



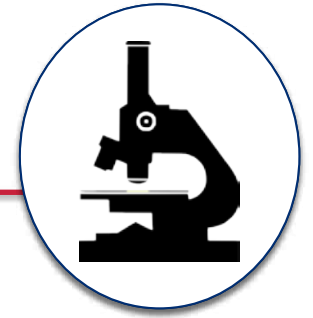
THE UNIVERSITY OF ARIZONA
HEALTH NETWORK



Department of Pathology
Presentation to Dr. Garcia

Research
September 8, 2014

Presented by Lisa Rimsza, MD



- Research
 - Describe the department's primary area(s) of research focus
 - Identify major collaborators/collaborations locally, nationally, internationally
 - Showcase up to 3 department "Stars" (at least one of whom is junior) - 15 min presentations

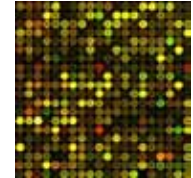


Translational Research: Pathology

Microscopy &
Immunohistochemistry



Laboratory & Molecular
techniques

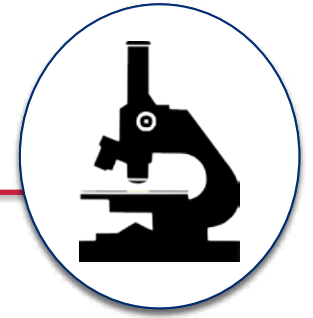


Tissue Banking

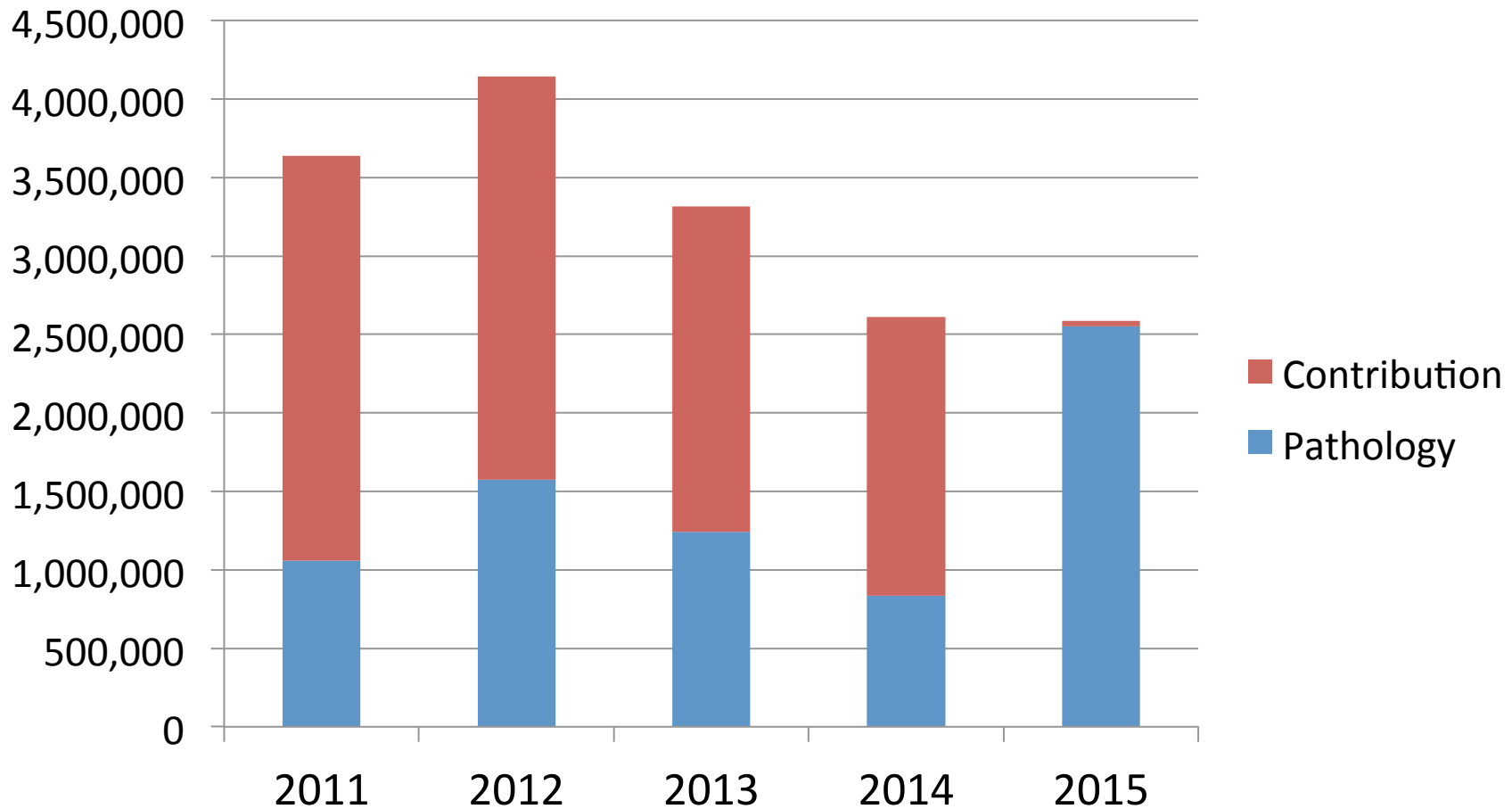


Precision Medicine
Neuroscience
Population Health
Health Disparities



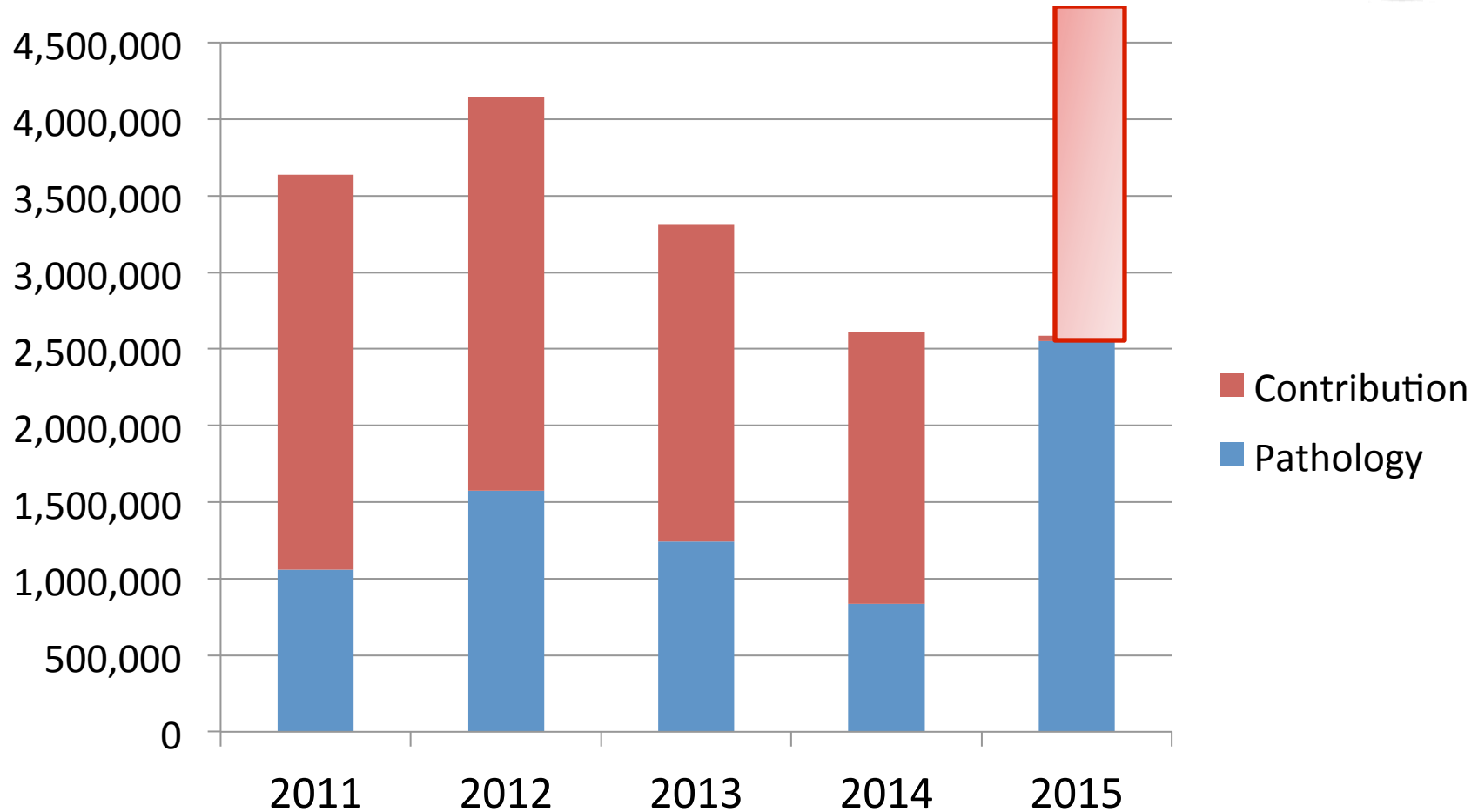


Funded Research last 5 years over \$16M



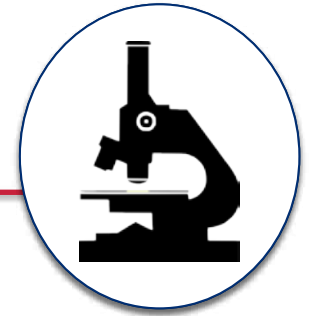


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Space & Funding

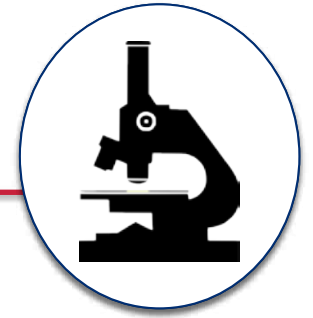


- Pathology has 11,135 net square feet of laboratory and office space primarily in COM and LSN 5th floor
 - Approximately 1800 sq ft, for hospital archives & BMT lab
- \$268-482 per square foot (benchmark \$325)
- Dedicated research support staff
 - Stacey Hines-Holdcraft, administrative, grant support
 - Robert Hershoff, equipment, photomicroscopy, IT support
- Core equipment: microscopes, thermocycler, plate reader, millipore filtered water, dry ice shipments, biological safety cabinet, -80C freezer, 3 ultra-centrifuges, high capacity liquid nitrogen box, spectrophotometer, microtomes, embedding station, cryostat, etc.



Research Activities Align with 4 Pillars of Excellence

- Precision Health (Biobanking, Cancer biology, Advanced Diagnostics)
 - Rimsza, Nelson, Bhattacharyya, Schmelz, Zheng
- Neuroscience (Aging Brain)
 - Rance
- Health Disparities (Native American Cancer Prevention, Envenomation, Infectious disease)
 - Briehl, Boyer, Whitfield
- Population Health and Health Outcomes (Laboratory test and blood utilization)
 - De, Brothman, Novak



