UNC Lineberger Cancer Center
Shared Resources

David Darr
Assistant Director
Basic

- Animal Histopathology Stephanie Montgomery; stephanie_montgomery@med.unc.edu
- Animal Models Dale Clowely; dale_cowley@med.unc.edu
- Animal Studies Charlene Santos cmross@email.unc.edu
- Mouse Phase 1 Unit David Darr darrdb@med.unc.edu
- Electron Microscopy Jim Bear jbear@email.unc.edu
- Flow Cytometry Nancy Fisher nancy_fisher@med.unc.edu
- Light Microscopy Jim Bear jbear@email.unc.edu
- Proteomics Lee Graves lmg@med.unc.edu
- Macromolecular Interactions Facility John Sondek sondek@med.unc.edu
- NMR Spectroscopy John Sondek sondek@med.unc.edu
- Peptide Synthesis John Sondek sondek@med.unc.edu
- Protein Expression John Sondek sondek@med.unc.edu
- X-Ray Crystallography John Sondek sondek@med.unc.edu
- Small Animal Imaging Hong Yuan hong_yuan@med.unc.edu
Translational

- Analytical Chemistry and Pharmacology Bill Zamboni zamboni@email.unc.edu
- Bioinformatics Joel Parker parkerjs@email.unc.edu
- Biostatistics Dominic Moore dominic_t_moore@unc.edu
- Genomics Corbin Jones cdjones@email.unc.edu
- Pre-clinical Genomic Pathology Laboratory Corbin Jones cdjones@email.unc.edu
- High Throughput Genotyping (Mammalian) Corbin Jones cdjones@email.unc.edu
- Next Generation Sequencing and Genotyping Corbin Jones cdjones@email.unc.edu
- RNAi Screening Facility Corbin Jones cdjones@email.unc.edu
- Tissue Procurement Todd Auman jtauman@email.unc.edu
- Translational Pathology Nana Feinberg nana_nikolaishvili@med.unc.edu
Population Sciences

- Biospecimen Processing Patricia Basta patricia_basta@unc.edu
- Communication for Health Applications and Interventions (CHAI Core) Anne Gluaber acabell@email.unc.edu
- Patient Reported Outcomes (PRO-Core) Antonia Bennett avbenn@unc.edu
- Rapid Case Ascertainment Mary Bell Elizabeth mbell@unc.edu
Founded in 2006 to use genetically engineered mouse models to test novel therapies for cancer

Over 50 active collaborations with investigators in academia and industry.

Commitment to infrastructure:
• 4,000 cages of tumor-bearing mice
• Serial tumor assessment (Ultrasound, PET, MRI, Optic)
• Small animal imaging located behind barrier
• Pharmacokinetic and pharmacodynamic assessment
• Specialized tech transfer support for industry partnering
Models in the MP1U

Breast
- C3Tag; basal-like disease
- p53 null (T11); Claudin-low
- MMTV-Neu; HER2+ enriched luminal
- K14 cre driven Brca1/p53

Melanoma
- Nras^{Q61R}; LKB1 p16
- Hras, Ink/Arf null (TRIA)
- Pten/Braf

Ovarian
- Serous – RB/p53
- Clear Cell - ARID1A/PI3K

Pancreatic
- Kras^{G12D}; Ink/Arf null

Bladder
- Upk3Cre^ERT2; Pten, p53
- DMBA induced

Mouse Phase 1 Unit

David Darr daviddb@med.unc.edu Mouse Phase 1 Unit (www.med.unc.edu/mousephase1)
Drug Discovery and Development

Research and Development

PK and Toxicity Analysis
- Cell Chemistry and Biology; 2015
- Clin Cancer Res; 2014
- Oncologist; 2012

Efficacy Screening
- Journal of Controlled Release; 2014
- Oncogene; 2013

Mechanisms of Action and Resistance
- J Clin Invest; 2009, 2010 and 2013
- Clin Cancer Res, 2013
- Cell, 2012

Combinatorial Therapy
- Mol Cancer Ther.; 2015
- J Clin Invest; 2014
- Clin Cancer Res.; 2012

Co-Clinical
- Nature; 2012
- JNCI; 2012

New Indications
- Nature Comm; 2015
- Clin Cancer Res; 2015

FDA approval

Mouse Phase 1 Unit
Collaborating with MP1U

- Funding for the MP1U is from private donors and State of NC
- We have provided:
  - Tumor-bearing animals
  - Animal handling and other expertise
  - Help with compounds and imaging
  - Long-term serial analysis of treated cohorts
- **Industry collaborations**: Signed MTAs with a dozen small to large pharmaceuticals.

