical trials and 5 retrospective study] were included for analysis. Only studies that provided stratified CNS response data for mBC were included. RevMan was used to analyze the Risk Ratio (RR) and Odds Ratio (OR) with 95% Confidence Interval (CI), derived from random effects (RE) model with Mantel-Haenszel (MH) method. Binary RE pooled proportions (PP) using DerSimonian-Laird method were determined using OpenMeta. Visual inspection of our funnel plots revealed no publication bias. Results: The T-DXd cohort had a total of 377 patients with a median age of 54.2 years (42.5-69). Control group (T-DM1-1, Chemotherapy-2 studies) had 86 patients with a median age of 54.5 years (54.2-54.7). All studies had previously treated patients and most of the patients received local therapy. PP with T-DXd for CNS complete response (CR) was 4.8% (2-7.6%). Partial response was 50.1% (32.4-67.7%) and stable disease was 28.9 (20.5-37.3%). PP of objective response rate (ORR) (CR+PR) was 60.9% (48.3-73.5%). Drug discontinuation rate was 18% (12.2-23.9%) and pneumonitis rate was 14.5% (9.4-19.6%). RR for Event/Progressive disease (PD) comparing T-DXd and control group was not significant [0.96 (0.77,1.2) p=0.74, I^2=0%], nor was OR for disease control rate (DCR) (CR+PR+SD) [1.11 (0.63,1.96) p=0.64, I^2=0%] (Table). The median progression free survival (PFS) was 14.1 (8.5-18.1) months for the T-DXd and 4.3 (3-5.6) months for the control group. Conclusions: Although direct comparison between the pooled T-DXd and control group failed to reveal a difference, the pooled ORR from 10/12 studies was clinically significant at 60.9%. The median PFS for T-DXd was also longer. T-DXd could be a viable treatment option for pretreated HER2+ and low mBC with CNS metastasis.

3. A Meta-Analysis Studying The Difference In Response To Trastuzumab-Deruxtecan (T-Dxd) Based On HER2 Immunohistochemistry (IHC) Staining In HER2 Low Metastatic Breast Cancer (Mbc) Patients.

Ashok Kumar, Prashanth; Sandhu, Michael; Venkata Metlapalli, Sravanthi; Suresh Kumar, Vishnu; Benjamin, Sam.

SUNY Upstate Medical University, Division of Hematology/Oncology and Departments of Internal Medicine and Gastroenterology

Background: HER2 low BC are tumors with an IHC staining of 1+ or 2+ with negative fluorescence in situ hybridization (ISH). Although T-DXd is approved for HER2 low mBC, difference in activity between 1+ and 2+ is uncertain. Methods: A systematic search with controlled vocabulary encompassing BC and T-DXd was conducted in PubMed, Embase, Scopus, and Cochrane on November 11, 2023. There were no search restrictions. 2318 records were identified, and duplicates were removed using Mendeley 1.19.8. The remaining 1189 records were imported into Rayyan, and the titles were screened independently by 2 reviewers. 47/75 full texts were relevant, of which 4 [3 clinical trials and 1 retrospective study] were included for analysis. Only studies that provided outcome data for HER2 1+ and 2+ ISH- were included. RevMan was used to analyze the Risk Ratio (RR) and Odds Ratio (OR) with 95% Confidence Interval (CI), derived from random effects (RE) model with Mantel-Haenszel (MH) method. Pooled proportions (PP) were determined using OpenMeta. Results: There was a total of 264 patients in 1+ and 204 patients in 2+ISH-. The median age was 57 years. All studies had previously treated mBC and encompassed all hormone receptor statuses. T-DXd dose was at least 5.4 mg/kg every 3 weeks. Visual inspection of our funnel plots revealed no publication bias. PP (3/4 studies) for patients achieving an Objective Response Rate (ORR) [Complete Response (CR)+Partial Response (PR)] was 42.9% (31.6-54.2%) in 1+ and 38% (26.3-49.7%) in 2+. The median progression free survival (PFS) (2/4 studies) was 8.6 and 7.95 months for 1+ and 2+ respectively. RE RR (3/4 studies) for PD showed no difference between 1+ and 2+ [0.93 (0.80, 1.10), p=0.4, I^2=0%]. Similarly, RE OR (3/4 studies) for parameters like disease control rate (DCR) [CR+PR+Stable disease (SD)] [1.20 (0.78, 1.85), p=0.41, I^2=0%], ORR [1.17 (0.58, 2.34), p=0.66, I^2=0%], and PR [1.05 (0.52, 2.11), p=0.89, I^2=0%] showed no significant difference between 1+ and 2+. Conclusions: Our results indicate no difference in response to T-DXd between 1+ and 2+, solidifying its role as a treatment option in HER2 low mBC, which constitute >50% of BCs. Limited number and heterogeneity between studies are limitations of our analysis, which ought to be addressed in future trials though clear subgroup stratification between 1+ and 2+.

4. Selective Inhibition Of Protein Phosphatase-5 As A Therapeutic Strategy In Renal Cancer

Backe, Sarah; Heritz, Jennifer; Sager, Rebecca; Ahanin, Elham; Dushukyan, Natela; Daneshvar, Michael; Chisholm, John; Bratslavsky, Gennady; Woodford, Mark; Bourboulia, Dimitra; Mollapour, Mehdi.

SUNY Upstate Medical University, Departments of Urology and Biochemistry & Molecular Biology; University of California, Irvine, Department of Urology; Syracuse University, Department of Chemistry

Over 81,000 people will develop kidney cancer, also known as renal cell carcinoma (RCC), and almost 15,000 patients will die from this disease in the US this year. Traditional radiation and chemotherapy treatments are ineffective causing ~50% of patients develop metastatic disease, for whom the 5-year survival rate is only ~10%. Such grim statistics point to an urgent need for deeper understanding of the RCC biology and also for developing better therapeutic strategies. Our previous work has shown that downregulation of Protein Phosphatase-5 (PP5) caused induction of apoptosis in clear cell renal cell carcinoma (ccRCC), the most common type of RCC. Here we demonstrated that PP5 interacts with FADD, RIPK1 and caspase 8, components of the extrinsic apoptotic pathway complex II. Specifically, PP5 dephosphorylates and inactivates the death effector protein FADD, preserving complex II integrity and regulating extrinsic apoptosis. We therefore used an in silico approach to screen and develop a selective inhibitor of PP5. Compound P053 is a competitive inhibitor of PP5 that binds to its catalytic-domain and causes apoptosis in renal cancer. Our data suggests that PP5 promotes renal cancer survival by suppressing the extrinsic apoptotic pathway which can be reversed by pharmacologic inhibition of PP5. P053 activates the extrinsic apoptotic pathway, presenting a viable therapeutic strategy for renal cancer.

5. Primary Sarcoma Of Prostate: A Genomic Landscape Study

Batayneh , Osama ; Jacob, Joseph; Bratslavsky, Gennady; Spiess, Philippe; Kamat, Ashish; Grivas, Petros; Necchi, Andrea; Ross, Jeffrey; Cheng, Liang; Basnet , Alina.

SUNY Upstate Medical University, Division of Hematology/Oncology and Department of Urology; H. Lee Moffitt Cancer Center and Research Institute, Department of Hematology and Medical Oncology; The University of Texas MD Anderson Cancer Center, Department of Hematology and Medical Oncology; University of Washington & Fred Hutchinson Cancer Center, Division of Hematology & Oncology; Vita-Salute San Raffaele University, IRCCS San Raffaele Hospital Milan, Italy, Department of Hematology and Medical Oncology; Brown University, Department of Hematology and Medical Oncology

Background: Primary sarcoma of prostate is exceedingly rare and not well-studied. We sought to describe the genomic landscape of this rare entity and identify potential therapy targets. Methods : From 19,057 cases of prostate cancers, only 11 (< .01%) cases of primary sarcomas were identified and underwent comprehensive genomic profiling (CGP) using FDA-approved hybrid capture-based system to assess all classes of genomic alterations (GA). Genomic-based ancestry, genomic signature, gLOH , MSI and TMB status were determined by CGP. Germline status was predicted using a Somatic-Germline-Zygosity algorithm. PD-L1 expression was determined by IHC (Dako 22C3 TPC scoring). Results : The routine histology and IHC stains from all 11 cases were reviewed centrally. There were 9 stromal sarcomas, and 1 each leiomyosarcoma and rhabdomyosarcoma. All patients(median age 57) were clinically advanced stage at the time of CGP. The primary tumor site was used in 6 patients and metastatic sites (3 bone, 1 ureter and 1 lung metastasis) in 5 patients. The mean number of GA per case was 2.3 (1 to 4 GA/sample). The most frequent GA were in TP53 (36.4%), RB1 (27.3%), ATRX (18.2%). Potentially targetable GA were rare and included MTOR pathway inhibitors for GA in TSC2 and PTEN (1 case each) and PIK3CA inhibitors (GA in PIK3CA in 1 case). There were 3 cases with non "targetable" gene rearrangements including a STAT6-NAB2 fusion in a stromal sarcoma (possible solitary fibrous tumor of prostate), a BCOR-MAML3 fusion and a TMPRSS2-ERG fusion in a stromal sarcoma with an adjacent focus of Gleason 6 prostate adenocarcinoma. 1 case featured a predicted germline mutation of the FLCN gene. All cases were microsatellite stable. TMB ranged from 0 to 9.8 mutations/Mb with median of 3.4 mutations/Mb with no cases at ≥10 mutations/Mb. gLOH scores were low, ranging from 0% to 10.9% (median 2.6%). Genomic ancestry was European in 7 patients and Admixed American in 4 others. There were no specific genomic signatures identified. PD-L1 was tested in 4 cases (all negative). Conclusions : Prostate sarcoma is an exceedingly rare primary cancer of the prostate with limited opportunities for targeted therapy or immunotherapy strategies. These tumors do not appear to be driven by "targetable" gene fusions and individual "targetable" mutations are uncommon.

6. Development And Analysis Of A Single-Center, Retrospective Research Cohort Of Intermediate, High-Very High Risk, And Metastatic Prostate Cancer

Bearden, Jonathan; Bixby, Amber; Chernet, Rachel; Kyewalabye, Keith; Faso, Susan; Rajendran, Rahul; Nasr, Michel; Basnet, Alina; Jamaspishvili, Tamara.

