2022-2023 FTC Consortium Progress Report

Sonenshein Lab. Breast cancer is the leading cause of cancer deaths in women. Breast cancers that express the hormone receptors (HRs) Estrogen Receptor-α (ER) and Progesterone Receptor (PR), but not Human Epidermal Growth Factor Receptor-2 (HER2) [HR+/HER2-] are the most common subtype (68%), followed by HR+/HER2+ and HR-/HER2- (10% each) and HR-/HER2+ (4%) [NCI]. Endocrine therapies, e.g., the selective estrogen receptor modulator (SERM) Tamoxifen, block estrogen signaling in HR+ breast cancer cells, decreasing recurrence and improving survival. Similarly, the anti-HER2 antibodies Trastuzumab and the antibody-drug conjugate Ado-trastuzumab emtansine improve outcomes of patients with HER2+ cancers. While patients with HR-driven and/or HER2-driven breast cancer have benefited enormously from such endocrine and HER2-targeted therapies these tumors still account for the preponderance of breast cancer deaths. The HR-/HER2- or ER-/PR-/HER2- subtype, also known as Triple-Negative Breast Cancer (TNBC), occurs preferentially in younger women and in women of African-American descent, and is even more challenging to treat due to a lack of ER, PR or HER2 target expression.

"ADAM8" is a protein on the surface of cancer cells. Previously, we demonstrated that ADAM8 promotes TNBC growth and spread in mouse models. RNA analysis demonstrated that *ADAM8* is one of the more highly expressed genes in breast cancer as compared with normal tissue, and that high *ADAM8* messenger RNA levels correlate significantly with poor disease-free survival and overall survival in the total patient population. Similarly, high ADAM8 protein expression has been detected in several other solid tumors and is always associated with either poorer prognosis, a more metastatic phenotype, or higher tumor grade.

A) Early detection. The FTC Consortium has postulated that tissues destined to become cancerous have tell-tale molecular changes that herald cancer formation even before pre-cancerous lesions can be detected by conventional imaging techniques. As a corollary, it was hypothesized that these molecular changes can be detected in circulating blood, making screening for pre-pre-cancers feasible. To test this hypothesis, the Sonenshein lab, in collaboration with the Sherr lab, is setting up a mouse model of exposure to a common environmental chemical that is known to induce cancers in humans. In this model cancers emerge about 40 weeks after chemical exposure. The Sonenshein lab will be taking blood samples at various time points and analyzing them for a specific molecular profile of "micro RNAs" (miRNAs) that are known to circulate and to suppress certain biological functions including immune function. While high risk, these studies are potentially high reward as they may be able to determine when someone has been exposed to a carcinogen (a chemical exposure signature) or when they are likely to soon develop cancer (a pre-pre-cancer signature). As indicated below, the Kuperwasser lab will measure another potential marker of exposure or pre-pre-cancer, i.e., changes in epigenetic signatures.

B) Preventative/Therapeutic Antibody Development. ADAM8 appears to be an ideal target for therapeutic intervention as it is a non-essential gene for the health of normal mice. By staining cells with fluorescent ADAM-8-specific antibodies, the Sonenshein lab showed that ADAM8 is expressed on 34.0% (17/50) of TNBC biopsies, whereas adjacent histologically normal breast tissue was negative (0/50). As reported last year, the Sonenshein laboratory has worked for the past six years on the development of an antibody-based intervention strategy capable of specifically binding to and inhibiting ADAM8 activity. A panel of extremely specific mouse monoclonal anti-ADAM8 antibodies (mAbs) have been isolated and a lead mAb has been isolated (manuscript in preparation). More recently, the lab has prepared a humanized version of this antibody and is in the process of performing safety testing prior to entering Investigational New Drug (IND) enabling studies with the hope that our antibody-based intervention will effectively block early pre-cancers as well as newly developing (secondary) cancers when administered either alone or in combinatorial regimen.