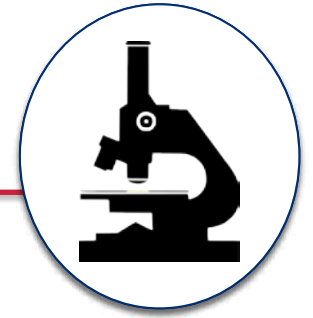
Arizona Lymphoma Repository (Rimsza)

- Consented patients for storage of tumor and normal blood samples
- Collection of excess diagnostic tissues
 - Fresh for snap freezing
 - Excess cells from clinical flow cytometry lab
 - FFPE blocks and slides of lymphoma patients
- Data related to hematologic malignancy, treatment, outcome
- Sharing of samples in coded manner
- Inventory entered into TissueMetrix





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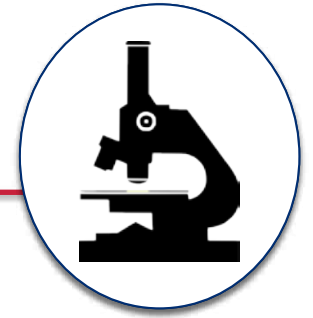
AIDS Cancer Specimen Resource Network (Rimsza, Schmelz, Patel)

- Southwest Regional Biorepository
- Science and Technology Core
- Executive Committee
- Archived FFPE & frozen materials from Arizona and Sub-Saharan Africa
- ANCHOR grant




AIDS and Cancer
Specimen Resource

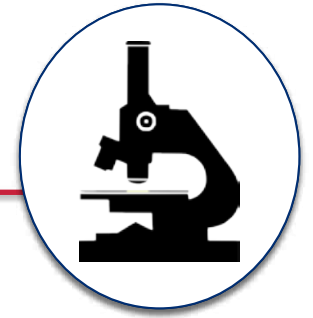
The logo for the AIDS and Cancer Specimen Resource (ACSR), featuring a stylized 'A' with a red and blue ribbon and the text 'ACSR' in blue, with 'AIDS and Cancer Specimen Resource' below it.



ANCHOR (Monika Schmelz)

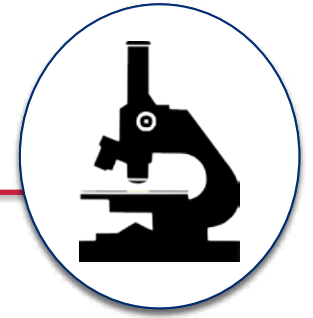
- Anal Cancer/HSIL Outcomes Research Study
- Phase III Study, 5000+ participants; 350,000 specimens
- Sponsored by: National Cancer Institute
- Office of HIV and AIDS Malignancy
- Protocol Chair: Joel Palefsky, MD, UCSF



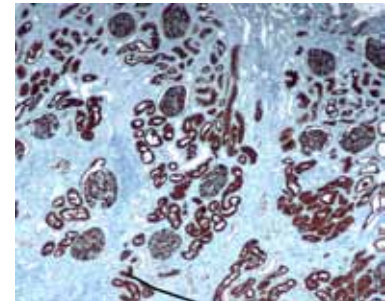


- TACMASS Core in UACC (Rimsza/Patel)
- UACC Biorepository
 - Consented patients, cancer and normal blood samples
 - Breast, pancreas, lung, brain
 - Legacy archives of snap frozen cancer blocks (non-consented)
 - Pick-up service for Skin repository (Curiel)
 - GI SPORE and colon polyp repository (Gerner & Lance, Bhattacharyya, Nelson)
 - Prostate Tissue bank (Nagle)
 - Inventory entered into TissueMetrix





- TACMASS Core in UACC (Rimsza/Patel)
- Tissue Analysis
 - Full histology services
 - Routine stains & Immunohistochemistry (10,000 slides/yr)
 - Image analysis & photomicroscopy
 - Recent merge with CMM histology laboratory
 - Relocation planning to basement locations

