

# ***Center for Innovative Biomedical Resources (CIBR)***

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# Diversity of Cores Available to UMSOM

## **Imaging Network**

Confocal Microscopy  
Electron Microscope  
Animal Imaging  
Diagnostic Imaging  
Neuroimaging

## **Structural Biology Network**

NMR  
X-Ray Crystallography  
Mass Spectrometry  
Biacore  
Edman Sequencing

## **Clinical Resources Network**

Pathology Biorepository  
Brain & Tissue Banks  
Cytokine & Hormone  
Immunoassay Core  
Flow Cytometry  
Stem Cell Core

## **Drug Development Network**

Pharmacokinetics/Biopharmaceutics Lab  
Industrial Pharmaceutics Lab  
Center for Nanomedicine and Cellular Delivery  
Computer-Aided Drug Design (CADD)  
High Throughput Screening Core

## **Model Development Network**

Veterinary Services  
Translational Core Lab  
Small Animal Physiology Core  
Phenotyping Core

## **Bioengineering & Biorobotics Network**

## **Biostatistics & Informatics Network**

## **Genomics Network**

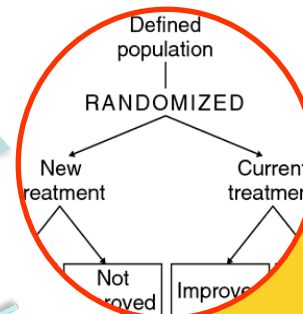
Genomics Core Facility  
Genomics Resource Center  
Biochemical Genetics Lab (clinical)  
Cytogenetics Lab (clinical)  
Translational Genomics Lab (clinical)

# Biostatistics Shared Service

A key resource to address issues related to increase rigor, optimize reproducibility, and minimize bias in data analysis



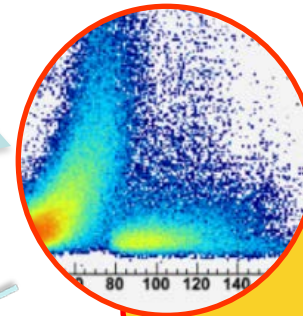
Problem formulation



Study design



Data collection



Data analysis



Interpretation & reporting

# Flow Cytometry: A Variety of Options



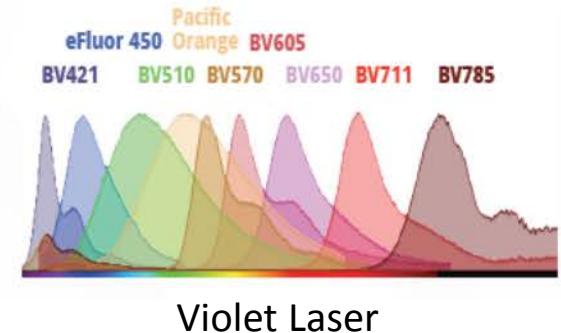
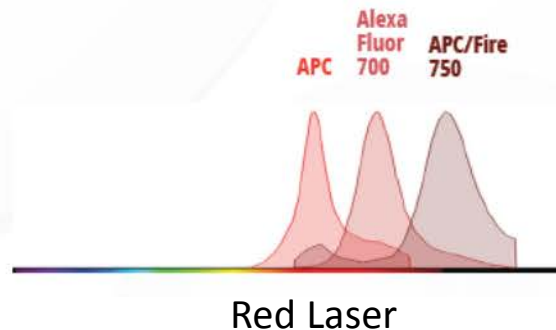
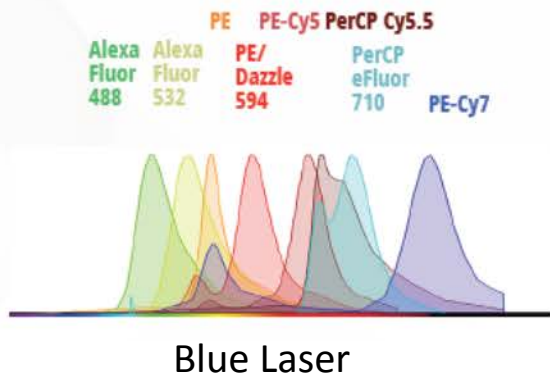
Facsaria II (with Biobubble)  
LSRII with autosampler  
FacsCanto II  
FlowSight Imaging Cytometer