C) Fluorescent ADAM8 Detection Assay. To identify those patients who could benefit from an anti-ADAM8 treatment, the Sonenshein lab has also developed a preclinical diagnostic assay using the monoclonal antibody to "light up" ADAM8 positive cells. To validate the ability of this assay to detect ADAM8 expression in tissue samples, a set of tissue microarrays (TMAs) with 490 samples of breast cancer biopsies, including 412 with data on expression of ER, PR and HER2 (including 61 TNBCs across the panel), were analyzed. ADAM8 expression was confirmed in 36.1% (22/61) of TNBCs, consistent with our earlier studies using a research-only antibody. The analysis revealed a similar positivity rate (~30%) in the non-TNBC breast cancer subtypes, including

HR+/HER2-, HR-/HER2+, and HR+/HER2+ that had not been examined previously. Of note, high ADAM8 expression in these patients was associated with poorer survival, suggesting a potential prognostic value for this assay in addition to its intended companion early diagnostic purpose.

Conclusions. ADAM8 is widely expressed in all breast cancer subtypes indicating a larger patient population that could potentially benefit from treatment with our humanized antibody. Furthermore, fluorescent imaging data will provide support for both a diagnostic as well as prognostic. As ADAM8 has been implicated in multiple other solid malignancies, including those of the bone, colon, head and neck, pancreas, liver, lung, and stomach, continued development of a clinical ADAM8 detection assay may have broad impact on cancer prevention and management.

Kuperwasser Lab. Over the course of the past year the Kuperwasser laboratory has been conducting a comprehensive investigation into the potential effects of environmental exposures on the development of normal and cancerous breast tissue. To this end, patient-derived mammary epithelial cells have been utilized in a 3-D biomimetic organoid tissue model to study the molecular, cellular, and tissue-level changes that result from exposure to a variety of environmental chemicals. With this technology, the lab is able to assess the effects of a variety of chemicals on normal human breast development and to extrapolate those results to implicate potential environmental causes of breast cancer.

A) A Novel Model of Human Breast Development in the Presence of Environmental Chemicals. The Kuperwasser laboratory's research efforts over the last year have resulted in the development of a unique and powerful model for growing human breast cells in culture. Using a gel-like substance (hydrogel) and a combination of nutrients, the lab is now able to take single human mammary cells, obtained from reduction mammaplasty surgery, and culture them for several weeks during which the cells divide and begin to form 3-D structures analogous to ducts formed in normal mammary glands (**Figure 1**). Furthermore, the system has been adapted to study the developmental and genetic effects of different environmental endocrine-disrupting chemicals (EDCs) on human breast development. Preliminary findings from these experiments indicate that “organoids” derived from patient breast cells grown with physiologically relevant levels of bisphenyl A (BPA) and bisphenyl F (BPF) appear to be, on average, larger than the controls, and some show structural alterations as well. In addition, there have been additional cellular and molecular changes observed following treatment with EDCs. In collaboration with the Sherr lab, the Kuperwasser lab is now assessing the effects of co-exposure to EDCs and environmentally common components of smoke on breast tissue development. These studies represent the Consortium’s first foray into evaluating the effects of environmental chemical mixtures, similar to those experienced in the real world, on primary human breast tissue. Notably, the preliminary results obtained thus far have highlighted intriguing phenotypic differences in patient samples induced by EDC exposure.

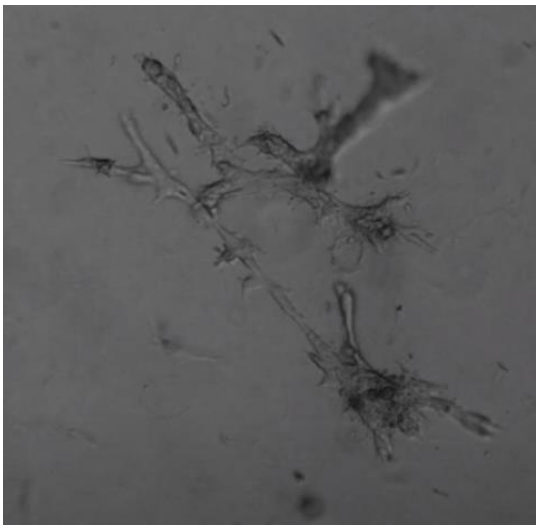

Figure 1. Real-time Development of Human Mammary Gland 3-D Organoids. Single cells from patients undergoing reduction mammaplasty are cultured in three dimensions in the presence of specific growth factors. Videos taken over 30 days reveal the expansion of those single cells into a network of ducts similar to those in developing human breast tissue. These organoids are now being exposed to environmental chemicals to assess early chemical-induced changes consistent with cancer development. Presented here is a photo taken at approximately day 20 of culture.