- **Academic collaborations**: Over 40 at UNC-CH, Duke, Emory, Harvard, Univ of Colorado, Wistar Institute, OHSU, UT-SW and others.
Translational Cancer Imaging

- PET/CT
- Optical
- 9.4T MRI
- SPECT
- Ultrasound
**Translational Imaging Core**

**Imaging Equipment**

- Siemens Biograph MR/PET scanner
- Siemens Tim-Trio 3T whole body MR scanner
- Siemens PET/CT scanner
- Bruker BioSpec 9.4T preclinical MR scanner
- GE eXplore Vista PET/CT
- GE speCZT/CT SPECT system
- Scanco microCT
- Carbon nanotube microCT
- Dual-energy x-ray absorptiometry (DEXA) system
- VisualSonics Vevo 770
- VisualSonics Vevo2100
- IVIS 100 optical imaging system
- IVIS-Kinetic imaging system
- IVIS-Lumina imaging system
- FMT-2500 Fluorescence Tomography system

*Imaging core in the new Marsico building.*

Green: Clinical Research Imaging unit; Blue: Preclinical imaging unit; Yellow: Imaging probe unit; Red: Animal vivarium.
Translational Imaging Core

Radiochemistry/Radiopharmacy service
- Radioisotope prediction with Two cyclotrons and one 30mCi Ga68 generator
- Provide imaging probes for research, including $^{18}$F-FLT, and $^{18}$F-MISO, $^{11}$C-acetate, $^{11}$C-choline, etc
- cGMP production of radiopharmaceutical probes for clinical usage including $^{18}$F-FDG, $^{15}$O-H$_2$O, and $^{13}$N-NH$_3$
- Develop new imaging probes based on investigator’s interests, support on radiolabeling optimization and probe validation

Preclinical imaging service
- Provide optical, ultrasound, MRI, PET/CT, SPECT/CT, and high resolution CT imaging for preclinical imaging studies
- Provide both small animal and large animal imaging

Clinical Imaging service
- Provide human imaging studies using MRI, MRI/PET, PET/CT imaging modality
- Provide assistance on IRB submission, study design and consultation, and image interpolation

Image Analysis Service:
- Image processing including registration, segmentation, image classification, volume rendering, and visualization
- Image quantification support on parameter extraction and data analysis
- Image data storage and archiving, and remote access
Translational Imaging Core

- Developing angiogenesis PET imaging probe. Various Cu-64 labeled peptide constructs were screened on animal tumor model at serial imaging time to select the best probe for tumor angiogenesis. (PI: Dr. Anka Veleva, BME, NC State)

- PET imaging with Zr-89 labeled antibody to fibroblast activation protein in xenograft glioma tumor model on mice. Whole body PET/CT images shown in the left, and longitudinal imaging over 3 days to monitor the antibody uptake shown in the right. (Dr. Thad Wadas, Wake Forest Medical Center)

- Respiration gated CT imaging on rat lung to monitor the therapeutic efficacy in stem cell regeneration study. (Dr. Ke Cheng, Dept. Molecular Biomedical Sciences, NC State Vet School)
Center for Structural Biology: six integrated cores

1. Protein Expression & Purification

2. Peptide synthesis

3. X-ray crystallography

4. NMR

5. Structural bioinformatics

6. Macromolecular interactions

sample preparation

structure determination

structural analyses

biophysical analyses

$K_d \approx 13 \mu M$

$K_d = 0.40 \mu M$
Center for Structural Biology: state-of-the-art

1. **Protein Expression & Purification**
   - expression in bacteria, insect, yeast & mammalian cells
   - automated purification

4. **NMR**
   - 500, 600, 700 and 850 MHz spectrometers with cryoprobes

2. **Peptide synthesis**
   - isotope-labeled peptides
   - peptide arrays
   - one-bead, one-peptide libraries

3. **X-ray crystallography**
   - automated crystallogenesis with remote visualization
   - member of SER-CAT at the Advanced Photon Source

5. **Structural bioinformatics**
   - UNC supercomputing cluster
   - homology and de novo models
   - molecular dynamics

6. **Macromolecular interactions**
   - automated ITC
   - light scattering and analytical ultracentrifugation
   - SPR- and BLI-based biosensors
   - circular dichroism
Center for Structural Biology: outside collaborations welcome

1. Protein Expression & Purification
   - Jeffery Yoder (NCSU)
   - Thaddeus Wadas (Wake Forest) - antibody production
   - UNC Kannapolis - protein expression in algae

2. Peptide synthesis

3. X-ray crystallography
   - Syngenta

4. NMR

5. Structural bioinformatics

6. Macromolecular interactions
   - Clay Clark (NCSU)
   - Bob Rose (NCSU)
   - John Cavanagh (NCSU)
   - Guozhou Xu (NCSU)
Genomics and Bioinformatics

- 5 major technologies:
  - Agilent Microarrays,
  - Affymetrix Microarrays,
  - Illumina bead array genotyping,
  - NextGen sequencing (Illumina, PacBio, and Ion Platforms) and
  - RNAi screening for functional validation

- 1 of 12 TCGA Centers

- Sequenced over 1 Trillion bases, 2 Million SNP, thousands of tumor samples
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