# Flow Cytometry Shared Service: 20-Color Spectral Cytometer

## Cytek Aurora

- Just arrived
- 3 lasers: 488 nm, 640nm, 405 nm
- Measures 38 channels that covers the whole spectrum
- Recognizes the signature differences in spectrum
- Separates dyes with very close emission



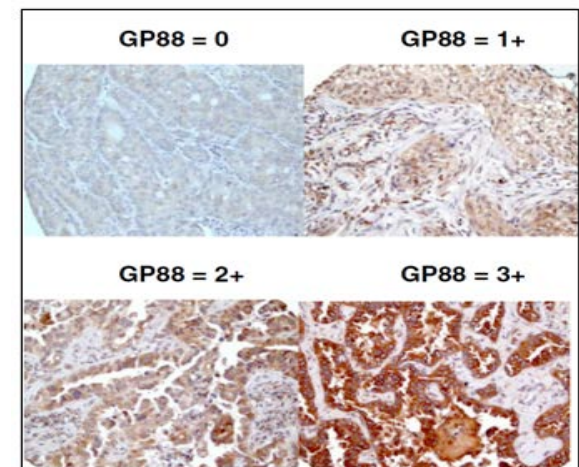
# Pathology Biorepository Shared Service

## Services Offered:

- **Frozen Tissue Archives (most with normal match control)**
- **Paraffin Embedded Archival tissue**
- **Tissue Microarray Construction**
- **Digital Image and Quantitative Analysis (Aperio)**
- **Clinicopathologic Data Set Construction**
- **Prospective Tissue Procurement (surgery)**
- **Blood/Bone Marrow and fluid processing**
- **Biospecimen Storage**
- **Histology**
  - **tissue processing and embedding**
  - **IHC – new antibodies**

## Immunohistochemistry

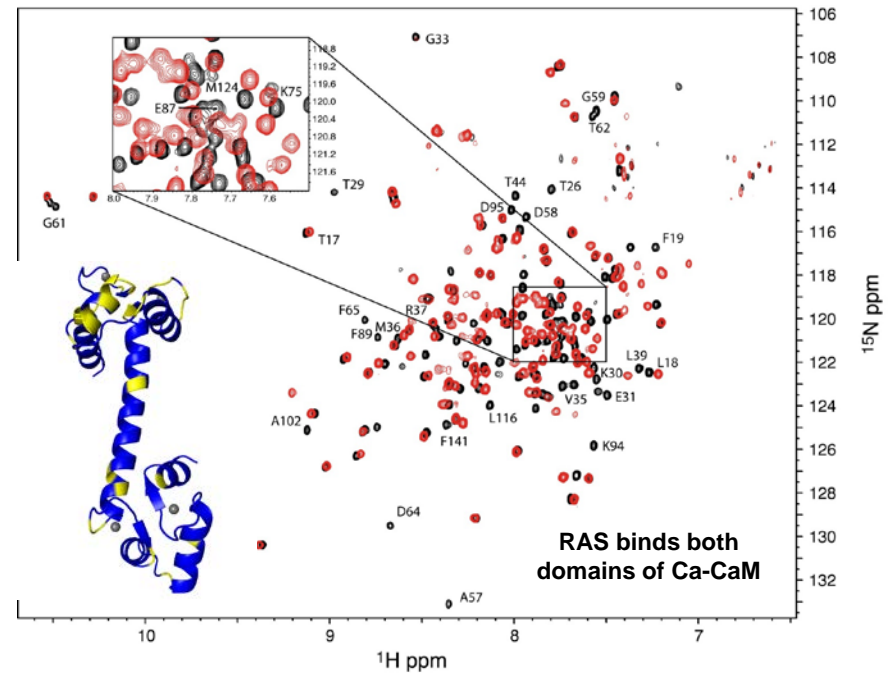
Immunohistochemical staining for GP88 Expression in Paraffin-Embedded Non-Small Cell Lung Cancer tissue sections. Ginette Sererro, PhD, (HRC). Edelman, et al., Human Pathol. 2014; 45:1893-9.