B) Detection of Epigenetic Changes on DNA That Indicate Chemical Exposure and a Pre-pre-cancerous State. In a second objective and as noted above, the Kuperwasser lab is working with the Sonenshein, Sherr, and Monti labs to implement an experiment in which permanent DNA changes (epigenetic marks) in chemical-exposed mice are assessed for their potential to: a) identify genetic signatures of chemical exposure and b) predict a pre-cancerous state. These epigenetic marks (DNA methylation) may help us not only determine what chemicals to which someone has exposed, potentially even in the distant past, but also to predict when someone is likely to develop cancer well before physical lesions can be imaged. This early identification of pre-

cancers is expected to lead to non-toxic approaches to cancer prevention before pre-cancerous or malignant lesions are detectable by conventional technologies.

Conclusions. The Kuperwasser lab has developed a powerful new technology that mimics human breast development and is being used to assess the effects of common environmental chemicals on developing breast tissue.

Monti Lab. The work in the Monti lab over the past year has encompassed analysis of multi-omics data (i.e., gigabyte-sized datasets indicating changes in DNA sequence (genomics), production of protein-encoding messenger RNA (transcriptomics), and a distribution of protein species (proteomics)) to study the mechanisms of action of breast and other cancers and the contribution of environmental exposures to cancer development.

A. Breast Cancer. The Monti lab is investigating mechanisms driving cancer initiation in basal-like (TNBC) breast cancer, a particularly aggressive type of breast cancer, and has identified aberrant activation of an important developmental cell signaling pathway as playing an important role in cancer formation. In addition, the lab is investigating the role of type 2 diabetes (T2D) as a comorbidity contributing to worse cancer outcomes in multiple organs, including breast. We suggest that our approach has value for identifying novel blood-based biomarkers that may link environmental chemicals and high fat diets to biochemical progression of breast cancer.

B. Lung Cancer. In collaboration with the Sherr lab, the Monti lab is continuing its investigation into the role played by the aryl hydrocarbon receptor (AhR) in pre-cancer- or cancer-induced suppression of the immune system. The lab is using state-of-the-art single cell messenger RNA-sequencing to investigate the change in immune cell type proportions as a consequence of the molecular inhibition (i.e., blocking) of the AhR with a novel inhibitor produced by the Sherr lab.

C. Head & Neck Cancer. In collaboration with the Sherr lab, the Monti lab continues its investigation into the mechanisms driving initiation and progression of oral cancer based on the analysis of multi-omics human data, as well as animal models of chemical carcinogen-induced oral cancer. Below are some of the main highlights.

Modeling malignancy. We applied computational and experimental approaches to the elucidation of the mechanisms driving oral cancer cell heterogeneity. In particular, we applied novel computational methods that we developed to segregate subsets of oral cancer cells based on their molecular signatures. Not only do these studies reveal how varied are the cells making up a tumor, they also suggest novel mechanisms through which some of these cells become aggressive. These findings were validated using specific drugs to target one or another of the revealed cancer pathways in an animal model of human cancer. Our findings are of particularly timely significance, given the increasing evidence pointing to a crucial role for these signaling pathways in driving cancer aggression and given the potential for cancer interception with the drugs tested in our animal models. A manuscript describing this work was published in Molecular Cancer Research and another is under review at Translational Research.

Modeling premalignancy. To gain insights into the molecular mechanisms promoting the progression of pre-cancer lesions into full blown cancers, we profiled and analyzed, on a molecular level, 66 human pre-cancer lesions. Our data revealed gene signatures associated with transition of sedentary cells to highly migratory (metastasizing) cells and with increased pro-tumorigenic inflammation. Interestingly, the studies also suggested a role for oral cavity bacteria (microbiome) in cancer development. A manuscript on this work is in preparation.