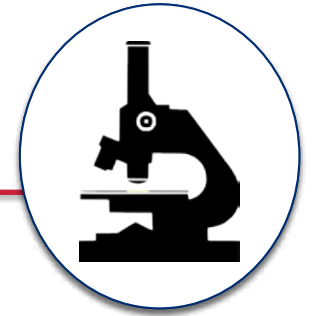




Hospital Tissue Archives & Additional Projects

- Custodianship of FFPE blocks and slides from UAHN since 1970's (Bhattacharyya)
- TCGA national sequencing project (Nelson)
- Clinical Proteomic Tumor Analysis Consortium (CPTAC) phase II project: (Nelson & Patel)
- ABLE, Arizona BioRepository and Laboratory Exchange (Nelson)

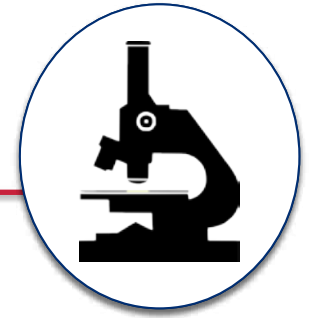




Arizona Biorepository and Laboratory Exchange Update (Nelson)

- Technical director and staff search underway
- Space request for “freezer farm” submitted
- ABLE content on AziCATS website
- ABLE “CATTRACK” Biospecimen Locator being built





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Patients

Treatment & Diagnosis

SWOG

Clinical trials

Investigator Initiated

SPECS II grant

Translational
Research

Ventana Medical Systems

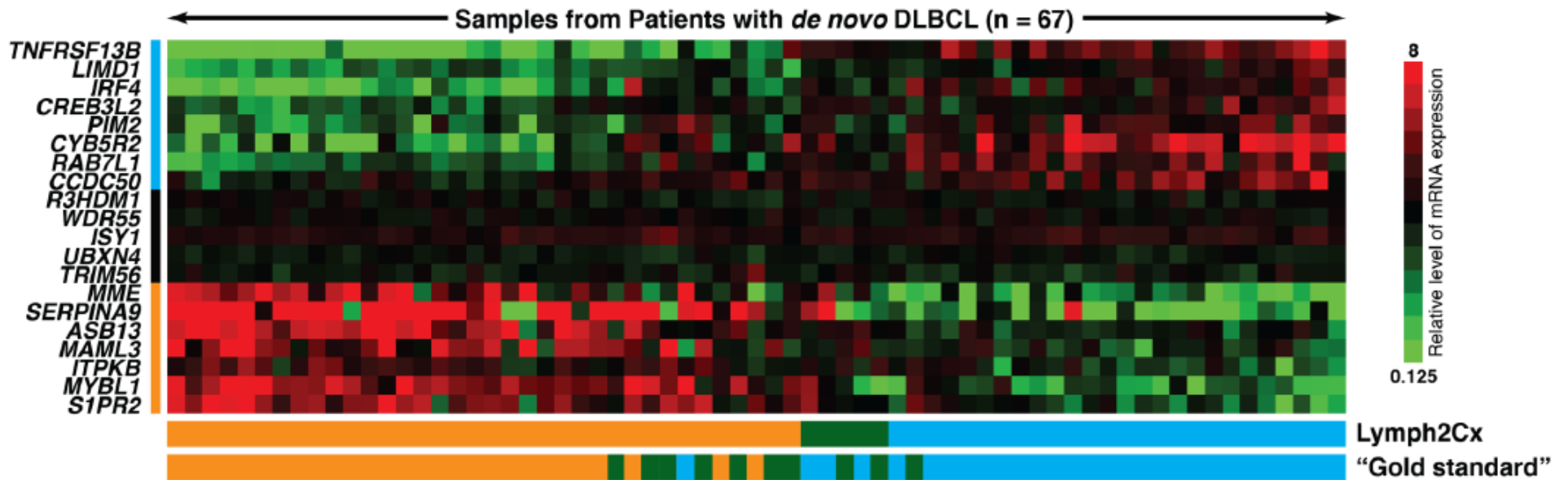
Lymphoma/Leukemia Molecular
Profiling Project

Discovery

Arizona Lymphoid Tissue & Blood Repository
AIDS Cancer Specimen Resource Network-UCSF
Tissue Acquisition & Molecular Shared Resource-UACC

Tissue
Repositories

The Lymph2Cx Assay



- Activated B-cell-like DLBCL/Non-GCB
- Germinal-Center B-cell-like DLBCL
- Unclassified DLBCL



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- Executive Team & Board
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Press Release

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NanoString Technologies Enters Into Biomarker Companion Diagnostic Collaboration with Celgene Corporation to Support Development of REVLIMID as Treatment for Patients with Diffuse Large B-Cell Lymphoma

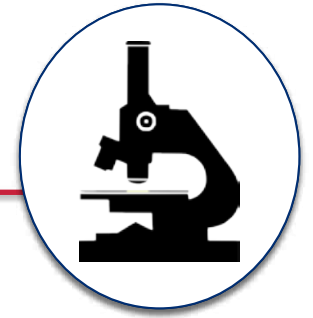
NanoString Eligible to Receive up to \$45 million for Upfront, Developmental and Regulatory Milestones, and Commercial Payments from Celgene

SEATTLE | June 3, 2014 – NanoString Technologies, Inc., (NASDAQ:NSTG) a provider of life science tools for translational research and molecular diagnostic products, today announced that it has entered into a collaboration with Celgene Corporation to develop a companion diagnostic assay using the nCounter® Analysis System to support the clinical validation of REVLIMID® for treatment of Diffuse Large B-Cell Lymphoma (DLBCL). Under the terms of the collaboration agreement, NanoString will develop, seek regulatory approval for, and commercialize the diagnostic test and is eligible to receive payments totaling up to \$45 million of which \$5.75 million is an upfront payment, \$17 million is for potential success-based developmental and regulatory milestones, and the remainder is for potential commercial payments.

DLBCL is a heterogeneous group of cancers classified together on the basis of morphology, immunophenotype, genetic alterations and clinical behavior, and represents the most common form of Non-Hodgkin Lymphoma. According to the National Cancer Institute, DLBCL will represent approximately 37 percent of the 70,000 new cases of Non-Hodgkin Lymphoma this year. The subtypes of DLBCL have long been known to have varying prognoses. Accordingly, the accurate and precise assignment of subtype has the potential to become increasingly important with the emergence of novel therapies, and repurposing of existing products, that have selective clinical activity in specific subsets of patients.

In January 2014, researchers associated with the Lymphoma/Leukemia Molecular Profiling Project (LLMPP) published a paper in the journal *Blood* describing the development and validation of a biomarker assay based on a 20-gene expression DLBCL subtype classifier using NanoString's nCounter Analysis System. In this paper, titled "Determining cell-of-origin subtypes of diffuse large B-cell lymphoma using gene expression in formalin-fixed paraffin embedded tissue," the authors concluded that the nCounter-based assay accurately and robustly assigned subtypes of DLBCL from formalin-fixed paraffin-embedded tissue samples with excellent site-to-site reproducibility and rapid turnaround time, making it attractive for implementation in clinical trials and, ultimately, patient management. NanoString has secured a license to the relevant intellectual property to enable the collaboration.