# Greenebaum Comprehensive Cancer Center: Structural Biology Shared Service

## 950 MHz NMR



### PPIs: Protein-Protein Interactions

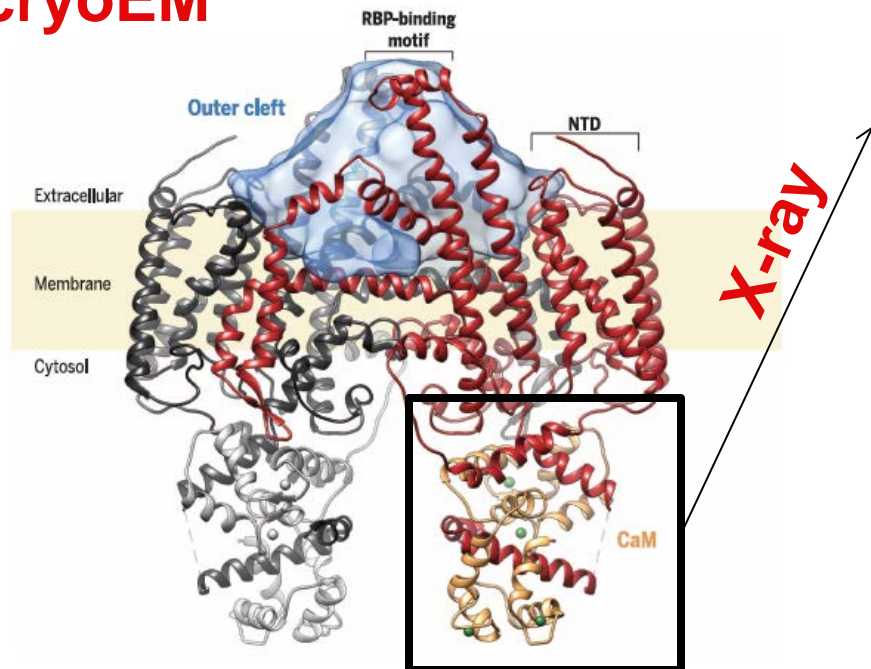
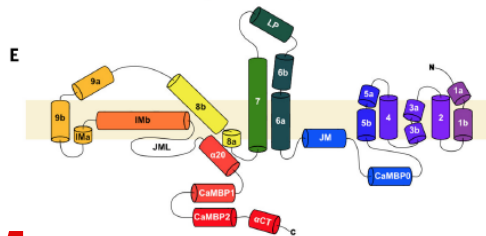
Reference: Stephen et al, Cancer Cell, 2014

# CryoEM

Detailed  
sidechains

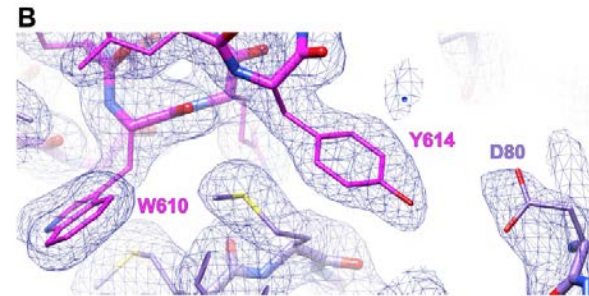
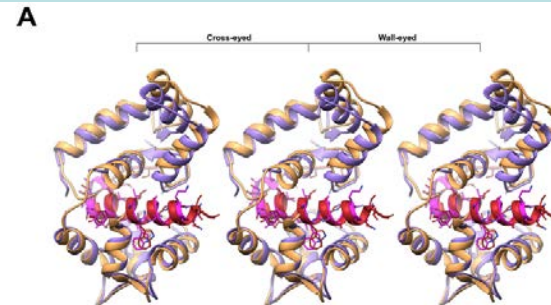
NMR