SUNY Upstate Medical University, Department of Pathology & Laboratory Medicine and Division of Hematology/Oncology

Background: Prostate cancer (Pca) remains the second leading cause of cancer-related deaths in men. Due to the disease's biological heterogeneity, there exist challenges in assessing risk stratification and optimal treatment modalities. Thus, the creation of well-annotated PCa cohorts is crucial for developing novel methods for disease stratification and treatment prediction. Objective: Assemble and annotate a multi-modal, longitudinal research cohort comprising patients with PCa, intended for future biomarker exploration and artificial intelligence (AI) -driven computational techniques for categorizing the disease and predicting treatment responses. Methods: Patient identification involved a query of Epic's Cancer Problem Registry (ECPR) and the NYS Cancer Registry (NYSCR) at Upstate Medical University. ECPR query focused on Urology, Hemato-Oncology, and Radiation Oncology, utilizing NCCN criteria for high, very high-risk, and metastatic Pca, as well as patients receiving hormone treatment or androgen receptor axis inhibitors (ARAIs). Criteria included all patients undergoing surgery, radiation or hormone treatment at SUNY Upstate. Results: Combined ECPR and NYSCR searches yielded 1,683 patients. CoPath query found 1,003 corresponding patients with 1,417 available specimens. Manual chart abstraction of 924 patients derived longitudinal meta-data of clinical, follow-up and outcome information. The final cohort comprised a majority intermediate (n=353, 38.1%) and high/very high-risk (VHR) (n=459, 49.6%) NCCN risk stratification groups, with de novo metastatic N1/M1, constituting 12.3% (n=114). Within the metastatic subgroup of available pathology archive samples, lymph node metastasis (n=85) and bone metastatic sites (n=83) were most prevalent. 909 patients (98.2%) have corresponding pathological samples for future use of specimen analysis and clinical correlation. Of the cohort, 284 patients experienced castrate-sensitive recurrence/metastasis, and 94 became castrate-resistant following varied treatment modalities. Conclusions: This cohort reflects the evolving approach to Pca treatment, studying the array of systemic and local therapies including chemotherapy, ADT, and ARAI use. Next steps include conducting proof-of-concept biomarker-driven cancer research studies. We also hope to create tissue microarrays and a digital repository of pathology slides along with radiological images to facilitate AI-driven translational cancer research.

7. Role Of Cytoreductive Nephrectomy In Metastatic Clear Cell Renal Cell Carcinoma In The Era Of Immunotherapy: An Analysis Of The National Cancer Database

Bou Zerdan, Maroun; Niforatos, Stephanie; Arunachalam, Swathi; Jamaspishvili, Tamara; Wong, Roger; Bratslavsky, Gennady; Jacob, Joseph; Ross, Jeffrey; Shapiro, Oleg; Goldberg, Hanan; Basnet, Alina.

SUNY Upstate Medical University, Departments of Internal Medicine, Pathology & Laboratory Medicine, Public Health & Preventive Medicine, Urology, and Division of Hematology/Oncology; Foundation Medicine, Inc.

Background: The effectiveness of the clinical outcome of CN (Cytoreductive Nephrectomy) in cases of mccRCC (Metastatic Clear Cell Renal cell Carcinoma) is still uncertain despite two trials, SURTIME and CARMENA. These trials, conducted with Sunitinib as the standard treatment, did not provide evidence supporting the use of CN. Methods: We queried the NCDB for stage IV mccRCC patients between the years of 2004-2020, who received (immunotherapy) IO with or without nephrectomy. Overall survival (OS) was calculated among three groups of IO alone, IO followed by CN (IOCN), CN followed by IO (CNIO). Cox models compared OS by treatment group after adjusting for sociodemographic, health, and facility variables. Results: From 1,549,101 renal cancer cases, 7,983 clear and non-clear cell renal cell carcinoma cases were identified. After adjusting for sociodemographic and health covariates, patients who received IO followed by CN or CN followed by IO had a respective 64% (adjusted Hazard Ratio [aHR]= 0.36, 95% CI =0.30-0.43, p= 0.006] and 47% (aHR=0.53, 95% CI=0.49-0.56, p=0.001) mortality risk reduction respectively compared to patients who received IO alone. Compared to White adults, individuals who identified as Black exhibited 17% higher risk mortality (aHR= 1.17, 95% CI= 1.06-1.30, p=0.002). Patients who received CN prior to IO had a 59% associated mortality risk compared to patients who received IO followed by CN who had a lower risk, 35.7% (p<.001). Conclusions: Patients receiving CN regardless of sequence with IO did better than IO alone in this national registry-based adjusted analysis for mccRCC. Presently available data indicates that the combination of CN and IO holds promise for enhancing clinical results in patients with mRCC.

8. Examining The Relationship Between ECOG Performance Status And Immunotherapy Outcomes: Insights From Real-World Data Analysis

Chernet, Rachel; Devashish, Desai; Rajendran, Rahul; Bixby, Amber; Faso, Susan; Wallace, Josh; Nasr, Michel; Jamaspishvili, Tamara; Basnet, Alina.

SUNY Upstate Medical University, Departments of Pathology & Laboratory Medicine, Public Health & Preventative Medicine, and Division of Hematology/Oncology

Introduction: The impact of Eastern Cooperative Oncology Group Performance Score (ECOG) on immunotherapy (IO) outcomes is intricate, as historically, clinical trials have primarily enrolled patients with ECOG scores of 0 or 1. The National Comprehensive Cancer Network (NCCN) advises against administering IO to patients with ECOG scores of 2 or higher. However, conflicting findings from research studies and variations in real-world clinical practice complicate this relationship. Our study aims to elucidate the association between ECOG status and the outcomes of immunotherapy. Methods: Data collected from SUNY Upstate Medical University treated cancer patients who underwent immunotherapy and other therapies (ie, chemotherapy, targeted therapy, hormonal therapy) were used for analysis. The Kaplan-Meier method and Cox regression were used to analyze survival probability based on therapy, age, and ECOG. Results: Of 813 patients included in the study, 46.91% (n=379) received immunotherapy alone. The mean age was 64.1 years in the IO group and 67.7 years in the non-IO group. 52.5% (n=187) of patients who were ≤ 64 years received IO compared to only 42.7% (n=195) of patients who were ≥ 65 years received IO (p=0.005). 48.6% (n=118) of patients with ECOG score 0 received IO, while only 40.5% (n=72) patients with ECOG score of ≥3 received IO (p=0.279). Patients who received IO with ECOG score of ≥3 had a higher probability of survival compared to other groups (p<0.0001, HR 0.866 (0.779 - 0.962)). There was no statistically significant difference between overall survival among the IO and non-IO groups across all stages and ECOG (p=0.6890, HR 1.035 (0.873 - 1.228). There was no difference in overall survival in patients receiving IO based on age categories (p=0.2627, HR 1.148 0.901 - 1.462). When considering three-year survival among ECOG 2 and 3 patients, the IO treatment group had a 49% increased survival advantage compared to those who did not receive any IO ((HR=1.485, 95% CI 1.087 - 2.028). Conclusions: Our findings suggest that relying solely on ECOG status to determine eligibility for immunotherapy may be overly restrictive. Patients with significant comorbidities could still derive benefits from immunotherapy. Further investigation is warranted to comprehensively assess the influence of ECOG status on immunotherapy outcomes.

9. GOAT-Ing For An Improved Cancer Biomarker: Ligand-Conjugate Development Targeting Ghrelin O-Acyltransferase

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Prostate cancer (PCa) is an ongoing global health concern, with PCa diagnoses constituting approximately 30% of all cancer diagnoses in men. The current standard biomarker to detect PCa is prostate specific antigen (PSA), presents drawbacks due to low specificity for the disease resulting in false positives and PCa overdiagnosis. Accurate and sensitive PCa detection requires identification of new biomarkers. We hypothesize that the enzyme ghrelin O-acyltransferase (GOAT) can provide a novel specific PCa biomarker. GOAT is a membrane bound O-acyltransferase required for the biological activation of the peptide hormone ghrelin. Recent studies report GOAT overexpression PCa and breast cancer cell lines, and in clinical studies, GOAT has been detected in plasma and urine samples derived from PCa patients. Based on its character as an integral membrane protein, we hypothesize that GOAT detected in circulation is present in cancer cell-derived extracellular vesicles. Our study aims to address two goals: development of a potent specific ligand for GOAT detection in PCa and breast cancer cells and PCa-derived extracellular vesicles; and development of a ligand- conjugates (LCs) targeting GOAT as a potential treatment avenue targeting PCa and other GOAT- overexpressing cancers. Ghrelin-derived ligands exhibiting nanomolar affinity for GOAT have been modified with a bifunctional linker molecule allowing attachment of customizable cargo. Multiple LCs have been synthesized differing in both cargo and ligand sequence, with the synthesis of each LC supporting the robustness of our synthetic scheme. These GOAT-targeted LCs have been used to explore GOAT-ligand binding interactions, GOAT detection in PCa, breast cancer, and noncancerous cell lines, and specificity of ligand-GOAT binding in cellular environments. Our studies support the specificity of these ligands for GOAT and the capability for ligand-based detection of GOAT in cancerous and noncancerous cells. Moving forward, we aim to evaluate the ability for GOAT to serve as an improved diagnostic biomarker for PCa with potential expansion to additional GOAT-overexpressing cancers.

10. Immunomodulatory Telodendrimer Nanomedicine In Treating Ovarian Cancer

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Although ovarian cancer (OC) treatment (surgery and chemotherapy) has a favorable initial response, the recurrence remains high in ~70% of patients. To tackle this drastic recurrence rate, many strategies following first-line chemotherapy were introduced including intraperitoneal treatments after cytoreductive surgery, such as hyperthermic intraperitoneal chemotherapy (HIPEC) and immunotherapy. Despite the prolonged survival benefit of HIPEC, the overwhelming inflammation derived from surgery and chemotherapy is challenging to manage in the clinic, resulting in systemic inflammatory response syndrome (SIRS). Inflammation plays a key role in all cancer stages, initiation, progression, recurrence, and metastasis. Accordingly, Inflammation control becomes a goal in cancer management. Inflammatory responses are triggered by the activation of the main pathogen recognition receptors, toll-like receptors (TLRs). Therapy-derived debris and damage-associated molecular patterns (DAMPs) activate TLRs and subsequently NF-kB signaling, resulting in proinflammatory cytokines such as IL-6 and IL-8 that induce proliferation and metastasis. Therefore, TLRs blockade can control inflammation and subsequently inhibit tumor proliferation and metastasis. In the Luo lab, we have developed a library of telodenderimer (TD) nanoparticles with a flexible scaffold decorated with different charged and hydrophobic moieties for both therapeutic delivery and immune modulation by different mechanisms such as TLR inhibition. Hence, we hypothesize that the dual functional TD nanoplatform as a nanocarrier for the targeted delivery of frontline chemotherapy regimen, CDDP/PTX, as well as TLR inhibitor in controlling inflammation, will synergize with OC treatment and inhibit the recurrence and metastasis. Here, we show that TD can inhibit TLR-2/4 activation and can inhibit the secretion of proinflammatory cytokines such as IL-6 from OC cell lines. TD can inhibit SKOV-3 OC cell line proliferation. It also directly inhibits SKOV-3 migration in a dose-dependent manner and upon treatment with conditioned media of differentiated macrophages stimulated with LPS. Moreover, TD inhibits cancer cachexia, shows preferential coating for wound sites, and can mitigate the OC engraftment promoted by surgical wound. Therefore, we believe that effective control of inflammation induced by OC treatment can reduce tumor progression which can be further augmented by the targeted delivery of frontline chemotherapy.