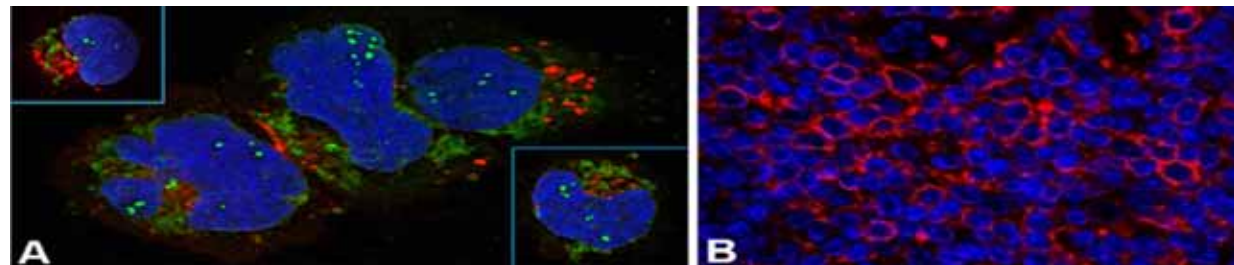




Monika Schmelz, PhD

Mechanisms for Immune Escape in Aggressive Lymphoma with Poor Survival

To understand the mechanistic role of the aberrant cytoplasmic MHCII trafficking and antigen machinery in DLBCL at the molecular/cellular level using *in vitro* tissue culture assays, proteomics, confocal microscopy.



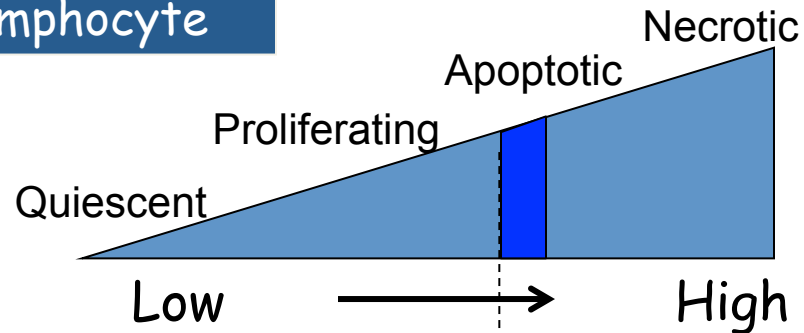
SUDHL6 **Lamp1** **MHCII** **DAPI**

FFPE tissue-germinal
center B cells

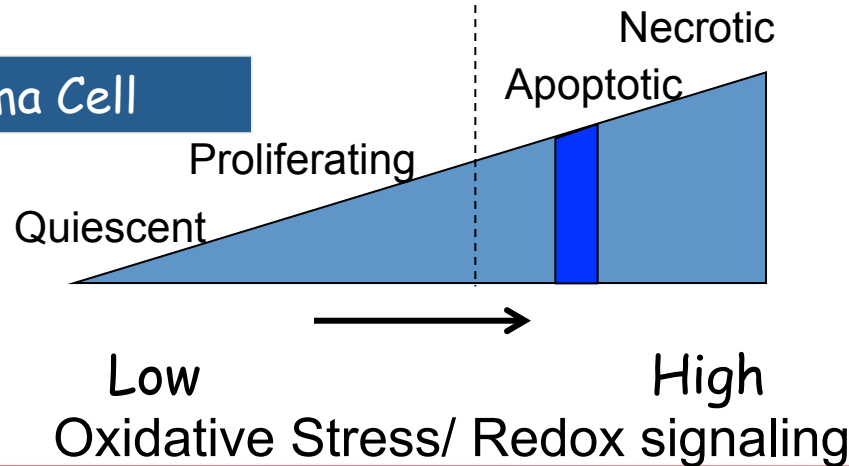


Margaret Briehl, PhD.

Normal Lymphocyte

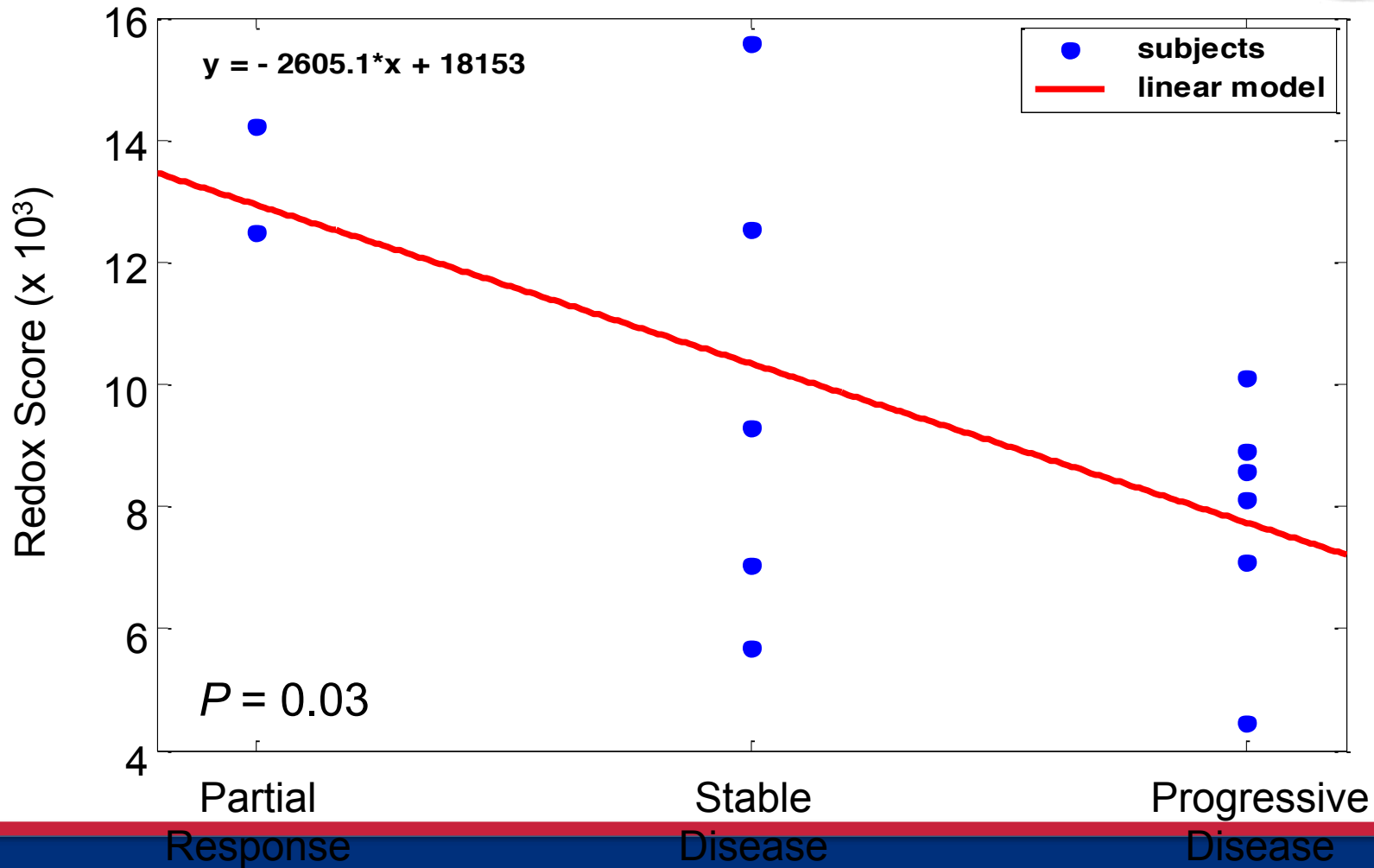


Lymphoma Cell



1. How does the redox state contribute to treatment resistance?
2. What is the mechanism for altered redox signaling in lymphoma cells?
3. How do we capitalize on the redox state of lymphomas to improve cure rates?