Dynamics  
of ligands

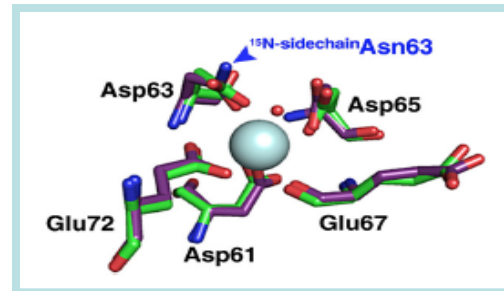


Global Structure of STRA6-CaM at 3.9  
Å

X-ray



Structure of CaM-CaMB2 at 1.7 Å

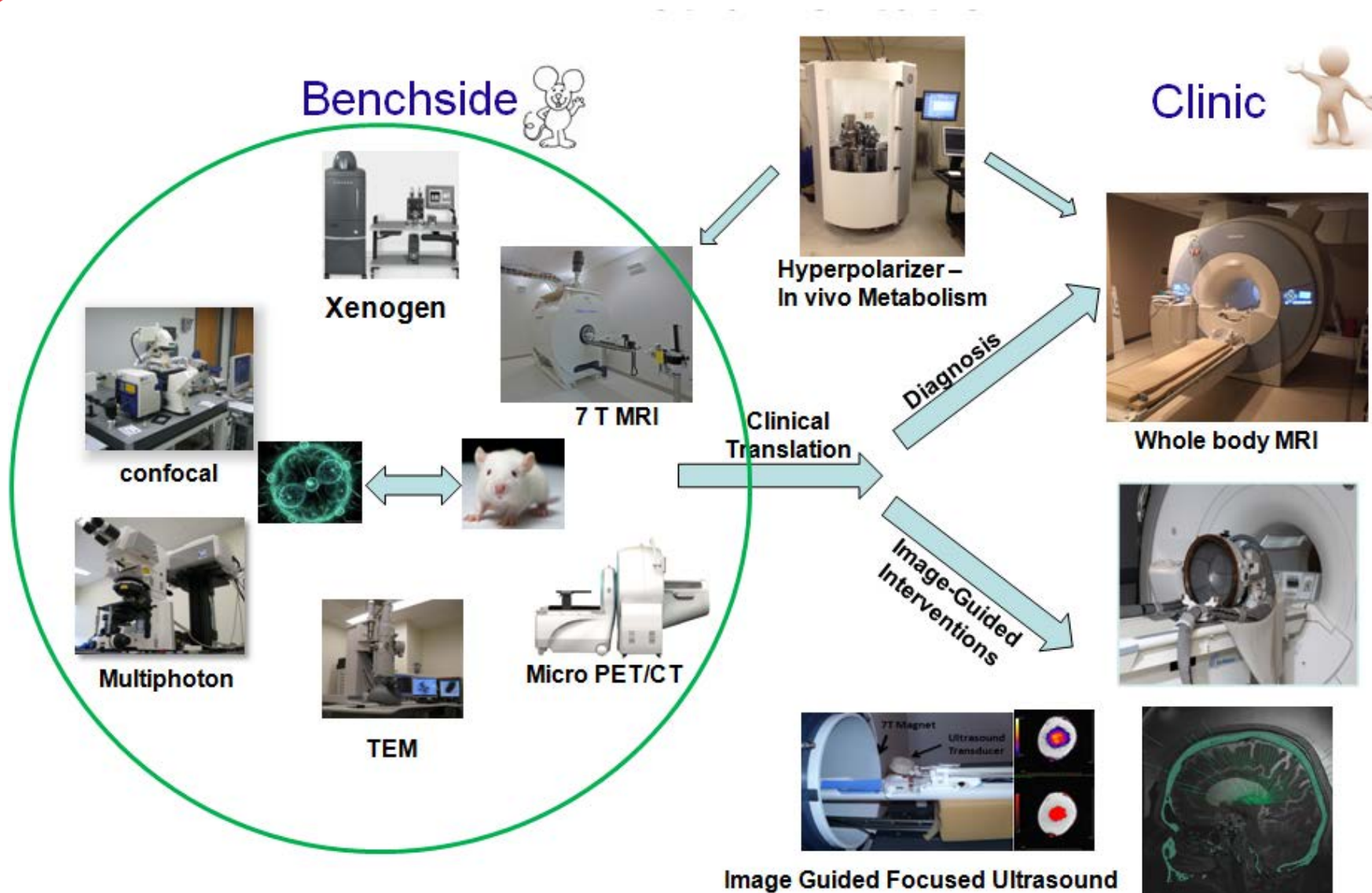


**FEI Talos Arctica on order**

Collaboration with Mancina *et al* Columbia;  
Chen *et al*, (2016) **Science** 353, 887