Computational Resources Development. We are completing the extension and optimization of the functionalities of our computer application, CaDrA (Candidate Driver Analysis), a tool we developed for the identification of genetic and epigenetic features driving cancer (e.g., after exposure to a chemical). We have optimized, hardened, and deployed the tool as an open-source R package developed based on best software engineering practices and design principles (GitHub.com/montilab/CaDrA) The package is being thoroughly documented, and user interface was designed to make the tool “biologist-friendly” (GitHub.com/montilab/CaDrA-shiny). The software is accessible at https://cadra.bu.edu/. Further, the package has been “containerized” via Docker to make it cloud-ready and automatically compatible with various high-performing computing (HPC) environments. A manuscript describing the package and the interface is in preparation.

Conclusions. The Monti lab has developed multiple computational models that show similarities between breast and other cancers and that reveal important mechanisms through which cancers develop in the presence or absence of environmental chemicals.

Sherr lab. As noted above, the Sherr lab serves as a hub for studies in the other three laboratories relating to environmental chemical-induced cancers in mouse models. In addition, the lab continues to study how pre-cancers and cancers suppress immune responses that would otherwise be sufficient to kill the tumor.

A) The Role of an Environmental Chemical Receptor, the AhR, in Suppressing Immunity to Tumors. Many studies indicate that the human immune system is capable of killing pre-cancerous or cancerous cells under "normal" conditions. However, virtually all types of cancers eventually develop a mechanism for inhibiting that response by activating "immune checkpoints", specific molecules that serve as brakes on the immune system. These immune checkpoints are the targets cancer immunotherapies that are remarkably effective in some, but not all patients. However, mechanisms that control the expression and activation of these immune checkpoints is not completely understood nor is their role in pre-pre-cancer initiation. The Sherr lab has demonstrated that at least two of the major immune checkpoints active in cancer are strictly controlled by the AhR and are activated with environmental chemicals. That several environmental chemicals can bind and activate the AhR (which then turns on the immune "brakes") explains why they have historically been found to be immunosuppressive. Furthermore, the laboratory has shown that deletion of the AhR with state-of-the-art gene editing techniques enables the development of robust anti-cancer immune responses and renders animals completely or partially immune to developing oral or lung cancers, respectively. For example, tagging AhR^+ tumor cells with a green fluorescent tag and immune cells with a red fluorescent tag demonstrates that unmanipulated AhR^+ tumors (**Figure 2, left**, **green cells**) are virtually devoid of immune cells (**Figure 2, left, red cells**) while AhR-deleted tumors show infiltration of many immune cells (**Figure 2, right, red cells**), further characterization of which using single cell RNA sequenced as described in Dr. Monti's work, revealed their identity as "killer T cells", i.e., the immune cell types most effective at killing cancers. A manuscript demonstrating immunity in AhR-negative lung cancers will be submitted for publication in April.

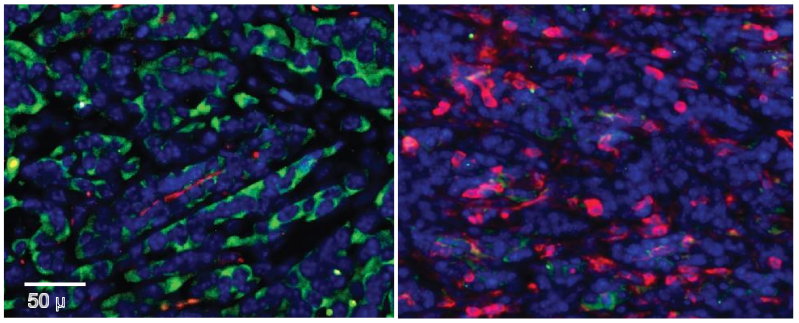

Figure 2. Deletion of the Aryl Hydrocarbon Receptor (AhR) from Cancer Cells Enables Recruitment of Killer Immune T Cells to the Lung Cancers. Tumors were sectioned into thin layers and stained for AhR expression (**green**) or infiltrating immune cells (**red**). On the left is a control tumor expressing AhR normally. On the right is an AhR-negative tumor.