11. Impact Of The 16bp Duplication Polymorphism In The Intron 3 Of TP53 Gene In Lung Cancer

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TP53 gene is one of the most extensively studied tumor suppressor genes. Previous studies demonstrated that the 16bp duplication polymorphism in TP53 intron 3 (TP53PIN3) was associated with increased incidence of several types of cancer, including lung cancer; the molecular mechanisms underlying, however, are unknown. Objective: To investigate the roles of TP53PIN3 in TP53 mRNA splicing efficiency and the correlation between TP53PIN3 and lung tumors. Methods: Three recombinant constructs (p53-R0, -R1 and -R2) containing different copies (R0=0, R1=1, R2=2) of the 16-bp sequence in TP53 intron 3 were prepared with a bi-cistronic reporter gene system and transfected into human lung epithelial cell lines H441 and A549, respectively. The mRNA splicing efficiency was determined by the ratio of Firefly (spliced form) to Renilla (spliced and unspliced form) luciferase activity. The spliced and unspliced mRNAs were analyzed by semiquantitative RT-PCR. Furthermore, trans-acting factors were isolated by RNA pull-down, identified by LC-MS/MS, and verified by Western blotting analysis. A significant difference in statistics was considered when $p<0.05$ by t-test or ANOVA. p53 expression and the distributions of TP53PIN3 genotypes and alleles were analyzed in human lung cancer by PCR and western blotting. Results: The results showed: 1) TP53PIN3 is an important cis-acting element for TP53 intron 3 splicing. p53-R1 (one copy of the 16 bp sequence) showed higher mRNA splicing efficiency ($p<0.05$) compared to p53-R0 (no 16bp sequence) and p53-R2 (16bp duplication). 2) Four RNA binding proteins, including FUSE binding protein 2 (KHSRP), hnRNP L, hnRNP A2/B1, and splicing factor 2 (ASF/SF2), which binds the 16bp duplication (32nt) were identified and verified, indicating these proteins were associated with p53 pre-mRNA splicing. 3)The level of p53 protein is higher in human lung tumor tissues compared with that of the matched healthy lung tissues ($p<0.05$). A1/A1 genotype and allele A1 showed high frequency (65.6% and 78.13%, respectively) and may be associated with the risk of lung cancer. Conclusion: TP53PIN3 and its associated binding proteins are involved in the regulation of TP53 pre-mRNA splicing, which may have an impact on the development of lung cancer.

12.Comparative Survival After Neoadjuvant Vs Adjuvant Systemic Therapy In Resectable Stage II And Stage III Non-Small Cell Lung Cancer: A Retrospective Study Using The National Cancer Database

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Background: Resectable Stage II and III Non-small Cell Lung Cancer (NSCLC) are managed with surgery and perioperative systemic therapy [Chemo/Chemo-Immunotherapy (IO)]. However, there lacks a consensus in optimal selection between neoadjuvant and adjuvant approaches. Hence, it underscores the necessity to undertake a comparative survival outcome associated with systemic therapy in these distinct settings. Methods: We conducted an analysis, of individuals aged 18 and above diagnosed with stage II and stage III NSCLC between 2004 - 2020, using data from the National Cancer Database (NCDB). Overall survival (OS) was compared for both Neoadjuvant and Adjuvant systemic therapy using Cox proportional hazards models after adjusting for sociodemographic (e.g., age, sex, race-ethnicity, and income) and health (e.g., insurance and facility type) related factors. The inclusion criteria involved restricting the analysis to individuals with no more than one lifetime cancer diagnosis and excluding those who received radiation therapy. Results: Among approximately 2 million total patients with NSCLC in NCDB, 8.38% and 20% were stage II and III respectively. After we identified a total of 137,473 eligible patients, 27,115 had relevant treatment information with 2,550 Neoadjuvant Chemo, 112 Neoadjuvant chemoIO, 24,175 Adjuvant chemo and 278 Adjuvant chemoIO. A statistically significant association between OS and treatment group was observed [$\chi2(3) =55.5$, $p<.001$]. The OS was notably higher in the Neoadjuvant chemoIO group (78.57%) compared to Adjuvant chemoIO group (55.76%), whereas the Neoadjuvant chemo-only group exhibited lower OS (45.41%) compared to the Adjuvant chemo group (47.98%). The Cox proportional hazards model showed 70% higher mortality risk in the Adjuvant chemoIO group compared to the Neoadjuvant chemoIO group ($p=0.030$, 95% CI 1.05-2.77). The 2-year and 5-year OS rates for Neoadjuvant ChemoIO were 77.9% and 68.8%, respectively versus 68.7% and 42.8% for Adjuvant chemoIO group. Conclusions: Our analysis reveals that Neoadjuvant chemoIO demonstrates superior survival outcomes compared to Adjuvant chemoIO. Additionally, our findings suggest the potential predictive value of Immunotherapy in combination with chemotherapy in the Neoadjuvant setting. Key Words: NSCLC, Neoadjuvant treatment, Adjuvant treatment, Chemotherapy, Immunotherapy, OS

13. Clinical-Genomic Characterization Unveils More Aggressive Disease Features In Elderly Prostate Cancer Patients With Low-Grade Disease

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Background: Over 20% of men diagnosed with prostate cancer (PC) are ≥75 yr old. More objective disease-specific indices for predicting outcomes beyond chronological age are necessary. Objective: To analyze age-related differences in clinical-genomic prognostic features of aggressiveness in localized PC. Design, setting, and participants: A retrospective multicenter cross-sectional study reported the use of the Reporting Recommendations for Tumor Marker Prognostic Studies (REMARK) guidelines. Clinical-genomic data of patients who underwent a prostate biopsy or radical prostatectomy (RP) were obtained from the Decipher Genomic Resource Information Database (NCT02609269). Intervention: Our analyses focused on the 22-gene Decipher genomic classifier (GC) and 50-gene (PAM50) models in the biopsy and RP cohorts stratified by age. Outcome measurements and statistical analysis: The primary endpoint was the impact of age on GC scores and PAM50 molecular subtypes. Prognostic indices including Decipher GC scores, PAM50 molecular subtypes, National Comprehensive Cancer Network risk categories, and ISUP grade groups (IGGs) were stratified by age using multivariable logistic regression analyses. Results and limitations: Within histological low-risk IGGs, there were a higher proportion of patients with high-risk Decipher biopsy scores with age (age <60 yr: 10.1% IGG 1 and 29.9% IGG 2 vs age ≥80 yr: 22% IGG 1 and 37.7% IGG 2). The prevalence of the adverse phenotype luminal B (PAM50-defined) increased with age (age <60 yr: 22.7% and 40.2% vs age ≥80 yr: 29.7% and 49.1%, in patients with IGG 1 and IGG 2, respectively). In IGGs 3-5, no age differences were observed. Multivariable models demonstrated that each age decile entailed a 19% (odds ratio [OR] 1.19, 95% confidence interval [CI] 1.10-1.29, $p < 0.001$) and a 10% (OR 1.1, 95% CI 1.05-1.16) increased probability for a high-risk Decipher biopsy and RP score, respectively. Aside from an obvious selection bias, data on race, family history, prostate volume, and long-term follow-up outcomes were unavailable. Conclusions: These data demonstrated that elderly men with favorable pathology (IGG 1-2), might harbor more aggressive disease than younger patients based on validated GC scores.

14. Targeting Hypoxia-Inducible Factor-2 Alpha In Kidney Cancer

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The transcription factor Hypoxia-Inducible Factor 2α (HIF2α) plays a crucial role in cancer cell adaptation to hypoxic conditions, particularly in clear cell renal cell carcinoma (ccRCC), promoting tumor growth and angiogenesis. Targeting HIF2α through pharmacologic inhibition offers a therapeutic strategy for HIF2α-driven cancers. Using an in silico approach, we identified Compound-c2 as a novel selective inhibitor that binds to the Per-Arnt-Sim-B (PAS-B) domain of HIF2α. Notably, Compound-c2 disrupts the interaction between HIF2α and the molecular chaperone Hsp70, leading to proteasomal degradation of HIF2α and the induction of apoptosis in ccRCC. This distinctive inhibitory mechanism sets Compound-c2 apart from previous HIF2α antagonists, positioning it as a promising alternative with potential applications in addressing drug resistance and providing a unique approach to inhibit HIF2α-related processes.

Upstate Cancer Center at Verona

15. Establishment Of A Microfluidic Platform To Model Physiology Of Human Tumors And Normal Tissues.

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Many drugs in the oncology pipeline fail in human trials due to unanticipated inefficacy or toxicity. The root-cause of these late-stage failures is often attributable to pre-clinical testing systems that do not adequately model human physiology, particularly in ADMET screening. The FDA Modernization Act 2.0 permits alternatives to animal testing prior to first-in-human trials, including microphysiologic systems (MPS). MPS are emerging bioengineering technology that offer enhanced fidelity and reproducibility, flexible design, high throughput and reduced costs, relative to the conventional pre-clinical model systems. The primary goal of this project is to establish a microfluidic testing platform that will be available to the Upstate Cancer Research Community for drug screening and physiologic modeling. In the initial phase, we have established instrumentation and methodology for on-demand fabrication of MPS devices, currently focused (a) hepatic drug metabolism/toxicity and (b) vascular endothelial function in tumors as test cases. Bespoke MPS devices are designed using CAD software, followed by stereolithographic 3D-printing of a mold. Optically transparent, gas permeable polydimethylsiloxane rubber is cast in the mold to create a three-dimensional culture vessel, and bonded to a glass slide or coverslip. Organotypic cells suspended in a photopolymerizable hydrogel composed of extracellular matrix proteins (e.g. collagen, fibronectin) are introduced to the device, and non-phototoxic visible light (405nm) is projected through a custom photomask to crosslink the hydrogel in situ to create solid, cell-laden 3D structures. Unexposed areas remain liquid, and are flushed away, leaving behind hollow channels down to 75um diameter. The empty vascular channels are then lined with vascular endothelial cells and connected to a precision microfluidic controller for perfusion with culture media. Cell viability is assessed by Live-Dead staining and deconvolution fluorescence microscopy. Material stiffness of the polymerized hydrogel is determined by compression testing to 10% strain. Vascular barrier function is dynamically assessed by time-lapse microscopy by perfusion with a range of FITC-Dextran conjugates ranging from 4-70kDa molecular weights. Hydrodynamic properties under perfusion are assessed by measuring transit velocity of fluorescent polystyrene beads through the vascular channels using real-time video microscopy. Further validation of this fabrication process and platform are currently underway.