# Imaging Shared Service





# UMM Biorepository

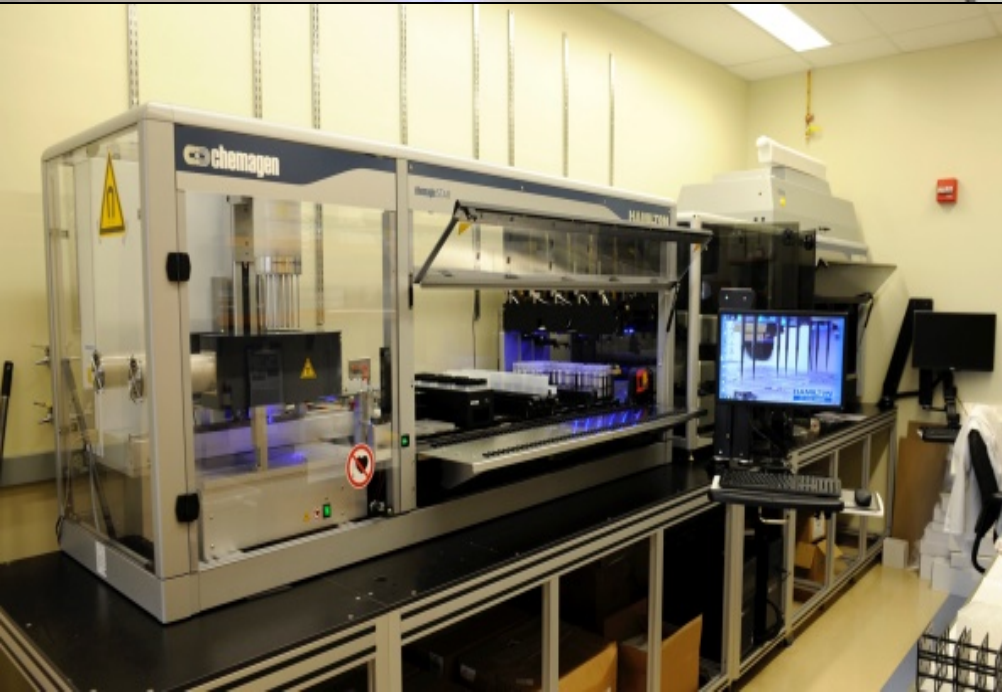
## CORE Services:

### Laboratory

- Sample processing & banking
- DNA/RNA extraction & banking
- Sample storage
- Sample retrieval

### Clinical Research Support

- IRB protocol preparation assistance
- Consenting
- Phlebotomy/sample collection
- Survey administration



## Services:

- Sanger Sequencing
- Genotyping
- Gene Expression Profiling
  - Cytogenomic Arrays (clinical)
  - GWAS
  - miRNA
  - Methylation
- Targeted Sequencing using Ion Torrent Technology
- STR (short tandem repeat analysis) – cell line validation

# Genomics Shared Service

Ion Chef – automated sample preparation



Ion Torrent Technology



S5 – increased sequencing capacity

# Genomics Shared Service

## MODY

*HNF4A*  
*HNF1A*  
*PDX1/IPF1/STF1*  
*HNF1B*  
*NEUROD1*  
*KLF11*  
*CEL*  
*PAX4*  
*BLK*

## Neonatal Diabetes

*ABCC8*  
*GCK*  
*INS*  
*KCNJ11*

*ZFP57*

## Lipodystrophy

*AGPAT2*  
*BSCL2*  
*CAV1*  
*LMNA*  
*PLIN1*  
*PPARG*  
*PPP1R3A*

## Syndromes

*ALMS1*  
*CISD2/WFS2*  
*EIF2AK3*  
*FOXP3*  
*GATA6*  
*GLIS3*  
*INSR*  
*PTF1A*  
*RFX6*  
*SLC19A2*  
*SLC2A2*  
*WFS1*

## Hyperinsulinemia

*GLUD1*  
*HADH*

## Severe Obesity

*MC4R*  
*LEP*  
*LEPR*  
*SIM1*

Cause of diabetes in 1-5%  
of young people

Most cases of monogenic  
diabetes are improperly  
treated, leading to poorly  
controlled blood sugar levels



# Translational Laboratory Shared Service

1. Provide UMGCCC clinicians with the means to perform early clinical trials of molecularly targeted drugs that require the assessment of pharmacodynamic endpoints
2. Make preclinical *in vitro* and *in vivo* model expertise available to UMGCCC members.
3. Facilitate the translation of novel therapeutic concepts from bench to bedside

