# Josephine Ford Cancer Center
## Cancer Research Programs

**presented to**

# WSU SOM PAD

**January 10, 2012**


**presented by**

**Sandra A. Rempel, Ph.D.**

**Associate Director of Research, JFCC**

# JFCC Cancer Research Programs

## ❑ Cancer Epidemiology, Prevention and Control Program

- **Members:** Gwen Alexander, Andrea Cassidy-Bushrow, George Divine, Sharon Hensley-Alford, Christine Cole Johnson, Lois Lamerato, Al Levin, David Nerenz, Christine Neslund Dudas, Laila Poisson, and Ben Rybicki
- **Clinical Members:** Robert Chapman, Paul Kvale, Melody Eide, David Nathanson, and Eleanor Walker

## ❑ Developmental Therapeutics Program

- **Laboratory Members:** Ken Barton, Stephen Brown, Indrin Chetty, Carri Glide-Hurst, Svend Freytag, Subhash Gautam, Jae Ho Kim, Hualiang Zhong, Fred Valeriote, Maria Worsham
- **Clinical Members:** Munther Ajlouni, Mohamed Elshaikh, Jae Ho Kim, Ben Movsas, Samuel Ryu, Eleanor Walker

## ❑ Urologic Oncology Program

- **Laboratory Members:** Evelyn Barrack, Mireya Diaz, Subhash Gautam, Jagadananda Ghosh, Clara Hwang, Sahn Ho Kim, Christine Neslund-Dudas, Prem-Veer Reddy, Ben Rybicki
- **Clinical Members:** Mani Menon, Craig Rogers

## ❑ Neuro-Oncology Program

- **Laboratory Members**: Arbab Ali, Chaya Brodie, Stephen Brown, Michael Chopp, James Ewing, Svend Freytag, Feng Jiang, Steven Kalkanis, Norman Lehman Ali Messer, Tom Mikkelsen, Laila Poisson, Sandra Rempel
- **Clinical Members:** Mani Brown, Jorge Gutiérrez, Rajan Jain, Steven Kalkanis, Norman Lehman, Tom Mikkelsen, Jack Rock, Mark Rosenblum, Tobias Walbert

## ❑ Cancer Imaging Program

- **Laboratory Members:** Arbab Ali, James Ewing, Ali Messer
- **Clinical Members:** Mani Brown, Rajan Jain

# Basic Approach to Cancer Research

Treat the cancer with different drugs to see if any are effective?

**Drug discovery and development**

**Cancer**

Study the cancer to find out what is different from normal

**Markers**

Use that information to develop markers that can be used to screen patients

- Diagnosis
- Prognosis
- Prevention

**Tumor biology**

Use that information to identify targets for cancer therapy

- Stop tumor cells from dividing
- Stop tumor cells from invading
- Stop tumors from creating a blood supply
- Make them die

# Cancer Epidemiology, Prevention and Control Program

Public Health Sciences

Chair: Christine Cole Johnson, Ph.D.

All Other Departments

# Cancer Epidemiology, Prevention and Control Program

## Members:

**Gwen Alexander, Ph.D.**
Andrea Cassidy-Bushrow, Ph.D.
George Divine, Ph.D.
**Sharon Hensley-Alford, Ph.D.**
Christine Cole Johnson, Ph.D
Lois Lamerato, Ph.D.
**Al Levin, Ph.D.**
David Nerenz, Ph.D.
**Christine Neslund Dudas, Ph.D.**
Laila Poisson, Ph.D.
**Ben Rybicki, Ph.D.**

## Clinical Members:

Robert Chapman, M.D.
Paul Kvale, M.D.
Melody Eide, M.D.
David Nathanson, M.D
Eleanor Walker, M.D.

**Bold**- Members with KCI membership

# Cancer Epidemiology, Prevention and Control Program

The Cancer Epidemiology, Prevention and Control (CEPC) program includes collaborative, multi-institutional research that addresses the entire cancer continuum.

Research emphases include a focus on population sciences including epidemiology, health services, health promotion, health economics, and cancer control.

# Cancer Epidemiology, Prevention and Control Program

## Prevention

**Gwen Alexander, Ph.D.** - diet changes, smoking cessation

**Christine Neslund-Dudas, Ph.D.**- racial differences and environmental impacts – prostate cancer

## Screening

**Andrea Cassidy-Bushrow, Ph.D.**- racial differences – prostate cancer and cardiovascular outcomes.

**Christine Cole Johnson, Ph.D.**-screening tests for lung, colon, prostate and ovarian cancers

**Christine Cole Johnson, Ph.D**. - sociodemographic risk factors

**Paul Kvale, M.D.**- prostate, colon, lung, ovarian cancer screening trials

## Diagnosis

**David Nathanson, M.D**. - sentinel lymph node biopsy for melanoma and breast cancer.

**Al Levin, Ph.D.**- Germline genetic variation and risk of cancer

# Cancer Epidemiology, Prevention and Control Program

## Initiation

**Ben Rybicki, Ph.D**.- DNA methylation and DNA adducts in prostate cancer initiation and progression

## Progression

**Sharon Hensley-Alford, Ph.D**.- stress and cancer progression

**Al Levin, Ph.D**. - DNA adducts and DNA methylation in prostate cancer progression

## Treatment

**Christine Cole Johnson, Ph.D.** - pharmacoepidemiology - non-steroidal anti-inflammatory drugs, hormone replacement therapy, statins