16. Artificial Intelligence (AI)-Powered PDL-1 Quantification Is Associated With Immunotherapy Efficacy

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Immunohistochemical (IHC) assessment of programmed cell death ligand 1 (PD-L1) expression is used as a predictive biomarker of anti-PD-1/PD-L1 response in non-squamous cell lung cancer. However, manual IHC scoring by pathologists introduces inter- and intra-observer variability which can affect patient indication for immunotherapy and thus reduce efficacy of treatment. We evaluated an artificial intelligence (AI)-powered PD-L1 quantification algorithm for clinical use and compared with "gold-standard" pathologists' manual scoring to determine better predictive ability for clinical outcomes. Digitized slides stained for anti-PD-L1 antibody (DAKO 22C3 PharmDx) from 158 patients who received first-line anti-PD-1/PD-L1 treatment were included in this study. PD-L1 quantification was categorized into clinically relevant groups as approved by FDA: <1% (absent), 1-49% (low), and ≥50% (high). We evaluated the agreement between both scoring mechanisms by expression level (absent, low, high) and examined their association with progression-free and overall survival. I-powered PD-L1 scores were significantly correlated (Pearson $r=0.899$, $p<0.001$) and concordant with pathologists' scoring (CC=0.835, $p<0.001$; 95% CI: 7.28-11.11). The AI-powered scores were reliable with an Intraclass Correlation Coefficient of 0.898 (95% CI: 0.86-0.92) and had substantial agreement (Cohen's kappa=0.652). AI-powered scoring also demonstrated a better association with objective response to immunotherapy (OR=2.45; 95% CI: 1.04-5.78) compared to pathologists scoring (OR=1.18; 95% CI: 0.52-2.70). Patients identified as PD-L1 positive by AI-powered methods also had significantly longer progression-free and overall survival compared to PD-L1 negative patients with Hazard Ratios of 0.54 (95% CI: 0.35-0.83) and 0.53 (95% CI: 0.30-0.93) respectively. Importantly two PD-L1 positive cases and 30 more "low" cases which were originally classified as "absent" were reclassified in "low" expression group, signifying a significant number of cases which would have missed immunotherapy using the manual scoring. AI-powered IHC quantification presents an opportunity to better identify patients who may respond better to immune therapy. Overall, the AI-powered assay identified more PD-L1 positive cases and demonstrated better response and survival associations within specific patient groups compared to pathologists' manual scoring, suggesting that AI-powered scoring could have greater clinical relevance.

17. Phosphorylation Of TRAP1 By The Tyrosine Kinase C-Abl Drives Pro-Survival Signaling In Renal Cell Carcinoma

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The molecular chaperone TNF-receptor-associated protein 1 (TRAP1) is a master regulator of mitochondrial metabolism and apoptosis and is often overexpressed in cancer. Insensitivity to apoptotic signaling underlies the pathogenesis of cancer, though the impact of TRAP1 on kidney cancer survival has not been explored. Here, we observed elevated TRAP1 expression in the most common subtype of kidney cancer, clear cell renal cell carcinoma (ccRCC), and inhibition of TRAP1 in these cells induced apoptosis. TRAP1 activity is modulated by post-translational modifications, which are often deregulated in disease. The proto-oncogene tyrosine kinase c-Abl is hyperactive in ccRCC though the mitochondrial targets of c-Abl are unknown. We detected TRAP1 phosphorylation and found that c-Abl-mediated phosphorylation of TRAP1 antagonized apoptosis by promoting TRAP1 binding to the apoptosis effector CypD. Co-targeting TRAP1 and c-Abl displayed drug synergy, suggesting a potentially viable therapeutic strategy for ccRCC.

18. The Role Of NKG2D Receptor And Ligands In Triple-Negative Breast Cancer (TNBC) Relapse.

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Triple-Negative Breast Cancer (TNBC) accounts for 15% of breast cancer cases and presents a significant challenge due to its higher mortality rate 40% greater than that of other breast cancers and limited treatment options, which contribute to decreased 5-year survival rates. A significant challenge in TNBC treatment is the downregulation of Human Leukocyte Antigen class I (HLA-1), essential for CD8+ T cells to target tumors effectively. We have identified that the expression of Natural Killer group 2, member D (NKG2D) a receptor primarily found on Natural Killer (NK) cells and on CD8+ T cells provide a novel pathway for targeting TNBC tumors independently of HLA-1. Our data showed a significant correlation between elevated NKG2D levels in TNBC patient CD8+ T cells and improved patient survival. This correlation is due to the upregulation of NKG2D ligands (NKG2DLs) in TNBC tumors, making them more vulnerable to CD8+ T cells with high NKG2D expression. Our findings highlight the potential for targeting NKG2D-mediated pathways to develop new and effective immunotherapy for TNBC. In our pursuit of therapeutic interventions, we have developed a novel small molecule activator of β-catenin, designated A124. Our data indicates that treatment with A124 significantly elevates the expression of NKG2D and the T-box transcription factor (T-bet) in CD8+ T cells derived from TNBC patients, notably in those exhibiting initially low levels of NKG2D. This augmented expression is tightly linked to the increased production of Granzyme B and Perforin, essential for the cytolytic activity of CD8+ T cells and their ability to effectively eradicate tumor cells. We further found using in a humanized mouse model which was infused with CD8+ T cells from TNBC patients, that A124 treatment significantly increases T-bet and NKG2D expression, reinforcing its potential as an immune base therapeutic approach. The primary objective of our proposal is to determine the mechanisms by which A124 activation amplifies the HLA-1-independent anti-tumor capabilities of CD8+ T cells against TNBC tumor in both in vitro and in vivo models.

19. Reshaping Current Practices in Pathology using Computational Tools and AI.

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Pathology, a fundamental field of medicine and research, is undergoing a transformative change driven by Artificial Intelligence (AI) and Computational Pathology. This presentation will focus on the revolutionary role these technologies may bring to the field, including the challenges and opportunities we may face. Many clinical and research pathology labs show that AI-powered algorithms augment the accuracy and efficiency of diagnoses, minimize bias and human errors, and improve patient risk stratification and prognostication, ultimately leading to improved patient care. This presentation will discuss the gaps we face in current pathology practices and viable options for addressing these challenges through digital pathology implementation, leveraging computational pathology and AI-powered quantitative approaches in clinical practice.

20. Unraveling MLL1-Fusion Leukemia: Epigenetic Revelations From An Ips Cell Point Mutation

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Our understanding of acute leukemia pathology is heavily dependent on 11q23 chromosomal translocations involving the mixed lineage leukemia-1 (MLL1) gene, a key player in histone H3 lysine 4 (H3K4) methylation. These translocations result in distinct MLL1-fusion (MLL1F) proteins that are thought to drive leukemogenesis. However, the mechanism behind increased H3K4 trimethylation in MLL1F-leukemic stem cells (MLL1F-LSCs), following loss of catalytic SET domain of MLL1 (known for H3K4 mono- and dimethylation), remains unclear. In our investigation, we introduced a homozygous loss-of-function point mutation in MLL1 within human induced pluripotent stem cells. Remarkably, this mutation mimics the histone methylation, gene expression, and EMT phenotypes of MLL1F-LSCs- without the need for a translocation or functional wild-type MLL1. This observation underscores the essential role of MLL1's enzymatic activity in restraining the cascade of epigenetic changes associated with the gene activating H3K4 trimethylation mark, which we show is catalyzed by mislocalized SETd1a H3K4 trimethyltransferase in the absence of MLL1's enzymatic activity. Challenging existing models, our findings imply that MLL1F-induced leukemias arise from a dominant-negative impact on MLL1's histone methyltransferase activity. We advocate for a therapeutic paradigm shift, targeting SETd1a for precision medicine. This work opens new avenues for addressing the complexities of MLL1-associated leukemias and improving targeted therapies.

21. Development Of ABI1 As Biomarker To Monitor Prostate Cancer ADT- And Enzalutamide-Resistance

Kotula, Leszek.

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In the United States, over 3 million men are living with prostate cancer. Nearly 40,000 die each year from metastatic prostate cancer, often due to tumors that become resistant to treatments such as androgen deprivation therapy (ADT) and androgen receptor (AR) inhibitors. Although effective at first, ADT frequently leads to a condition known as castration-resistant prostate cancer (CRPC), characterized by the continued activity of the AR. Our data from the clinical trial has shown that the gene ABI1 might play a role in this resistance, highlighting its potential as a biomarker. ABI1, a gene dependent on AR, changes its expression during the progression of prostate cancer and in response to ADT/AR treatment. Our data indicate that ABI1's various splice forms-versions of the gene with different sections included or excluded-are misregulated during treatment. Specifically, when ADT (using a drug called goserelin) is combined with the AR inhibitor enzalutamide, we see abnormal levels of ABI1 splice forms in tumors, especially those including a segment known as Exon 4. Despite a general decrease in ABI1 expression, the presence of Exon 4 in ABI1 transcripts significantly increases. This Exon 4-encoded region is crucial for ABI1's interaction with DNA, as revealed by our NMR structural studies. Early findings suggest that these specific ABI1 transcripts encourage a unique pattern of gene activity in prostate cells, contributing to ADT resistance. Our current research aims to confirm ABI1, particularly its Exon 4, as a marker of resistance to ADT and AR inhibitors. We're developing liquid biopsy assays for blood and saliva to measure ABI1 forms and Exon 4 expression. The goal is to track changes in ABI1 in response to ADT and link them to the cancer's return. Our upcoming trials will measure ABI1 Exon 4 mRNA in saliva from men undergoing ADT, comparing it with ABI1 levels in blood, prostate tumors, and PSA levels. By collecting saliva at different points in treatment, we aim to link ABI1 levels with disease progression. Using RNA sequencing, qPCR, and droplet PCR, we will analyze ABI1 isoforms and Exon 4 expression in detail. This study seeks to underline the importance of abnormal ABI1 expression as a biomarker for advanced prostate cancer and its resistance to therapy.

22. The Neuroendocrine Factor VGF Provides Paracrine Support For Glioma Growth And Is A Circulating Marker Of Tumor Burden

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A major factor that contributes to the unchecked growth and recurrence of glioblastoma (GBM) is the presence of a heterogeneous population of tumor stem-like cells (GSCs) that continuously replenish the tumor mass and are resistant to conventional therapies. GSC proliferation is supported by signals from neural cells and it has been shown that disruption of this microenvironmental support is sufficient to diminish or prevent GBM growth. VGF is a neurotrophic factor produced by neurons that is cleaved and secreted in the form of neuropeptides; these peptides promote neural progenitor proliferation and are involved in neural mechanisms such as memory formation and central control of body metabolism. We and others have observed VGF expression in GSCs and shown that knockdown of VGF in these cells reduces their viability and stemness properties. However, the potential role of paracrine VGF - produced by neural cells- on the tumor remains unknown. Here we demonstrate that GSCs induce the expression of VGF in astrocytes, which do not normally express this neurotrophic factor. We observed significant upregulation of VGF in astrocytes co-cultured with GSCs as well as in tumor-associated astrocytes in vivo. Furthermore, we observed that GSCs co-cultured with VGF-deficient astrocytes had lower viability and lesser resistance to the chemotherapeutic temozolomide, compared to GSCs co-cultured with control astrocytes. Exogenous VGF also increased the viability and temozolomide resistance of GSCs cultured alone. Importantly, this trophic role was only observed when we cultured GSCs in presence of the full-length VGF precursor but not with the known VGF neuropeptides, suggesting that the full-length protein -or novel cleavage products- may act through mechanisms distinct from those known for VGF neuropeptides. Separately, we observed a significant upregulation of circulating VGF in glioblastoma patients compared to healthy controls (AUC = 0.866) and confirmed its origin from both tumor and host cells. Taken together, our results suggest that this protein may have value both as potential target in the tumor as well as biomarker of tumor burden. Current research in our laboratory is focused on identifying and targeting the molecular mechanisms driven by VGF in GSCs with the goal of curtailing neural support to the tumor and ultimately prevent tumor growth.