Redox Score Predicts Lymphoma Response to the Redox-Targeted Drug Imexon



Correlation = -0.59



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Partnership for Native American Cancer Prevention (NACP)

- Objectives
- Focus



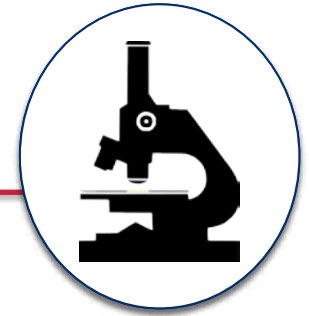
- Focus on cancer prevention and early detection
- Training and education for community health workers
- Outreach – cancer education & input on community priorities
- Evaluation – tracks progress toward specific aims

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Mark A. Nelson, Ph.D.

Interests

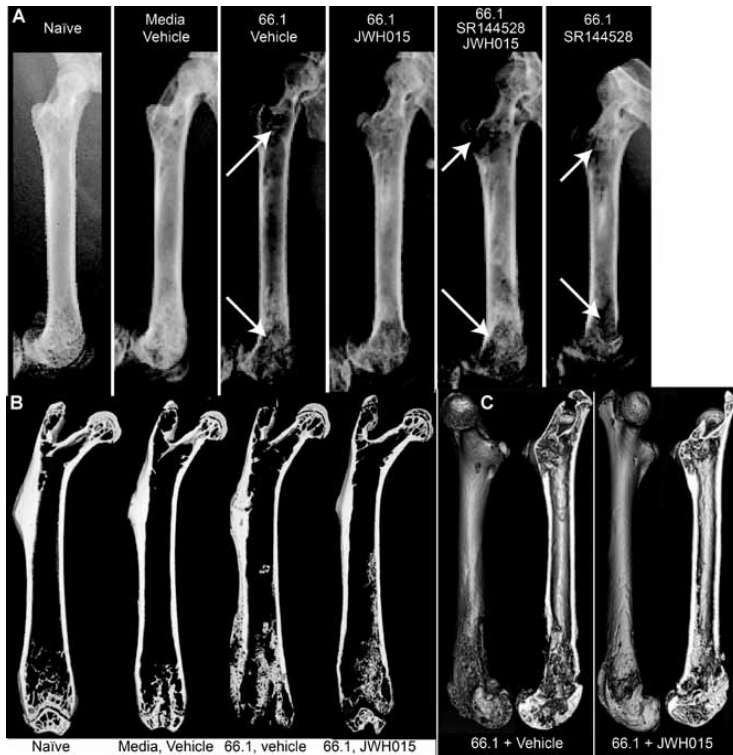
- Inflammation/Metastasis
- Cancer/Neuropathic pain



PATHOLOGY
COLLEGE OF MEDICINE



Cancer/Neuropathic pain

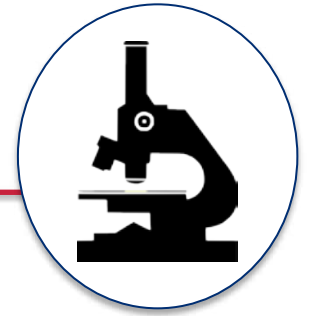


Effect of CB2 agonist

- Reduced cancer-induced bone pain
 - Bone loss
 - Tumor cell growth

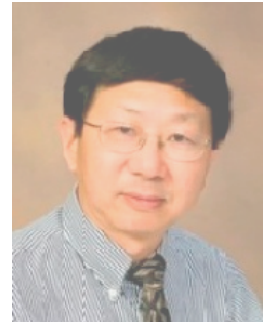
Rationale

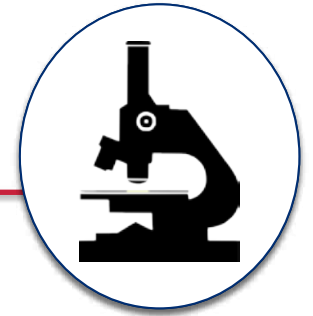
- Breast cancer is 2nd leading cause of death in U.S.
- Breast metastases cause bone loss, fractures, anemia, and pain
- Neither palliative care nor approved therapeutics for skeletal related events have improved survival
- Alternative therapies are needed



Wenxin Zheng, MD

- The cell origin of ovarian cancer
- The cell origin of ovarian endometriosis
- Endometrial serous carcinogenesis and early detection
- One-stop total care for cervical pre-cancers
- > 10 peer review articles/year in recent 3 years.



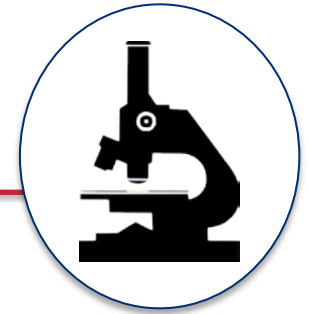


One-Stop Total Care for Cervical Precancers

- Reduce the clinic visits from 3-4 times to one time.
- Reduce the clinical care times from 8-12 weeks to less than 4 hours.
- Clinical trial is ongoing in China.
- Will focus on mobile populations first.
- May return to USA when the project is more mature.



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Arthur R. Brothman, Ph.D., FACMG

**Professor of Pathology, Director of Cytogenomics, U of A,
Interim Director, Genetic Core Clinical Sequencing, Tucson**

Adjunct Professor of Pediatrics, Human Genetics and Pathology, U of U, Salt Lake City

- 1. Cancer Biology (Prostate)**
- 2. Development (Stem Cells and Epigenetics)**
- 3. “R &D” (translational)**





“R&D” – translational

FISH assays validated (or in progress) at UAHN Cytogenomics Lab

Sex mismatched BMT (chimerism) X and Y chromosomes complete

AML (panel): t(15;17), t(8;21), inv(16), 11q23 complete

CML: t(9;22) complete

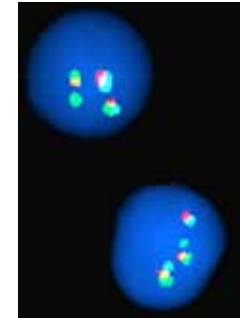
CLL: del(11), +12, del(13), del(17) complete

ALL (panel): +4, 10, 17, t(9;22), t(12;21), 9p21, 11q23, 14q32, 19p13

MDS (panel): del(5), del(7), +8, del(20) complete

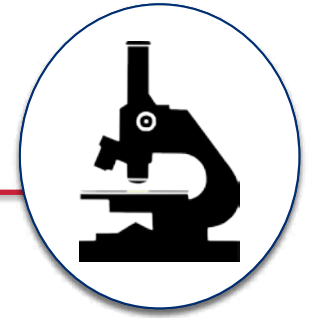
Multiple Myeloma panel: 1q21, t(4;14), t(11;14), del(13), t(14;16), 14q32, del(17),
hyperdiploidy (9q,11cen)

MPD: 4q12, 5q33.1, 8p12, t(9;22)





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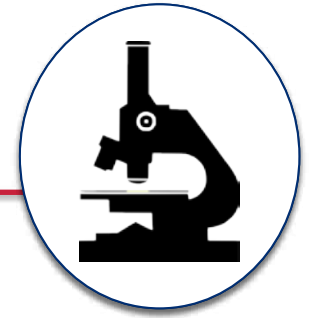
R&D: Precision Health



- Clinical Sequencing
- Started in Michael Hammer's research laboratory
- CLIA and CAP certified
- Interim Director with Dr. Maria Proytcheva
- In process of validating constitutional and cancer cases