B) Molecular Analysis of AhR Control of Immune Checkpoints. Using molecular techniques, the Sherr lab and Monti labs have identified specific signaling pathways within cancer cells that result in the expression of a prototypical immune checkpoint (immune suppressive) molecule, PD-L1 (Programmed Cell Death Ligand 1). Furthermore, they showed that the AhR controls PD-L1 expression and that environmental chemicals that activate the AhR induce high levels of immunosuppressive PD-L1. The nature of this deleterious molecular pathway

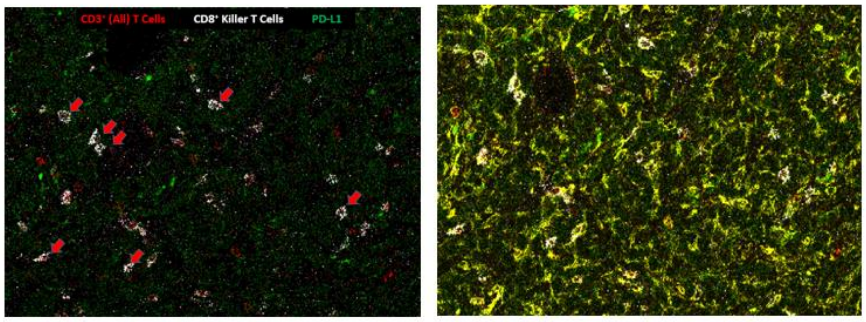

Figure 3. Imaging Mass Cytometry of Immune Killer T Cell Infiltration into a Tumor. Visualized here is a thin section of mouse lung cancer stained for 30 proteins distinguishing 14 different immune cell types. **Left**: While stained with 30 different colors, shown here are results filtered only for 3 colors, **red** for all immune T cells, **white** for all killer T cells, and **green** for all cancer cells expressing the immune checkpoint protein, PD-L1. Killer T cells are indicated with red arrows. **Right**: Results filtered for 4 colors, the same three colors as in the left image plus a darker green for all malignant cells.

and the ability of environmental chemicals to induce it are described in a second manuscript being prepared for submission.

C) Development of An Imaging Tool, Imaging Mass Cytometry, to Visualize the Immune System Attacking Cancers. In the last year, The Sherr lab has been exploiting a powerful new technology, Imaging Mass Cytometry (IMC), to define the multiple subsets of immune cells capable of killing pre-cancers and full-blown malignancies. With this technology, as many as 30 cellular proteins can be identified and quantified in tumor samples and the ability of immune cell subsets to "talk to" one another can be determined. For example, infiltration of killer T cells into the body of am AhR-negative tumor can readily be shown (**Figure 3**). This technology is now being used to determine, at a very granular level, how pre-cancers suppress immunity.

Conclusions. The Sherr lab has used multiple state-of-the-art technologies, including gene editing, imaging mass cytometry, and live animal imaging to drill down on the molecular mechanisms through which an environmental chemical receptor suppresses immunity in pre-cancers and full-blown malignancies.

Scientific Communications in which Find The Cause Breast Cancer foundation is gratefully acknowledged.

Invited lectures and posters given locally, nationally, and internationally.

Understanding mammary gland development through organoid biology and genetic approaches. **Kuperwasser, C.** (June 2022). *Gordon Research Conference on Mammary Gland Biology*, Barga, Italy.

Combining 3D organoids and genetic technologies to reveal developmental programs: **Kuperwasser, C. (**March 2022). *Special Seminar, University of Minnesota, Twin Cities.*

Combining 3D organoids and genetic technologies to reveal developmental programs. **Kuperwasser, C**. (March 2022). *Seminar, Department of Cell, Molecular & Developmental Biology, Tufts University School of Medicine.* Boston, MA.

Rauner, G., Trepicchio, C., Traugh, N., Parrish, M., Gupta, P., **Kuperwasser, C**. (February 2023) Advancements in breast tissue biomimetics. *Keystone Symposium: Organoids as Models of Development and Disease, and their Impact on Drug Discovery, CO, USA.*

Traugh, N., Rauner, G., Gupta, P., **Kuperwasser, C**. (June 2022) Developing a 3D biomimetic model to study human mammary immune-epithelial cell interactions and enhanced tissue regeneration. *2022 GRC Mammary Gland Biology*.