23. Identifying The Mechanism Of ABI1 Binding On Androgen Receptor

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Prostate cancer is the second most common cancer diagnosis in men worldwide. Prostate cancer growth is predominantly driven by androgen receptor (AR) signaling. Unfortunately, even as prostate cancer is treated with androgen-deprivation therapy (ADT) and anti-androgens such as enzalutamide, AR signaling is able to remain active through a variety of mechanisms. To better characterize the regulation of AR signaling, and the dysregulation allowing for its reactivation, we focused on better understanding the AR interactome. Previous studies from our lab identified Abelson Interactor 1 (ABI1) as a novel binding partner of AR. ABI1 has been shown to be a regulator of key pathways involved in prostate cancer progression and metastasis. ABI1 also serves as an AR co-transcriptional regulator, as the loss of the ABI1-AR interaction changes the expression of canonical AR targets. We hypothesized that ABI1 interacts with AR's N-terminal domain (NTD) via binding between ABI1's Src Homology 3 (SH3) domain and AR-NTD's PxxP motifs. To test this hypothesis, we designed serial truncation mutants of AR, systematically removing PxxP motifs. AR-negative PC-3 prostate cancer cells were transiently transfected with the various AR mutants and lysed after 72 hours. Following co-immunoprecipitation, levels of mutant AR bound to ABI1 were detected using western blotting and quantified in ImageJ. Our data shows that ABI1 has a higher affinity for a specific truncation mutant of AR, suggesting that a specific PxxP motif is the critical binding site for ABI1. These experiments will allow us to better understand how ABI1 is able to interact with AR and regulate its activation and signaling, both physiologically and during prostate cancer progression.

24. National Trends In Hospital Charges At Discharge For Hepatic Resections For Malignancy

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Hepatic resection is one of the major treatment options for primary and secondary malignancies of the liver. With the incidence of liver and intrahepatic bile duct cancers, as well as colorectal cancer, on the rise in the United States, the utilization of liver resections has significantly increased over the past decade. This surge can be attributed to various factors, including advancements in surgical techniques, expanding criteria for resection, and improved patient management strategies. While mortality rates following liver resection remain relatively low, morbidity rates continue to pose challenges, particularly in an aging population with significant comorbidities. The economic burden associated with liver resections is substantial, with inpatient costs escalating over time. Complications such as surgical site infections, respiratory failure, and renal failure contribute significantly to the overall cost. In this study, we analyzed trends in hospital charges for hepatic resections using the Nationwide Inpatient Sample database spanning from 2000 to 2019. Statistical analysis involved weighted sample estimates, standard errors calculation, and multivariate linear regression to assess the impact of various patient and hospital characteristics on total charges. The analysis revealed a noteworthy increase in total charges over the two-decade period, with hepatic lobectomies experiencing a disproportionate rise compared to wedge resections. Factors such as non-elective admissions, longer lengths of stay, and complications further exacerbated the financial burden associated with liver resections. Interestingly, these findings indicate that the increased cost of liver resections surpasses the average inflation rate, suggesting additional underlying factors influencing cost escalation. These trends provide valuable insights into the economic challenges associated with hepatic resections and emphasize the need for targeted interventions to optimize cost-effectiveness while maintaining high-quality care standards. Further research is warranted to validate these findings and investigate causality.

25. Study Of Pathogenic Variants In CHEK2: Association With Breast Cancer Clinical Features And Family History Of Cancers For The Optimization Of Management And Surveillance

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The CHEK2 gene ("cell cycle checkpoint kinase 2") encodes a nuclear serine/threonine kinase, which acts as a tumor suppressor with important roles in DNA damage repair. Specific germline pathogenic variants (PVs) in CHEK2 are known to elevate lifetime risks for breast and colon cancers. Additional studies have suggested possible risks for thyroid and other cancers, however, not proven definitively, thus challenging health care providers in counseling patients with CHEK2 PVs for additional cancer screening. Our Genetic Counseling Program aims to describe characteristics of the patient population found by our clinic to have inherited CHEK2 PVs in terms of loci, cancer diagnosis, phenotype, ethnic background, and family history. In an IRB-exempt study of our de-identified RedCap database, we identified 110 patients with CHEK2 PVs, 11 of whom were tested at point-of-care in our Multidisciplinary Breast Cancer Program. Patients (pts) with CHEK2 PVs were mainly women (90.5%) and of Northern (53.8%), Eastern, and Central European ancestry. The most frequent PVs detected in all-comers were c.1100delC (38 pts), c.470T>C (36 pts), c.444+1G>T (5 pts), c.190G>A (5 pts), and c.349A>G (4 pts); CHEK2 PVs were virtually all heterozygous, with 1 being homozygous; 13 pts (12.3%) also had inheritance of other additional pathogenic mutations for which they were counseled. 42 total pts in our database presented with a breast cancer diagnosis, and of these, the majority was ductal histology (37 vs 6 with lobular), with phenotype positive for estrogen receptor expression (85.7%) and of invasive breast cancers, negative for HER2 amplification (93.5%), 2 cases of which were metastatic at presentation, all consistent with findings in published literature. However, patients who also had additional history of thyroid cancer or nodules, with (4) or without (7) breast cancers, were seen more commonly to also carry PVs in c.1100delC, c.470T>C, but others had PVs at c.1232G>A, c.1427C>T, and c.190G>A, further adding to cases reported in previous studies concentrating only in Polish populations. Those patients presenting with other cancers and found to carry various CHEK2 PVs had colon (4), prostate (3), gynecologic (4), and pancreatic cancers (3). We readily apply cancer surveillance recommendations for patients and their family members with *CHEK2* PVs in alignment with national consensus guidelines. While these are clear-cut for breast and colon cancer screening and for certain well-studied PVs, we also counsel patients with diverse backgrounds for other cancer risks based on their family history and individual risk factors. We will present unique family pedigrees and our tailored recommendations for each.

26. Depicting The Function Of ABI1 In AR Localization

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Prostate cancer remains a significant healthcare problem in the United States. Despite substantial progress, many aspects of the mechanism of prostate cancer development remain unknown. Prostate cancer tumor growth is driven by androgen activity, which leads to Androgen Receptor (AR) nuclear translocation. In the nucleus, AR regulates transcription of multiple genes that promote growth and proliferation of prostate cells. However, the mechanism of nuclear translocation of AR is not well understood. Preliminary data shows that ABI1 and AR colocalize in the nucleus. This can be observed in cultured cell lines and in tumors. Interestingly, overexpression or enzalutamide treatment have resulted in colocalization of ABI1 and AR entirely in the cytoplasm. Additionally, a mutation of the ABI1 nuclear export signal (NES) leads to an accumulation of ABI1 in nuclei but the impact of this mutation on AR or ABI1-AR complex is currently unknown. Based on our preliminary data we hypothesize that ABI1 may play a role in the localization of AR to the nucleus but also in AR export from the nucleus to the cytoplasm. The goal of this project is to establish suitable antibodies and microscopy methodology to study the above regulation. Here, we identify conditions suitable for an in-depth investigation of ABI1-AR complex localization dynamics. We tested various antibodies and concentrations of androgens to find the best condition to define the localization of ABI1 and AR. We hypothesize that charcoal stripped serum (CSS) leads to dominant cytoplasmic localization of ABI1-AR complex. In contrast, when we stimulate with androgen, we expect to see the complex localize in the nucleus. Our goal is to evaluate the antibody signal for both proteins in these expected subcellular compartments under various conditions of androgen stimulation.

27. Retrospective Review Of The Effect Of Antibiotics Within 30 Days Of Immune Checkpoint Inhibitor Initiation In Stage IV NSCLC

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Aim: To determine the effect of antibiotic therapy within 30 days of initiation of immune checkpoint inhibitor in patients with stage IV non-small cell lung cancer (NSCLC) Method: A deidentified database platform, TriNetX, was queried for patients with stage IV NSCLC who received any of Pembrolizumab, Nivolumab, Durvalumab and Atezolizumab and compared two groups who received antibiotics in a period within 30 days of initiation of ICI therapy compared to those who didn't. These patients were 1:1 matched for age, age at index event and sex to get two groups of 893 patients each. The primary end point was overall survival. Results: 1796 patients were included, 893 In each group. All had stage IV disease. The mean age was 71 years (25 - 90 years). 54% were male, 36% were female and 10% had unknown sex. The group with antibiotic use had 657 deaths amongst 893 with a risk % of 73.6% compared to 541 deaths in the no antibiotic use group with a risk % of 60.6%. The risk difference was 13% (8.7 - 17.3) with a risk ratio of 1.21 (1.14-1.30) with a p value of <0.0001. The antibiotic group had a median survival of 236 days, and no antibiotic group had a median survival of 529 days (p value < 0.0001) Conclusion: The use of antibiotics within a period of 30 days after the initiation of ICI in patients with stage IV NSCLC conferred a poorer outcome. This may be due to the effect the GI tract and gut microbiome on immunomodulation and efficacy of ICIs which is disrupted by the use of antibiotics. There could be several confounding factors like variations in the burden of the disease, combination therapies with ICI, physical status and comorbidities of the patients that are not accounted for in this database.

28. Clofarabine Monotherapy In Aggressive, Relapsed And Refractory Langerhans Cell Histiocytosis

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Purpose: LCH is a neoplastic inflammatory disorder driven by recurrent somatic mutations in the MAPK pathway in myeloid precursors. Over 50% of patients with systemic LCH are not cured with front-line therapies and data to guide salvage options are limited. In this study, we describe 58 patients with relapsed/refractory LCH who were treated with clofarabine. Methods: Data were extracted from clinical records of patients treated with clofarabine for LCH by Texas Children's Hospital physicians or collaborators between May 2011 and 2023. Results: Patients were treated with a median of two chemotherapeutic regimens prior to receiving clofarabine; median age was 3.49 (4 months to 61 years). The typical treatment course was 25mg/m2 daily for 5 consecutive days per month; 19%(11/58) received treatment for less than 6 months; 26%(15/58) for 6-9 months; and 55%(32/58) for 9-24 months. OS in this cohort was 100%(58/58) and PFS was 75% with median 2-year follow-up (range: 5 months to 11 years); The objective response rate (ORR) for all patients was 84% with 9%(5/58) maintaining stable disease and 7%(4/58) developing progressive disease during the study period. Patients treated for LCH-associated neurodegeneration had relatively worse outcomes (ORR: 63%) compared to patients with systemic disease without LCH-ND (ORR: 88%). Patients treated with clofarabine showed significant decreases in the amount of detectable BRAF V600E alleles in their circulating peripheral blood mononuclear cells. Toxicities included cytopenia, vomiting, and bacterial infections, but the majority tolerated chemotherapy in the outpatient setting. Conclusion: Clofarabine monotherapy has activity against LCH in heavily pretreated patients, the majority of whom achieved durable remission. Prospective multi-center trials are warranted to determine optimal dosing as well as long-term efficacy, late toxicities, relative cost and patient reported outcomes of clofarabine compared to alternative salvage therapy strategies (e.g. MAPK inhibitors) in patients with relapsed/refractory LCH.