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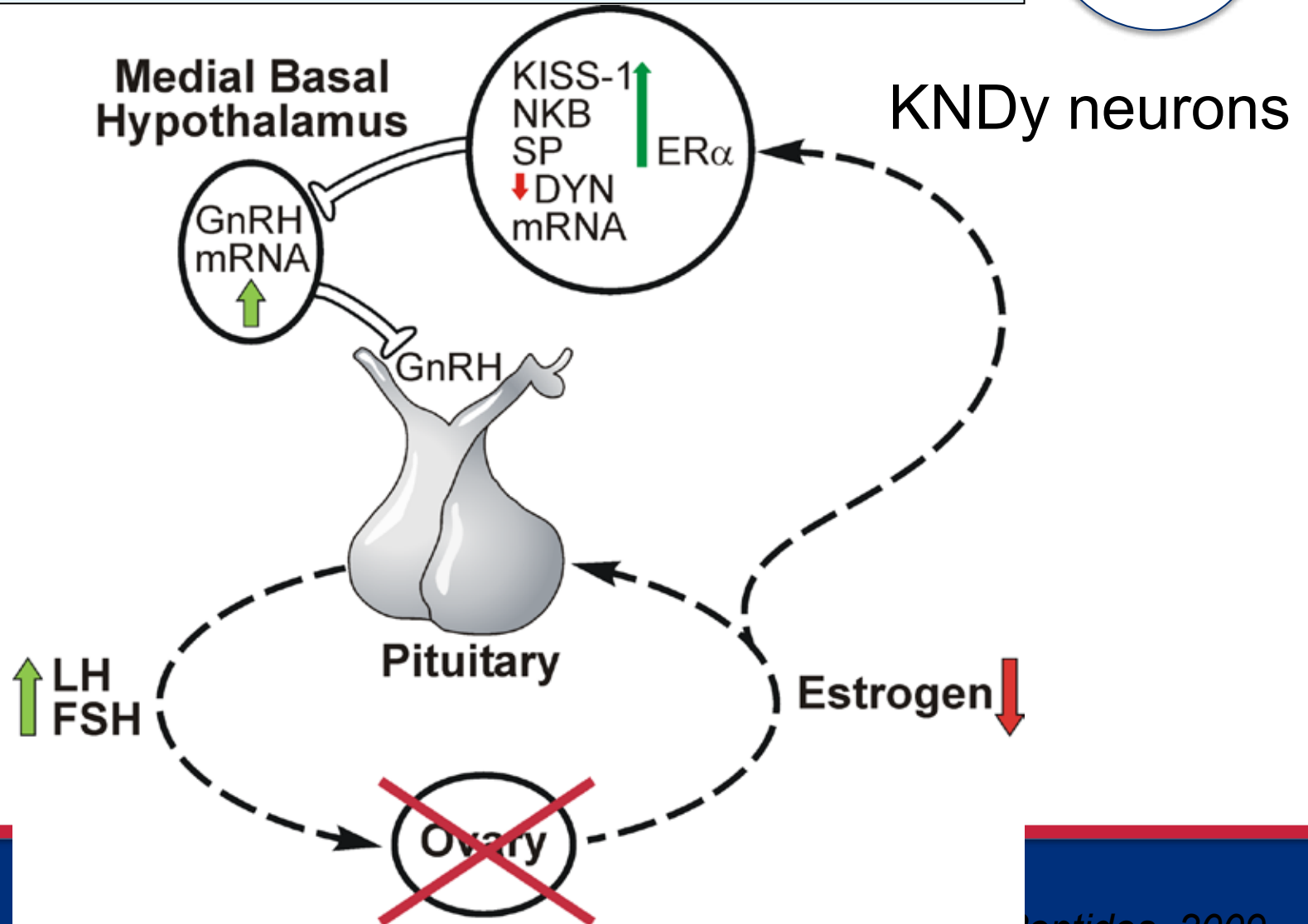
Naomi Rance, MD, PhD

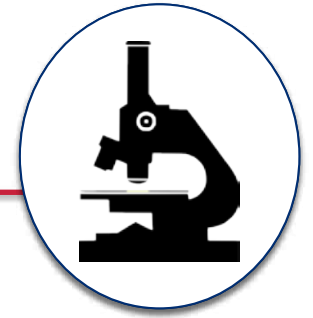
- Menopause and the Human Hypothalamus: Evidence of a Role for KNDy Neurons in the Estrogen Modulation of LH Secretion and Body Temperature





Neuroendocrine regulation in postmenopausal women

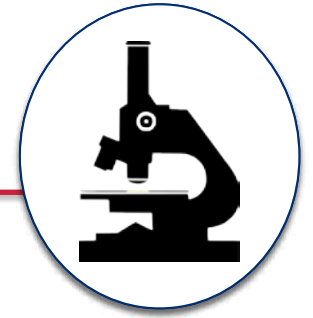




Barun De, PhD

- Co-investigator in a CDC and AZ Department of Health funded project on “HIV screening using a new algorithm” (2013-2015).
- Problem: HIV diagnostic tests ordered haphazardly with significant waste of resources
- Results: After one year, most clinicians are ordering as per CDC algorithm, potentially saving money, improving care and better containment of infection.





Deborah Novak, M.D.

- *PROPPR - Pragmatic, Randomized Optimal Platelet and Plasma Ratios*
- Multicenter, prospective, randomized trial comparing different ratios of blood products given to trauma patients who are predicted to require massive transfusions (greater than 10 units of PRBCs within the first 24 hours).
- UAHN was 1 of 12 sites nationally





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Leslie Boyer, MD
Associate Professor of Pathology
Director, Venom Immunochemistry,
Pharmacology and Emergency
Response (VIPER) Institute



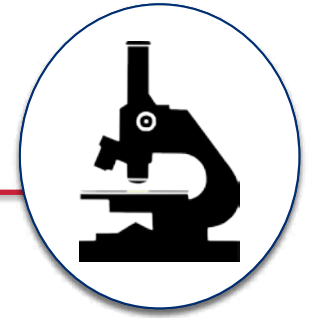


- Novel lymphotoxinology model, developed jointly by VIPER (UA) and IBt (National Autonomous University of Mexico)
- Diagnostic ELISAs validated by IBt, used by UA as secondary endpoints in clinical trials
 - *Crotalus* venom
 - *Micrurus* venom
 - *Centruroides* venom
 - Equine F(ab')₂
 - Ovine Fab

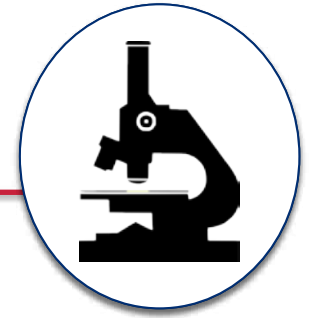




- Antivenoms, from concept to license
 - Early-phase design, in collaboration with Institute of Biotechnology, UNAM
 - Clinical development with multiple manufacturers as well as UA INDAs
 - Multicenter phase 2 and 3 clinical trials, originating at UA, performed across USA
 - Antivenom Index for zoo association
 - Pharmacoeconomics, with HOPE Center



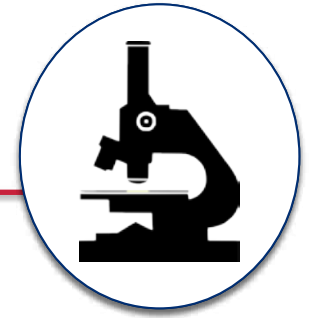
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Charmi Patel, M.D.

- Karyometric analysis of pancreatic neoplasms: Drs. Alberts and Krouse
- Karyometric analysis of Barrett's mucosa: Drs. Alberts and Banerjee.
- Kallikrein expression and secretion in colon cancer: Dr. Natalia Ignatenko (TACMASS)
- Targetting Probe for imaging colorectal cancer vasculature: Dr. Zhoglin (TACMASS) submitted for R21.
- ACSR and ANCHOR trials: Drs. Rimsza and Schmelz.