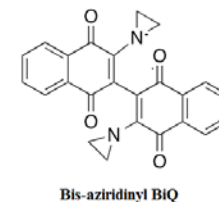
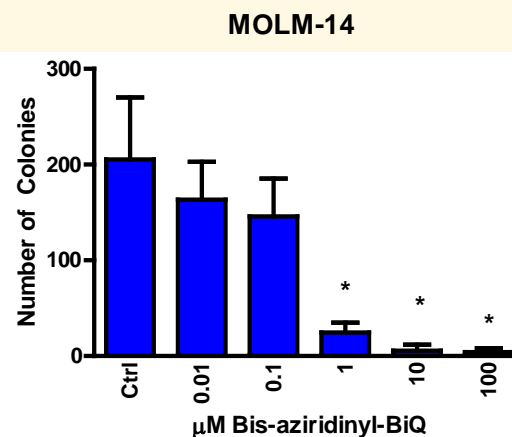
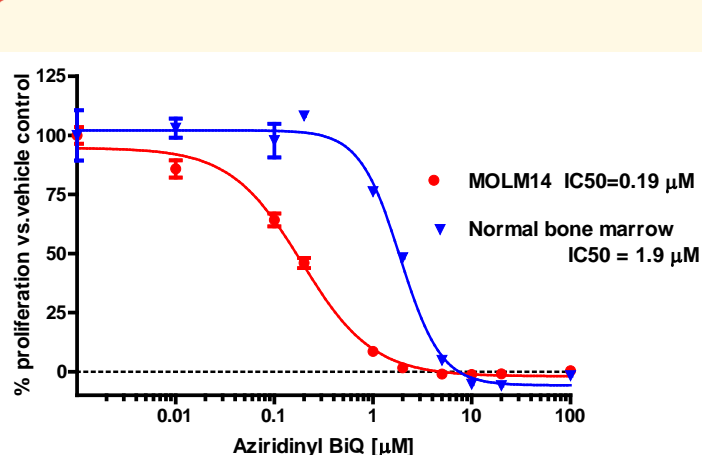
# Pre-clinical

- In Vitro
  - Cell Based assays – (proliferation, apoptosis, synergy, sequencing)
  - Angiogenesis assays
  - Flow Cytometry analysis post drug treatment
  - Fluorescence microscopy post drug treatment
- In Vivo
  - MTD
  - PK
  - In vivo efficacy – both flank and systemic models
- Develop novel assays that are requested

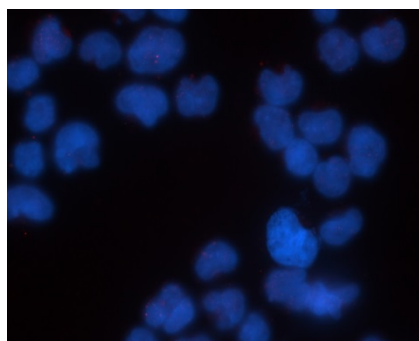
# Cell Lines and Primary Lines

- 100+ cell lines in our repository
  - STR validated in genomics core (in progress)
  - Including breast, prostate, colon, lung, melanoma, ovarian, leukemia among others
  - Endothelial cells - HUVEC
- Primary lines
  - leukemia

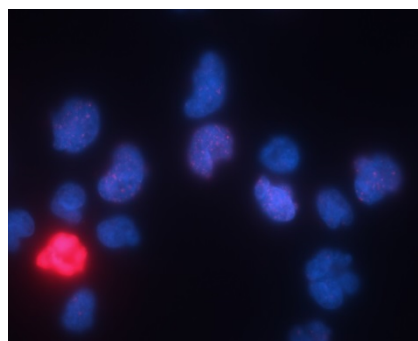
# Example: Effect of Novel Binaphthoquinone in AML



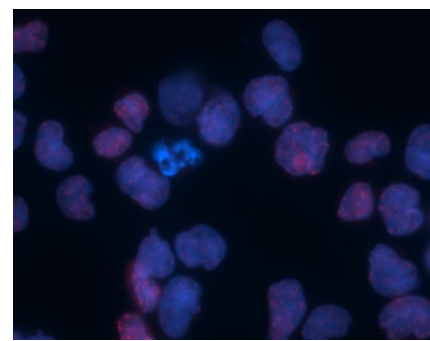
- Novel Bis-aziridinyI BiQ designed and synthesized at UMB in collaboration with UMSOP
- Novel Bis-aziridinyI BiQ has potent  $\text{IC}_{50}$  in AML compared to normal bone marrow
- inhibits clonogenicity in AML and induces DNA damage as measured by  $\gamma\text{-H2Ax}$  staining