Trepicchio, C., Rauner, G., Traugh, N., Gupta, P., **Kuperwasser, C**. (June 2022) Developing a 3D biomimetic model to study human mammary immune-epithelial cell interactions and enhanced tissue regeneration. *2022 GRC Mammary Gland Biology*.

Mal,Y, Rauner, G., Gupta, P., **Kuperwasser, C**. (June 2022) The Role of ZHX2 in Mammary cell Plasticity and EMT. *2022 GRC Mammary Gland Biology*.

Khan, M.M., Frustino, J., Villa, A., Nguyen, B. C., Woo, S. B., Varelas, X., Kukuruzinska, M., **Monti, S.**, *Characterization and integration of transcriptional and microbial profiles of oral lesions and cancer*, ISMB 2022 COSI Track: Microbiome, Madison, WI. Poster. Video. Slides.

Khan, M.M., Kroehling, L., Bais, M., Varelas, X., Kukuruzinska, M., **Monti, S.**, Investigation of Cellular Heterogeneity in 4NQO-induced Tumors in Mice and Inhibition through Therapeutic Interventions, Evans Day, 2022. Poster.

Chau R, Bulekova K, Kartha V, **Monti S**. *CaDrA: A Containerized and Cloud-Deployable Open-Source Software Package for Candidate Driver Analysis of Multi-Omics Data*. ISMB 2022 (COSI Track: BOSC), Madison, WI. Poster. Video.

Li M, Song Z, Gurinovich A, Sebastiani P, **Monti S**. *Development of a yQTL Discovery Pipeline Applicable to both Unrelated and Related Individuals*. IGES 09/2022. Same abstract was also submitted to ASHG 10/2022. [IGES Poster] [ASHG Poster to come]

Kroehling L, Khan MM, Kukuruzinska M, Varelas X, Bais M, **Monti S.** *Analysis of Heterogeneity in the Tumor Microenvironment in the 4NQO HNSCC Mouse Model*. ICSB 10/2022, Berlin, Germany. Poster and 1 min flash talk.
Kroehling L, Khan MM, Kukuruzinska M, Varelas X, Bais M, **Monti S**. *Analysis of Heterogeneity in the Tumor Microenvironment in the 4NQO HNSCC Mouse Model*. Evan's day 10/2022. Poster.

Spinella A, Kroehling L, **Sherr DH**, Kukuruzinska MA, **Monti S**, Varelas X. *Defining age-associated oncogenic drivers of an immune-evasive tumor population in oral squamous cell carcinoma*. Lightning talk presented at the Genome Science Institute (GSI) 2022 Research Symposium. November 17, 2023, Boston University Chobanian & Avedisian School of Medicine, Boston, MA.

Spinella A, Kroehling L, **Sherr DH**, Kukuruzinska MA, **Monti S**, and Varelas X. *Defining oncogenic drivers of an age-associated, immune-evasive tumor population in oral squamous cell carcinoma.* 2023 APSA Northeast Regional Conference, Boston, MA. March 4, 2023.

Monti S, Sebastiani P, Song Z, Huang Z, Li VM, Andersen-Toomey S, Perls TT, *Serum metabolomics signatures of extreme old age and longevity*. Metabolomics of longevity and lifespan Symposium, 2023 GSA Annual Scientific Meeting, Tampa, FL.

Qiu Y, Yu R, Chen A, Llevenes P, Kolla M, Jafari N, Pompa I, Ennis C, Mahdaviani K, Ko N, **Monti S**, Denis G. *Exosomes produced by adipocytes induce EMT, and tumor metastasis, in both in vivo and in vitro models of TNBC*. ISEV Annual Meeting 2023, Seattle, WA.

Snyder M, Lara B, Kenison-White J, Wang Z, Yang K, and **Sherr, DH**. 2022. Malignant cell expression of the aryl hydrocarbon receptor induces PD-L1 and immunosuppression
in models of oral and lung cancer. American Association of Immunologists, Portland, OR.

Snyder M, Kenison-White JE, Wang Z, Lara L, Yang K, Quintana FJ, **Sherr DH**. 2022. The AhR as a regulator or immune checkpoints in cancer. 2022 International AhR Symposium. State College, PA.