29. Investigating The Tumor Environment And Signalling Dependencies In Diffuse Midline Glioma: A Comprehensive Approach Leveraging Bulk Multiomics Deconvolution And Single-Cell Omics Validation

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Background: Diffuse Midline Glioma (DMG) is a incurable tumor affecting children. Recent genomic investigations have identified a recurrent H3K27M mutation which induces global alterations in histone methylation patterns and DNA methylation. These epigenetic modifications hint at pivotal roles in DIPG pathogenesis, yet effective therapeutic strategies remain elusive, with median survival rates stagnant at approximately one year. This shortfall stems from two main factors: 1) Inadequate multiomics studies hindering our understanding of DMG evolution and tumor progression, and 2) Limited comprehension of the tumor microenvironment in DMG. Methods: To elucidate DMG's clonal evolution, we adopted a comprehensive multi-region sampling approach, acquiring 33 specimens from seven patients. Whole-exome and transcriptome sequencing, alongside DNA methylation profiling, were performed. Additionally, we embarked on generating one of the most extensive single-cell multi-omics datasets (>300,000 cells from 21 additional samples), with a focus on pre- and post-treatment effects in DMG. Results: Our analysis delineated a tumor-promoting microenvironment characterized by hypoxia and pro-inflammatory conditions, nurturing genomic alterations and specialized biological processes such as proliferation and epithelial-mesenchymal transition. Notably, a majority of immune cells exhibited M1-like polarization, bolstering pro-inflammatory programs within the tumor milieu. Subclones within the DMG cohort demonstrated dissemination potential, often exhibiting up-regulation of NOTCH, P53, and WNT beta-catenin signaling pathways. These findings suggest that DMG clones harboring dissemination capabilities outside the pons acquire additional phenotypic features, possibly mediated by epigenetic or transcriptional alterations, contributing to enhanced migratory and aggressive behaviors. Conclusions: Our study unveils the parallel evolution of DMG at genetic, epigenetic, and transcriptional levels, unveiling novel subclonal phenotypes governing tumor behavior. Crucially, we identify critical environmental shifts such as hypoxia and inflammatory changes, coupled with specialized signaling programs, driving dissemination and resistance phenotypes. These insights may pave the way for generating accurate genetically mouse models and targeted therapeutic interventions to combat this challenging malignancy.

30. Nivolumab In Platinum-Refractory Head-And-Neck Cancers: A Retrospective Observational Audit From A Tertiary Cancer Center.

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Background: Nivolumab and pembrolizumab are approved treatment options for platinum-refractory head-and-neck squamous cell cancer (HNSCC) based on the demonstration of improved outcomes in clinical trials. However, limited data exist on their efficacy in the real-world setting. Objectives: To determine the impact of immune checkpoint inhibitors in the treatment of platinum-refractory HNSCC and the associated outcomes in a real-world setting. Materials and Methods: This was a retrospective study conducted between August 1, 2016, and December 31, 2018 in the Department of Medical Oncology at the Tata Memorial Hospital, a tertiary cancer center in India. We included patients with advanced platinum refractory HNSCC who had been treated with nivolumab. Data regarding adverse events, response, overall survival (OS), and progression-free survival (PFS) were collected. Survival analysis was performed by the Kaplan-Meier method. Cox regression analysis was used to identify the factors which affected OS. Results: A total of 2796 patients qualified for potential treatment with immunotherapy, but only 41 (1.47%) were able to receive it. The dose used was 240 mg in seven patients (17.1%) and 3 mg/kg in the remaining 34 (82.9%). The response rate was 19.5% (n = 8). The median PFS and OS were 2.27 months [95% confidence interval (CI), 1.51-4.14] and 5.29 months [95% CI, 3.78-11.67], respectively. The 1 year OS was 33.6% (95% CI, 19.5-48.4). Oral cavity tumors were associated with a lower PFS (hazard ratio, 3.86; 95% CI, 1.67-8.92; P = 0.001) and OS (hazard ratio, 2.79; 95% CI, 1.26-6.17; P = 0.001). Conclusion: Nivolumab has a good impact on both OS and PFS even in the real-world setting of patients with extensively pretreated platinum-refractory HNSCC similar to what has been reported in the pivotal studies. Among the patients who are treated with nivolumab, those with oral cavity tumors have a worse OS and PFS relative to those of other sites.

31. mTOR Activation And Blockade In Checkpoint Inhibitor-Induced Autoimmune Diseases (CIAD)

Perl, Andras.

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Checkpoint inhibitors revolutionized cancer therapy. Typically, these treatments rely on monoclonal antibodies that target PD-L1 (pembrolizumab, nivolumab, cemiplimab, dostarlimab) on cancer cells, PD-1 (durvalumab, avelumab) or LAG-3 (relatlimab) on effector T cells, or CTLA-4 on regulatory T cells or Treg (ipilimumab, tremelimumab). Among unintended consequences 6%-75% of checkpoint inhibitor-treated patients develop autoimmune diseases. These side effects may lead to the discontinuation of lifesaving therapies. The activation of PI3K-Akt/mTOR pathway underlies the triggering of CD8 and CD4 effector T cells and paralysis of Tregs. Resulting from mTOR activation, effector T cells produce pro-inflammatory cytokines (IL-1, IL-4, IL-6, IL-10, TNFα, IFNγ, TGFβ) and metabolites (2-hydroxyglutarate, kynurenine, prostaglandin E2, 4-hydroxynonenal, malondialdehyde). Further downstream, these cytokines and metabolites promote B-cell activation, plasma cell development, and autoantibody production. These pro-inflammatory signals can trigger or reactivate systemic and organ-specific autoimmune diseases, including lupus, rheumatoid arthritis, vasculitis, thyroiditis, myositis, and inflammatory bowel disease. Corticosteroids, prostaglandin synthesis inhibitors, and B-cell depletion currently represent the main stain of therapeutic interventions. mTOR blockade with N-acetylcysteine or sirolimus has anti-proliferative mechanisms of action and expanded Tregs with therapeutic effects in autoimmune disease. Clinical trials with combination of mTOR inhibitor sirolimus and durvalumab are ongoing in patients with lung cancer. Along this line, personalized treatments based on genetics and immunophenotyping represent the optimal interventions aimed at preventing of CIAD.

32. Predictors And Patterns Of Complementary And Integrative Health Therapy Use Among Individuals With Recent And Non-Recent Cancer Diagnoses: A National Cross-Sectional Study

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Purpose: The aim of this study is to describe the prevalence of complementary and integrative health (CIH) therapy use, and to compare predictors and patterns of use in those with a recent and non-recent diagnosis of cancer, and no previous cancer diagnosis. Methods: This study used data from the 2022 National Health Interview survey to derive US national prevalence estimates for the utilization of any CIH therapy. Therapies were also classified into three main categories: manipulative body-based therapies (chiropractor, acupuncture, massage), creative therapies (music therapy, art therapy), and mind-body therapies (meditation, guided imagery, yoga). Additionally, prevalence and reasons for use (e.g., pain management or general health improvement) were described by cancer type. Regression models identified predictors of any CIH therapy use among all participants as well as within subgroups categorized by cancer status (recent diagnosis within the past two years, non-recent diagnosis, and no past diagnosis of cancer). Results: Among 26,523 participants, prevalence of any therapy use was similar amongst individuals with recent cancer (40.17%), non-recent cancer (37.75%), and no cancer diagnosis (37.93%), but manipulative body-based therapies were more prevalent in the recent diagnosis group when compared to non-recent and no cancer groups (23.62%, 19.68%, 19.18%, respectively, p=.02). Mind-body therapies were mostly used for pain management, whereas manipulative therapies were primarily used for both pain and general health. Overall CIH usage varied by cancer type, with breast (42.03%), skin (41.18%), and gynecological (40.81%) cancers showing the highest rates of use. Adjusted models found higher odds of use among recent (OR=1.37) and non-recent (OR = 1.14) cancer diagnoses compared to those without. Subgroup analyses by diagnosis status revealed that female sex, younger age, depression, self-rated excellent health, higher education, and income were significant predictors of CIH therapy use. Conclusion: Prevalence of CIH therapy use was similar regardless of cancer status, but recent cancer survivors were more likely to use CIH therapies in adjusted models. Additional predictors of using any CIH therapy are similar across cancer status groups. This may indicate continued inequalities in access to these therapies, as use remains highest amongst those with higher socioeconomic conditions.

33. Peri-Hilar Cholangiocarcinoma (Phcca): A Comparative Comprehensive Genomic Profiling Study

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Background: CCA is a heterogenous group of malignancies that arise from epithelium of the biliary tree. The comparison of the genomic landscapes that can influence therapy selection of phCCA from other types of intra- and extra-hepatic CCA (ih/ehCCA) are not well-known. We queried differences in comprehensive genomic profiles (CGP) of CCAs and comparing genomic alterations (GA) in phCCA and other types of CCA Methods: DNA extracted from 110 cases of phCCA, 743 cases of common bile duct CCA (cbdCCA) and 9178 cases of intrihCCA underwent hybrid capture-based CGP to evaluate GA, MSI status, TMB levels, genomic ancestry, genomic signature, HRD score and germline status. phCCA cases were confirmed at surgery and pathology as originating from either the left, right or common hepatic ducts. cbdCCA cases were confirmed either by CBD biopsies or Whipple procedures. PD-L1 expression was determined by IHC using the Dako 22C3 assay using the tumor proportional score (TPS) system Results: Patient characteristics were similar. The GA/tumor and frequencies of European ancestry were similar. Both phCCA and cbdCCA featured significantly greater frequency of ERBB2 GA than ihCCA (P=.002) and lower frequencies of FGFR2 GA (P=.001) and IDH1 GA (P=.006). ihCCA featured significantly higher frequencies of FGFR2 (11.7%) and IDH1 (13.9%; P=.006) GA than either phCCA or cbdCCA. cbdCCA had a significantly higher frequency of KRAS GA than phCCA (P=.015) and ihCCA (P<.001). The KRAS G12C frequency reached 5.9% of KRAS mutated ihCCA. GA in BRAF, PIK3CA, CDKN2A and MTAP were not significantly different. TP53 GA were higher in cbdCCA than phCCA (P=0.011) and combined phCCA and cbdCCA (ehCCA) were higher than ihCCA (P=.071). MSI status, TMB levels and PD-L1 expression was similarly low in all 3 groups. Positive homologous recombination deficiency (HRD) scores based on %gLOH and high frequencies of MMR genomic signatures were similar in all 3 groups. Conclusions: phCCA appears to be a distinctive form of ehCCA featuring significantly higher frequencies of potentially targetable ERBB2 and lower frequencies of targetable FGFR2 and IDH1 mutations, when compared to ihCCA. Predictive IO markers were similarly low in both ihCCA and ehCCA.