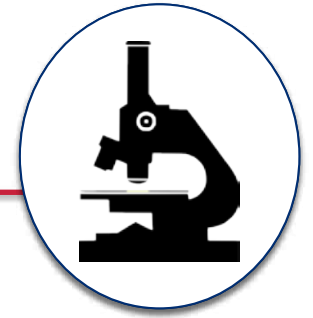




Nathalie Whitfield, PhD, ABMM

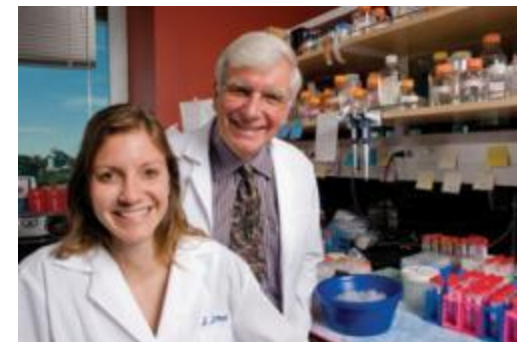
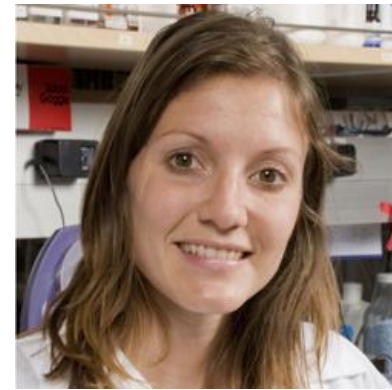
- Director of the Clinical Microbiology laboratory
- Director of Infectious Disease Research Core (IDRC)
 - designs, develops, validates, implements, and performs new laboratory methods for diagnosing, treating and preventing infectious diseases and public health threats.
- Border Infectious Disease Surveillance Testing
 - Collaborative effort between CDC, US-MX Border States, and local Health Departments performing enhanced surveillance activities & laboratory capacity for testing of diseases of public health importance.

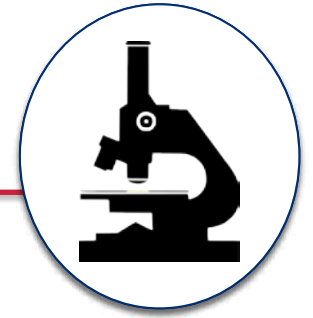




Samantha Kendrick, PhD

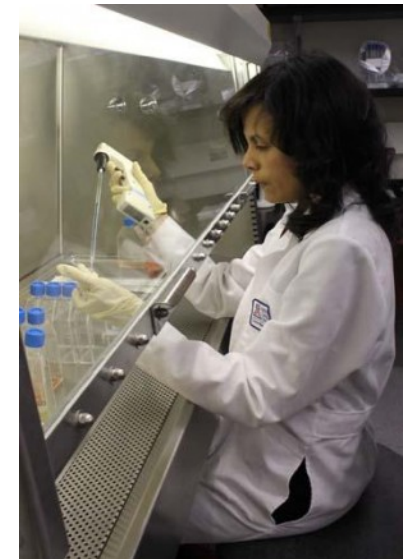
- PhD. Cancer Biology
 - Dr. Laurence Hurley, Advisor
 - Award: Student Technology Innovation Award 2010
- Post-doctoral fellowship
 - Dr. Lisa Rimsza, Advisor
 - Funded by Lymphoma Research Foundation
 - K99-R00 submission Oct 1, 2014

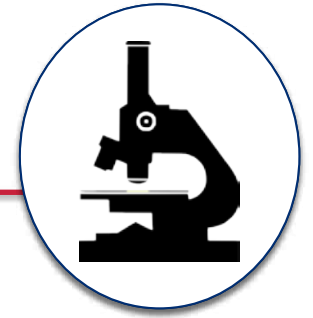




Melba Jaramillo, PhD.

- PhD. in Cancer Biology (Advisor: Margaret Briehl)
- Post-doctoral Fellow (Advisor: Lisa Rimsza)
 - HIV/AIDS and Lymphoma Outreach
- Pre-Medical Admissions Pathway
2014-2015



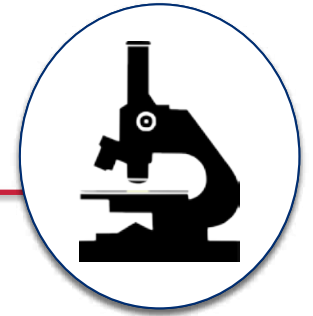


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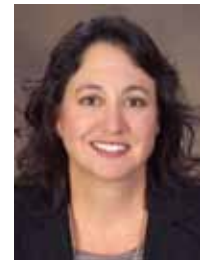


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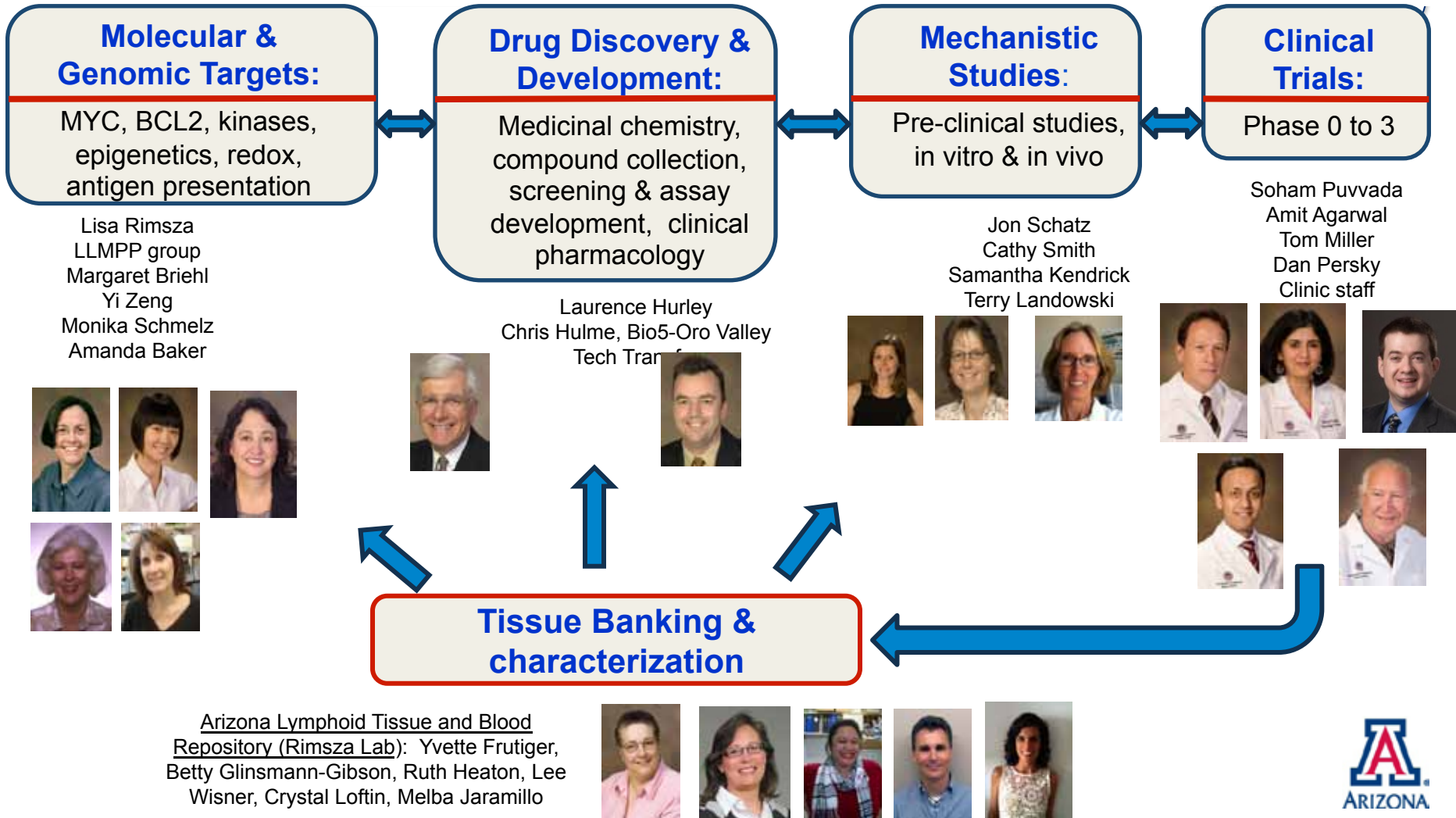
Collaborations-Rimsza