Sherr, DH. Evans Center Affinity Research Collaborative Symposium. "The AhR as a Master Regulator of Immune Checkpoints"., Boston, MA

Sherr, DH. International AhR Symposium. "AhR-AhR Ligand Feedback Mechanisms in Cancer and Cancer Immunity" College Station, PA.

Sherr, DH. International AhR Symposium. "Executive summary of the 2022 International AhR Symposium" College Station, PA.

Peer Reviewed Journal Publications.

Nora D. Mineva, Stefania Pianetti, Sonia G. Das, Sri Srinivasan, Nicolas M. Billiald, **Gail E. Sonenshein**. A novel class of disintegrin binding, dual metalloproteinase and disintegrin antagonist, human ADAM8 antibodies for treatment of ADAM8-driven triple-negative breast cancer

Stefania Pianetti, Kathy D. Miller, Hannah H. Chen, Sandra Althouse, Sha Cao, Steven J. Michael, **Gail E. Sonenshein,** and Nora D. Mineva. ADAM8 is expressed widely in breast cancer and predicts poor outcome in hormone receptor positive, HER-2 negative patients.

Kern J, Tilston-Lunel A, Federico A, Ning B, Mueller A, Peppler G, Stampouloglou E, Cheng N, Johnson, R, Lenburg M, Beane J, **Monti S**, Varelas X (2022). *Inactivation of LATS1/2 drives luminal-basal plasticity to initiate basal-like mammary carcinomas*. Nature Communications 13(1):7198. PMID: 36443313. PMCID: PMC9705439

Jafari N, Chen A, Kolla M, Pompa IR, Qiu Y, Yu R, Llevenes P, Ennis CS, Mori J, Mahdaviani K, Halpin M, Gignac GA, Heaphy CM, **Monti S**, Denis G (2022). *Novel Plasma Exosome Biomarkers for Prostate Cancer Progression in Co-Morbid Metabolic Disease.* Advances in Cancer Biology – Metastasis 6: 100073

Alhousami T, Diny M, Ali F, Shin J, Kumar G, Kumar V, Campbell J, Noonan V, Hanna G, Denis GV, **Monti S**, Kukuruzinska MA, Varelas X, Bais M (2022). *Inhibition of LSD1 attenuates oral cancer development and promotes therapeutic efficacy of immune checkpoint blockade and Yap/Taz inhibition*. Molecular Cancer Research 20(5): 712–72. PMID: 35105672

Reed ER, Jankowski SA, Spinella AJ, Noonan V, Haddad R, Nomoto K, Matsui J, Bais MV, Varelas X[+], Kukuruzinska MA[+], **Monti S**[+] (2023). *β-catenin/CBP activation of mTORC1 signaling promotes partial epithelial-mesenchymal states in head and neck cancer.* Under review at Translational Research.

Karagiannis T, Dowrey TW, Villacorta-Martin C, Montano M, Reed E, Andersen SL, Perls TT, **Monti S**[+], Murphy GJ[+], Sebastiani S[+] (2023). *Multi-modal profiling of peripheral blood cells across the human lifespan reveals distinct immune cell signatures of aging and longevity*. Lancet eBiomedicine (In press).

Arinze, N. V., Yin, W, Lotfollahzadeh, S., Napoleon, M.A., Richards, R, Walker, J.A., Belghasem, M., Ravid, J.D., Hassan Kamel, M., Whelan, S.A., Lee, N., Siracuse, J.J., Anderson, S., Farber, A. **Sherr, D.H**., Francis, J., Hamburg, N.M., Rahimi, N., and Chitalia, V.C., 2022. Tryptophan metabolites suppress Wnt pathway and promote adverse limb events in CKD patients. *J Clin Invest*.

Snyder, M., Wang, Z, Lara, B., Fimbres, J., Song, G., Khan, M.M., **Monti, S**., **Sherr, DH**. IFNγ-induced Immunosuppression in Lung Adenocarcinoma is Mediated by the Aryl Hydrocarbon Receptor Through PD-L1 and Indoleamine 2,3-dioxygenase Control. In preparation.