34. Evaluation Of Treatment Outcomes In Adults With Blastic Plasmacytoid Dendritic Cell Neoplasm: A Systematic Review And Meta-Analysis

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare neoplasm with a poor prognosis. Treatment options include CD123 directed agents (tagraxofusp) or intensive chemotherapy, followed by allogenic stem cell transplant (allo-HSCT). Sufficient evidence comparing them is lacking and there is no consensus on the best first line treatment. Our primary objective was to evaluate the treatment outcomes in patients with BPDCN receiving tagraxofusp compared to various chemotherapeutic regimes, in terms of response rates, mortality, and patients proceeding to allo-HSCT. Controlled vocabulary encompassing BPDCN and tagraxofusp or SL-401 was used to perform a systematic search in PubMed, Embase, Scopus and Cochrane from inception to April 2023. We identified 818 total patients: 36% (292/818) received tagraxofusp, 60% (494/818) received intensive chemotherapy (HyperCVAD, AML and ALL-like, and CHOP), and 3% received less intensive chemotherapy (azacytidine, venetoclax, or other mild regimes). The median age was 61 (range of 36-80). Most patients were male, and most patients had extensive systemic disease (97%). The OR of having CR for tagraxofusp versus intensive chemotherapy using the random effects model was 0.46 (confidence interval=0.21-1.02, p=0.06, I2=0%), shown in figure 1. Proportions calculated using random effects model (figure 2) were used to determine CR (tagraxofusp 71%, intensive chemotherapy 64%, less intensive chemotherapy 25%), PR (17%, 8%, 31%), NR (23%, 21%, 40%), mortality rate (43%, 30%, 71%), and allo-HSCT rate (51%, 50%, 6%). From our analysis, the OR of attaining CR between tagraxofusp and chemotherapy was not significant and did not answer the question of which modality has a higher chance of CR. What is clearly seen is that less intensive chemotherapy had a lower rate of CR (25%) and allo-HSCT (6%), and higher mortality (71%) and failure rates (PR 32%, NR 40%). This may be attributed to the baseline poor functional status of these patients, leading to the selection of less intensive therapy. We can conclude that whenever possible, either tagraxofusp or intensive chemotherapy needs to be used. While our study does not answer the question of whether tagraxofusp or intensive chemotherapy is better as first line therapy for BPDCN, it highlights the fact that controlled data in the literature is very sparse and emphasizes the need for further research in this space.

35. Contrasting Comprehensive Genomic Profiles (CGP) Of Adenocarcinomas Of The Appendix (AAC) In Younger Versus Older Patients

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Background: AAC is a rare form of intestinal malignancy which can pursue an aggressive clinical course. Little is known about the clinical and biologic features of this disease when it presents in young patients under 40. Methods: 1,840 cases of clinically advanced AAC were selected and analyzed by hybrid capture based CGP to evaluate all classes of genomic alterations (GA). MSI high status and tumor mutation burden (TMB) were determined from sequencing results and PD-L1 was measured by immunohistochemistry (Dako 22C3). Results: 135 (7.3%) of the AAC were identified in patients of 39 years of age or younger ("Younger"). The mean age of the younger patients was 32.9 years and for the 40 and over ("older") patients it was 60.4 years. The slight female gender preponderance was higher in the older patients than the younger patients. The GA per sample were similar. The younger patients had a significantly higher frequency of KRAS GA (71.1% vs 60.4%; p=.017) and TP53 GA (56.3% vs 41.3%; p=.0008). The KRAS G12C mutation frequency was similarly low in both cohorts. Targetable GA in BRAF and ERBB2 were infrequent in both groups as were GA in PIK3CA, PTEN and FBXW7. GA in the APC gene was significantly more frequent in the older patients (10.8% vs 3.7%; p=,007). Biomarkers of immune-oncology (IO) drug efficacy were infrequently identified in both groups including MSI-High status, TMB levels and PD-L1 expression. Conclusions: At a 7.3% incidence, AAC is a relatively infrequent form of gastrointestinal malignancy in young patients. The data analysis shows significant differences in the genomics found in younger and older patients suffering from this disease. These results can have a crucial impact on current and future clinical trials used to design novel treatments. Further exploration into this subject can change the overall approach and even treatment guidelines for this type of cancer.

36. Unraveling The Specificity Of ITK-SLP76 Interaction Through Isothermal Titration Calorimetry: Implications For GVT-GVHD Uncoupling In Allo-HSCT

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Allogenic hematopoietic stem cell transplantation (allo-HSCT) is a promising treatment for hematological malignancies, leveraging graft-versus-tumor (GVT) responses mediated by donor T-cells. However, this approach often triggers graft-versus-host-disease (GVHD), primarily orchestrated by mature donor T-cells. Inhibition of interleukin-2-inducible T-cell kinase (ITK) offers a potential strategy to uncouple GVT from GVHD by targeting its interaction with SH2 domain-containing leukocyte protein of 76 kDa (SLP76). Although ITK inhibitors present an alternative to chemotherapy, their lack of specificity poses challenges. To enhance specificity, understanding the intricacies of the ITK-SLP76 interaction is important. Currently, it is known that the SH2 domain of ITK (ITK_SH2) binds to an intrinsically disordered region (IDR) on SLP76, specifically at tyrosine 145 (Y145). We hypothesize that there is tight binding between ITK_SH2 and SLP76 Y145, and that this is mediated by Y145 phosphorylation and influenced by the structural complexity of both proteins. Using Isothermal Titration Calorimetry (ITC), we have begun to characterize this interaction by determining binding between ITK_SH2 and novel SLP76pY145-based peptides. These peptides have subtle variations in length and amino acid composition, enabling assessment of their impact on binding strength and specificity. Our preliminary results demonstrate in vitro binding between ITK_SH2 and various SLP76 peptides, with a preference for a SLP76pY145 peptide consisting of amino acids 132-155 from the IDR of SLP76 (SLP76pY145_132-155). Future ITC experiments will expand this investigation to include other SH2 domains that are in the same family of kinases as ITK (i.e., BTK_SH2 and Src_SH2) and additional ITK constructs (e.g., ITK_SH3_SH2 and ITK_SH3_SH2_SH1). Additional experiments will be done to examine binding between full-length and truncated versions of SLP76 and the various ITK constructs. These comparative studies will allow us to compare the specificity of SLP76 peptides and ITK to other SH2 domain-containing proteins, as well as elucidate any changes in ITK_SH2 and SLP76pY145 binding as this interaction is put in the context of the other ITK and SLP76 domains. Overall, this research aims to unravel the nuances of ITK-SLP76 interaction, paving the way for targeted therapeutic interventions that effectively uncouple GVT from GVHD in the context of allo-HSCT.

37. Breast Cancer Driver Gene Discovery By A Novel Multi-Omic Approach

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We are interested in understanding the mechanism of oncogenic changes induced by recurrent chromosome breaks in the breast cancer cell model. We recently investigated the degree to which chromosomal structural rearrangement breakpoints are correlated with recurrent DNA double-strand breaks (DSBs) by sequencing the estrogen receptor-positive breast cancer cell line MCF-7 and a non-cancer control breast epithelium cell line MCF-10A. We showed that concurrent DSBs and structural breakpoints in MCF-7 almost exclusively occurred in the pericentromeric region of chromosome 16q. Chromosome 16q is frequently lost in breast cancer cells, including MCF-7 cells. However, our data suggested that the pericentromere of 16q remains intact, and undergoes translocation to other chromosomes, as a result of the recurrent chromosome breakage in the pericentric 16q region. Our data underscored the importance of a complete understanding of the structural alterations on chromosome 16 in a wide collection of cancer genomes. We identified select genes located immediately downstream of 16q pericentromere, including SHCBP1, ORC6, and MYLK3, which showed heightened expression in MCF-7 cells. SHCBP1 and ORC6 are both strong poor prognosis and treatment outcome markers in the estrogen receptor-positive breast cancer cohort. We propose that SHCBP1 and ORC6 are potential oncogenes whose expression is driven by the recurrent breaks at 16q pericentromere. In the future, we will systematically determine chromosome rearrangement hotspots by simultaneous mapping of DSBs, copy number variation and structural variation breakpoints, and gene expression changes in multiple breast cancer cell lines/samples. We will also study the impact of overproducing ORC6, which is increasingly recognized as a putative oncogene in various cancers.

38. Defining ABI1's Role In Prostate Cancer Using Bioinformatic Analysis

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Background: The gene ABI1 has been shown to play a critical role in prostate tumor progression through regulation of the epithelial mesenchymal transition (EMT) pathway. In addition to being a WAVE complex member and STAT3 regulator, it also possesses a novel DNA binding ability through its alternatively spliced exon 4. Isoforms with exon 4 are preferentially selected following androgen-deprivation therapy (ADT) and are associated with worse disease-free survival. Combined with evidence of ABI1 nuclear DNA binding, this raises the possibility of ABI1 regulating transcription. Methods: The metastatic prostate cancer line DU145 RNA sequencing of ABI1 KO, WT and ΔExon 4 rescue DU145 cell lines were preformed and the expression of a variety of prostate cancer (PCa)-related genes were compared. Results: ABI1 exon 4 appears to be critical for the upregulation of a subsect of genes, such as Fibroblast Growth Factor 1 (FGFR1), cAMP-responsive element-binding protein 5 (CREB5) and Cyclin Dependent Kinase 6 (CDK6). Previous studies have shown that FGFR drives bone metastasis of castrate-resistance prostate cancer and promotes a lineage-switched, neuroendocrine phenotype. CREB5 overexpression promotes resistance to ADT and Androgen-receptor (AR) inhibitors, such as enzalutamide. Lastly, CDK6 has also been shown to be upregulated in castrate-resistance prostate cancer. Conclusion: Taken together, this data suggests that ABI1 isoforms containing exon 4 could be transcriptional regulators, promoting resistance to ADT by upregulating genes allowing for prostate cancer to undergo lineage switch. Future experiments are needed to confirm ABI1 plays a role in the mechanism behind the transcription changes.

39. Analyses Of Possible Off-Target Effects On Cardiac And Skeletal Muscles By Berberine, A Drug Suggested To Treat Cancers And Weight-Loss

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Previous reports from our laboratory describing the formation of myofibrils in cultured embryonic cardiac and skeletal muscle cells have proposed that myofibrillogenesis occurs in three steps of increasing protein organization: beginning with premyofibrils, followed by nascent myofibrils and ending in mature myofibrils. (Rhee et al., 1994; Wang et al., 2022; Welchons et al., 2023). Inhibitors of the Ubiquitin Proteasome System (UPS) prevented nascent myofibrils from progressing directly to mature myofibrils in cultured cardiac and skeletal muscle cells, supporting a three-step model of assembly in which some of the proteins in nascent myofibrils are proteolyzed to allow the assembly of mature myofibrils (Wang et al., 2020; 2021). Applications of UPS inhibitors on cultured muscle cells suggests possible explanations for the off-target cardiac and skeletal muscle adverse effects of UPS drugs, which are used on cancer patients. Berberine, a plant derivative, has been used to treat various cancers, including multiple myelomas (Gu et al., 2018). In contrast to the use of UPS drugs, success was reported with Berberine in multiple myeloma patients with no off-target effects on their hearts (Gu et al., 2018). As a test, we have exposed cultured cardiac and skeletal muscle cells to Berberine, a ligase inhibitor (UHRF1, i.e., Ubiquitin-like with PHD and RING Finger domains; Gu et al., 2018). Berberine inhibited myofibril assembly at the nascent myofibril stage in embryonic skeletal muscle cells but had no effect in the assembly of mature myofibrils in embryonic heart cells. In support of our suggested preclinical assay, the specific ligase (UHRF1) that Berberine binds, is not present in cardiac muscle cells, but is present in skeletal muscle cells. Berberine is also being used as a popular weight losing compound, because it is much cheaper and available without a prescription than the semaglutide containing weight losing drugs (Wegovy and Ozempic). In contrast to Berberine, semaglutide had no effects on myofibril assembly in culture assays for both cardiac and skeletal muscle cells. We postulate that analyses of cultured embryonic cardiac and skeletal muscle cells will provide a preclinical assay for the testing of novel cancer drugs with improved outcomes for patients, an important "…goal of the emerging field of cardio-oncology…" (Narezkina and Nasim, 2019).