Control



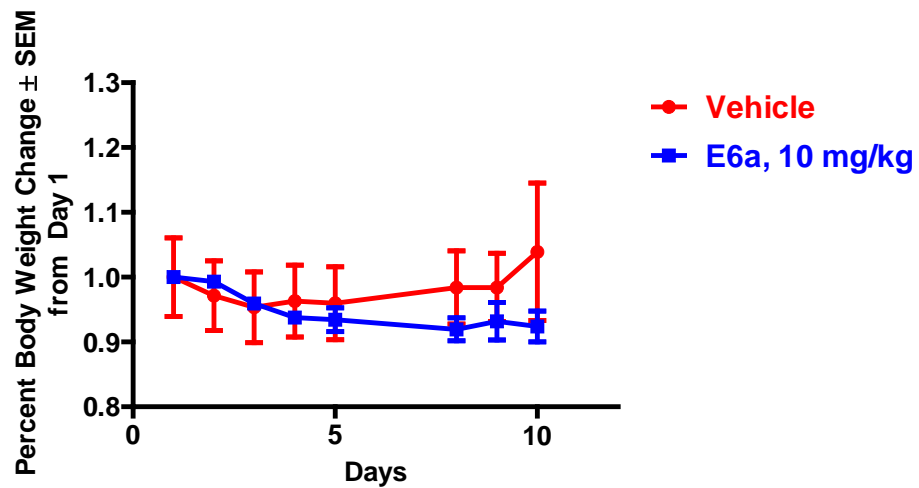
2  $\mu\text{M}$  Bis-aziridinyI BiQ



Radiation (6 gy)