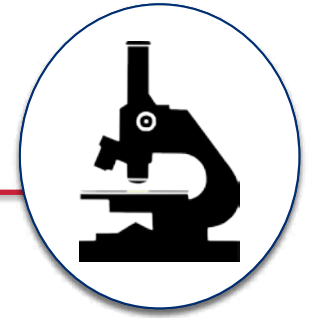


- Lymphoma & Leukemia Molecular Profiling Project (5 countries, 8 sites), Principal Investigator
- Southwest Oncology Group
 - Lymphoma Committee Pathology Chair
 - University of Rochester-Spore
- AIDS Cancer Specimen Resource Network: University of California-San Francisco, Baylor, GWU, Stellenbosch University Hospital Capetown, South Africa
- Lymphoma Research Group, “de facto” head
 - Pharmacy: Med Chem & Pharmacology; Arizona Cancer Center-Therapeutic Development & Cancer Biology Programs, Bio5 UA Genetics Core, Dept. Immunology



Translational Therapeutics in Lymphoid Malignancies

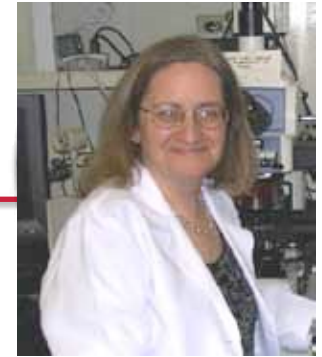




Collaborations-Briehl

- Partnership for Native American Cancer Prevention
- - U54 grant mechanism through the NIH Center for Health Disparities
- - collaboration between NAU and UACC with the goal of reducing cancer health disparities in Native communities (Dave Alberts is the PI at UA)

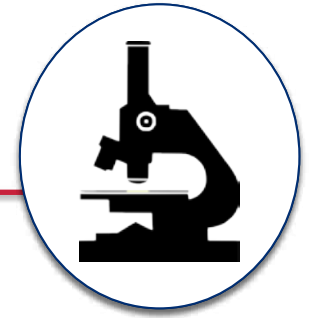




Collaborations-Rance

- Graduate Students of Neuroscience and Physiological Sciences IDPs
- Nathaniel McMullen, Department of Cellular and Molecular Medicine
 - Ralph Fergosi and Richard Levine, Departments of Physiology and Neuroscience
 - Andrej Romanovsky, Barrow Institute, Phoenix

Funding by NIH, National Institutes on Aging, Evelyn McNight Brain Institute, Arizona Biomedical Research Commission



Collaborations-Nelson

- Funded by RO1 CA142115 (TV & MN), Better Than Ever grant (MN) and the Main Cancer Foundation (TV)
- Collaborators:
 - Todd Vanderah, Ph.D.
 - Patrick Mantyh, M.D., Ph.D.
 - Frank Porreca, Ph.D.
 - Krisha Howell, M.D.
 - Leigh Newmayer, M.D.
 - Lauren LaBeau, M.D.
 - Michelle Ley, M.D.
 - Moab Ibrahim, M.D.
 - Bernie Futscher, Ph.D





Collaborations-Zheng



University of Arizona

Tubal cytology for ovarian cancer early detection

Zahra Aly (Path)

Setsuko Chambers (gyn-onc)

Ovarian cancer carcinogenesis

Drs. Chambers, Cragun, Hatch (gyn oncology)

Tubal serous carcinogenesis

Guang Yao (Cell biology)

Setsuko Chambers (gyn-onc)

Ovarian cancer imagine study

Art Gmitro (Radiology)

Drs. Chambers & Hatch (gyn-onc)

International

Ovarian cancer

Beihua Kong (Shandong University, China)

Yiyang Wang (Zhengzhou University, China)

Endometrial cancer

Beihua Kong (Shandong University, China)

Yiyang Wang (Zhengzhou University, China)

Cervical cancer

Yiyang Wang & Yue Wan

(Zhengzhou University, China)

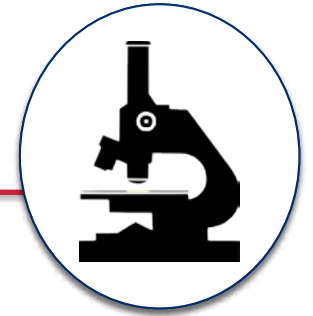
Beihua Kong (Shandong University, China)

Wen Di (Shanghai Jiaotong University, China)

Gynecologic pathology

Danhua Shen (Beijing University, China)

Donghui Guo (Tianjing University, China)



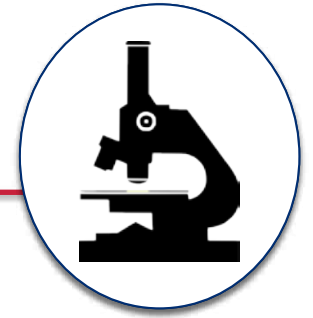
Barun De, PhD

- HIV Test Ordering
- Co-Pis
 - Dr. Carol Galper: Prof. Family & Community Med;
Assistant Dean, Medical Student Education
 - Dr. John Guisto: Prof. of Emergency Medicine;
Associate Head of Clinical Affairs
 - Brad Dreifuss, Assist. Professor of Emergency
Medicine; Director, Rural & Global Health Programs





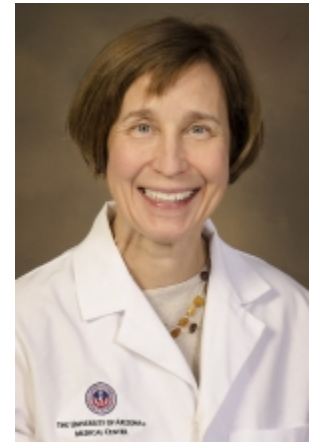
THE UNIVERSITY OF ARIZONA
HEALTH NETWORK



Collaborations-Novak

--PROPPR trial in 12 Level 1 trauma centers:
Memorial Hermann-Texas Medical Center; UCSF; USC-LA
County; University of Washington-Harborview Medical Center;
Memphis Regional Medical Center; University of Alabama,
University of Wisconsin; University of Cincinnati; Oregon
Health and Science University; Sunnybrook Health Sciences
Centre; University of Maryland

--In collaboration with UAHN Trauma Surgery and
the Emergency Department





Translational Research: Pathology

Collaborative, Multi-Disciplinary, Broad, Growing