Cancer Center Research Programs and Membership

The SUNY Upstate Cancer Center currently has three Research Programs that support a wide range of investigations on cancer, ranging from molecular mechanisms and novel experimental drugs to studies on patient survivorship and cancer health disparities.

Each program focuses on a different thematic area (genetics and cell biology; experimental therapeutics; cancer prevention and population health) but Cancer Center members actively participate in and collaborate across several programs. Collaborations are also promoted with investigators at neighboring institutions, which can access the programs as affiliate members.

- ***Program on Cancer Genetics and Cell Biology***
  This Research Program brings together investigators with interests on the basic biology of cancer cells and the tumor microenvironment. This program supports research on cancer cell biology, biochemistry, pharmacology, genetics and immunology. The Program also promotes research on bioengineering and the development of materials and devices to study cancer cells.

- ***Program on Experimental Cancer Therapeutics***
  This Research Program fosters research on novel therapeutic strategies and experimental treatments against cancer and cancer-associated diseases. The Program supports multidisciplinary research in medicinal chemistry, chemo-and radiotherapy, immunotherapies, toxicology, pre-clinical studies, investigational new drugs and devices, and early-stage clinical trials.

- ***Program on Cancer Prevention, Survivorship, and Population Health***
  This Research Program brings together researchers, clinicians, and experts in populational health to promote multidisciplinary studies on the different causes, treatments, and sequelae of cancer. The Program promotes collaborations to study cancer incidence, risk factors, preventative measures, chemo- and radioprotection, clinical trials, patient monitoring, quality of life, and health disparities.

The Research Programs are supported by state-of-the art research facilities, an institutional tumor bank, a streamlined pipeline for patient accrual for clinical trials, and several funding mechanisms for basic-science and clinical investigators. Together, the Research Programs at SUNY Upstate Cancer Center advance our knowledge of cancer to improve patient care and reach long-term, cancer-free, patient outcomes.

Cancer Center members are selected for their accomplishments in cancer research or healthcare; their sustained and productive record of research or clinical work in cancer; and their commitment to work together as part of the scientific community at SUNY Upstate, neighboring and collaborating institutions. Full members must be faculty at SUNY Upstate Medical University who can be identified as Principal Investigators for clinical or basic science research. Affiliate members from other academic institutions must be tenured or tenure-track faculty at their respective institutions and have similar qualifications to full members. Trainee members may be clinical residents, fellows, postdoctoral researchers, medical and graduate students at SUNY Upstate Medical University. Trainees must be sponsored by a Full Member of the Cancer Center that can act as training advisor.

Members of the Cancer Center have access to "Cancer Center only" sources of support for academic activities at SUNY Upstate. Specific support includes:

- One- and two-year pilot funding for research projects in the field of cancer.
- Two-year partial support for postdoctoral scholars in cancer research.
- Scholarships for summer students pursuing research or clinical projects in cancer.
- Priority to invite speakers through the "Distinguished Cancer Researcher" seminar series.
- Priority to submit requests of cancer-related resources and infrastructure (through the research program directors)
- Access to support for cancer-related clinical trials through the SUNY Upstate Clinical Research Unit.
- Promotion of on-campus activities and seminars using Cancer Center communications resources.

2024 Cancer Center Research Program Members

Cancer Experimental Therapeutics Program Members

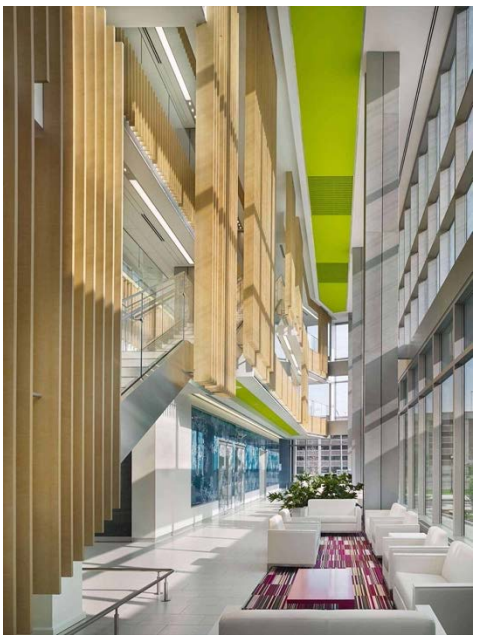
- Paul Aridgides, M.D.
- Harish Babu, M.D., Ph.D.
- Alexander Banashkevich M.D.
- Alina Basnet, M.D.
- Dimitra Bourboulia, Ph.D.
- Melanie Comito, M.D.
- Michael Cosgrove, Ph.D.
- Andrea Dvorak, M.D.
- Christian Geier M.D.
- Teresa Gentile M.D., Ph.D.
- Diana Gilligan, M.D., Ph.D.
- Stephen Graziano, M.D.
- Dandan Guo, Ph.D.
- George Holz, Ph.D.
- Jason Horton, Ph.D.
- Joseph Jacob, M.D.
- Mobin Karimi, M.D., Ph.D.
- Bruce Knutson, Ph.D.
- Leszek Kotula, M.D., Ph.D.
- Prashanth Kumar, M.D.
- Yamin Li, Ph.D.
- Stewart Loh, Ph.D.
- Hong Lu, Ph.D.
- Juntao Luo, Ph.D.
- Philip Monteleone, M.D.
- Megan Oest, Ph.D.
- Snehalata Pawar, Ph.D.
- Andras Perl, M.D., Ph.D.
- Bernard Poiesz, M.D.
- Jamie Romeiser, Ph.D., MPH
- Jean Sanger, Ph.D.
- Joseph Sanger, Ph.D.
- Rahul Seth, D.O.
- Jody Sima, M.D.
- Brittany Simone, D.O.
- Karna Sura, M.D.
- Thomas van der Meer, M.D., FACS
- Mariano Viapiano, Ph.D.
- Jushuo Wang, Ph.D.
- Augusta Williams, D.Sc., MPH
- Richard Wojcikiewicz, Ph.D.
- Mark Woodford, Ph.D.
- Xiaoran Hu, Ph.D.

Cancer Genetics and Cell Biology Program

- Rinki Agarwal, M.D.
- Michael Archer, D.O., FACS
- Harish Babu, M.D., Ph.D.
- Dimitra Bourboulia, Ph.D.
- Michael Cosgrove, Ph.D.
- Christian Geier, Ph.D.
- Diana Gilligan, M.D., Ph.D.
- Jason Horton, Ph.D.
- Tamara Jamaspishvili, M.D., Ph.D.
- Mobin Karimi, M.D., Ph.D.
- Bruce Knutson, Ph.D.
- Leszek Kotula, M.D., Ph.D.
- Mira Krendel, Ph.D.
- Vladimir Kuznetsov, Ph.D.
- Hong Lu, Ph.D.
- Gloria Morris, M.D., Ph.D.
- Andras Perl, M.D., Ph.D.
- Bernard Poiesz, M.D.
- Jean Sanger, Ph.D.
- Joseph Sanger, Ph.D.
- Norifumi Urao, M.D., Ph.D.
- Mariano Viapiano, Ph.D.
- Guirong Wang, Ph.D.
- Jushuo Wang, Ph.D.
- Richard Wojcikiewicz, Ph.D.
- Mark Woodford Ph.D.

Cancer Prevention, Survivorship and Population Health

- Tamer Ahmed, M.D.
- Michael Archer, D.O., FACS
- Alina Basnet, M.D.
- Melanie Comito, M.D.
- Mashaal Dhir, M.D., FACS
- Darlene Ely,
- Jason Horton, Ph.D.
- Leslie Kohman, M.D., FACS
- Hong Lu, Ph.D.
- Philip Monteleone, M.D.
- Christopher Morley, Ph.D.
- Gloria Morris, M.D., Ph.D.
- Bernard Poiesz, M.D.
- Katja Reuter, Ph.D.
- Jamie Romeiser, Ph.D., MPH
- Jean Sanger, Ph.D.
- Joseph Sanger, Ph.D.
- Vandana Sharma, M.D. FASA
- Jana Shaw, MD, MPH, FPIDS,FAAP
- Jody Sima, M.D.
- Steven Sperber, M.S., Ph.D., FACMG
- Telisa Stewart, Dr.PH
- Karna Sura, M.D.
- Jushuo Wang, Ph.D.
- Roger Wong, Ph.D., MPH, MSW



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10 A Decade of Dedication

As we recognize the 10-year anniversary of our state-of-the-art building, we reflect on a decade of unwavering dedication to excellence in cancer care. Share in our celebration as we highlight the work that has defined our journey over the past decade!

- **Cutting-Edge Diagnostics, Treatments & Technology:** Our 100,000-square-foot center offers cutting-edge treatment, including advanced imaging technology, robotic-assisted surgery and immunotherapy.
- **Multidisciplinary Care:** Our dedicated teams of surgeons, medical oncologists, radiation oncologists, genetic counselors, nurses and support staff collaborate closely to personalize treatment plans for each patient.
- **Research Partnerships:** Upstate Cancer Research encompasses the efforts of many Upstate faculty and collaborators at other institutions, with the goal of translating research into improving outcomes for patients through potential cures, technologies and other products.
- **Clinical Trial Studies:** Our robust Clinical Research Team allows Upstate patients access to national clinical research studies.
- **Patient Support Services:** Upstate Cancer Center provides a range of supportive services, including financial counseling, nutritional counseling, Psychosocial Oncology and integrative therapies to help you and your family throughout your treatment.
- **Survivor Wellness Program:** Upstate's Survivor Wellness team works in partnership with your existing health care providers to address the unique needs of cancer survivors, empowering them to lead fulfilling lives post-treatment.
- **Community Outreach and Education:** We are committed to serving the larger community through outreach efforts, educational programs and seminars. We also host awareness campaigns and promote early cancer detection and prevention.

Thank you

for allowing us to be part of your healing journey. We are grateful that our community has entrusted us with their cancer care over the past decade.