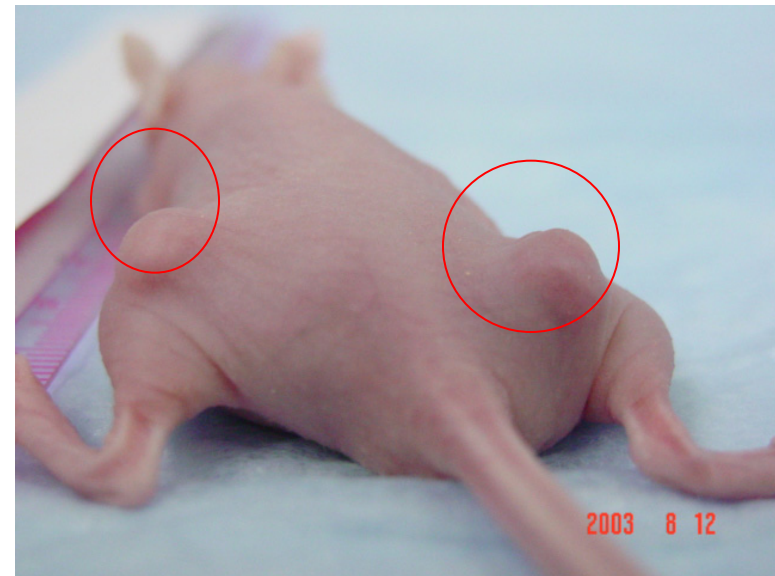
# Tolerability/PK

## Tolerability/MTD studies



Lapidus et al 2016 Pharmaceuticals

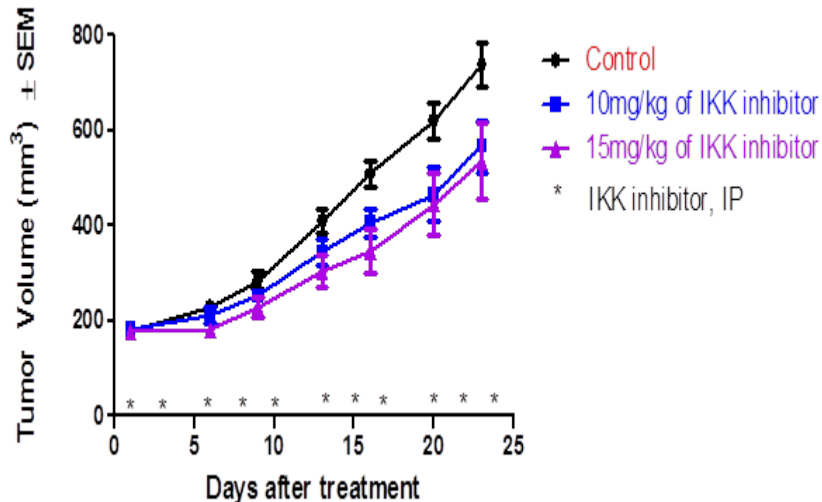
## Tumor bearing PK studies





# In Vivo – Flank and Orthotopic models/Imaging

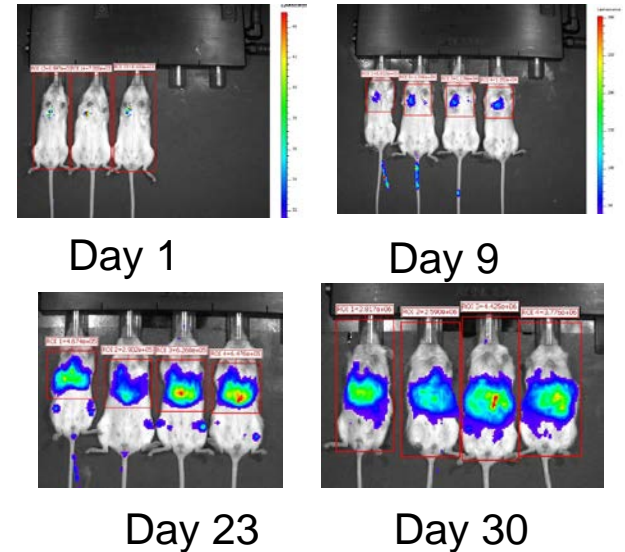
## Human prostate xenograft



Dan HC et al 2016 Mol Can Ther 15(7): 1504-1514, 2016

Flank models: lung, breast, prostate, colon, melanoma, liver, head and neck etc....

PDXs TOO!



Human breast cancer (231-luc) cells were injected IV into the tail vein.

Orthotopically, cells could be injected into the prostate, brain mammary fat pad, renal capsule

# Update On Services – GMP Production Lab

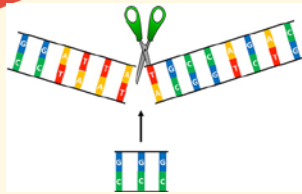
Construction complete; Summer 2018; Staff being hired



**The Fannie Angelos cGMP Facility**  
*A Laboratory for cell and vaccine production*

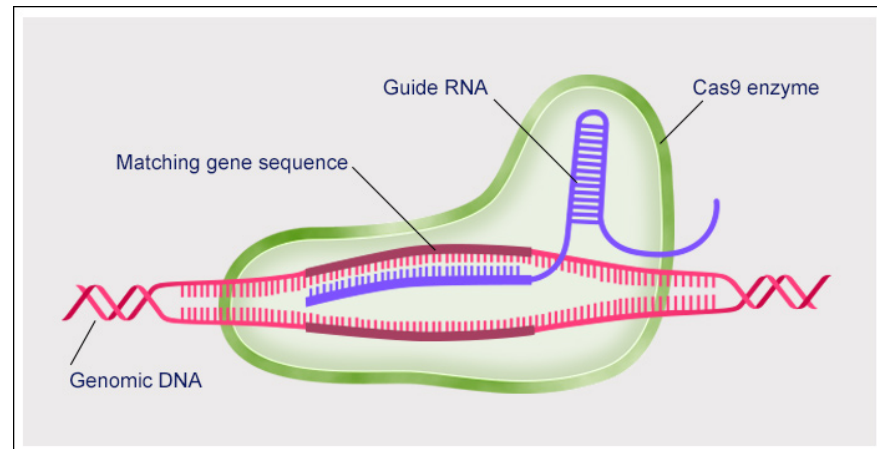


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# CRISPR CORE

- Cell Lines
- Knock Downs
- Guide Construction/Plasmid/Lentivirus
- Genetic validation



# CIBR Website

<http://www.medschool.umaryland.edu/cibr/>

## Center for Innovative Biomedical Resources

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▸ Clinical Resource Facilities

### News

[University of Maryland School Of Medicine \(UM SOM\) Scientist, Dr. Søren Bentzen, Receives Top Award for His Pioneering Work on Improving Radiation Therapy Outcome](#)

[UM SOM Translational Genomics Laboratory Receives Accreditation from College of American Pathologists](#)

[University of Maryland Medical Center Offers Genetic Testing as Standard of Care to Help Improve Outcomes for Heart Stent Patients](#)

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