## Long-term Outcomes

**Al Levin, Ph.D.**- genetic differences on cancer outcomes

# Developmental Therapeutics Program

Hematology/Oncology

Radiation Oncology

Surgery

Otolaryngology

Urology

Neurosurgery

# Developmental Therapeutics Program

## Laboratory Members:

Stephen Brown, Ph.D.
Indrin Chetty, Ph.D.
Carri Glide-Hurst, Ph.D.
**Svend Freytag, Ph.D.**
**Subhash Gautam, Ph.D.**
Jae Ho Kim, M.D.
Ramandeep Rattan, Ph.D.
Fred Valeriote, Ph.D.
**Maria Worsham, Ph.D.**
Hualiang Zhong, Ph.D.

## Clinical Members:

Munther Ajlouni, M.D
Mohamed Elshaikh, M.D.
Jae Ho Kim, M.D.
**Ben Movsas, M.D.**
Samuel Ryu, M.D.
Eleanor Walker, M.D.

**Bold**- Members with KCI membership

# Developmental Therapeutics Program

## Drug Discovery and Development

Treatment of all cancers – Fred Valeriote, Ph.D.

## Radiation Oncology

Treatment of prostate cancer – Svend Freytag, Ph.D.

Protection of normal tissue – Stephen Brown, Ph.D.

## Surgery

Treatment of prostate cancer- Subhash Gautam, Ph.D.

## Otolaryngology

Treatment of breast and head & neck cancer – Maria Worsham. Ph.D.

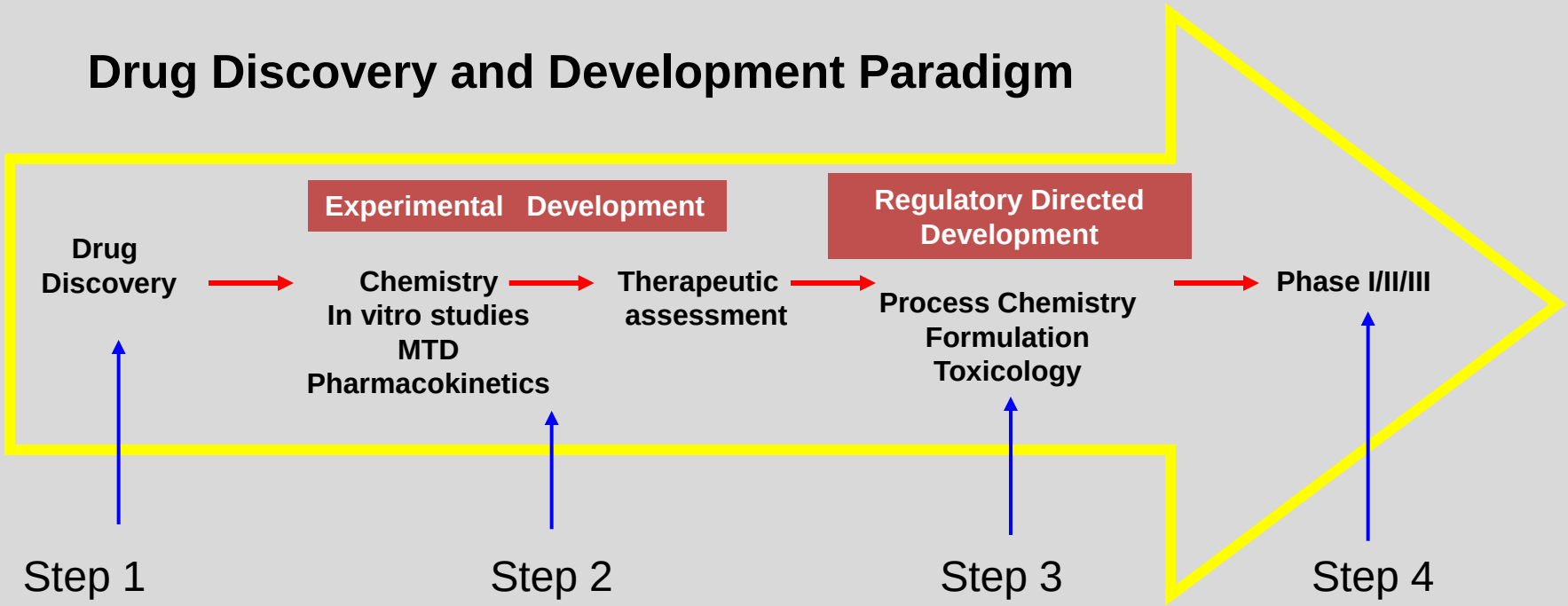
## Women's Health Services

Treatment of ovarian cancer - Ramandeep Rattan, Ph.D.

# Drug Discovery and Development

**Fred Valeriote, Ph.D.**

## Drug Discovery and Development Paradigm




### Step 1
### Drug Discovery

**Discover new anticancer molecules from natural product sources**
- **land plants**
- **ocean plants and animals**

- **Many resources**
- **Many collaborations**

### Step 2
### Is it safe?

- **Animal models**
- **Are there side effects?**
- **What is the best dose?**

Is it effective?

- **Animal models**
- **Does the drug treat cancer**

### Step 3
### How to mass produce?

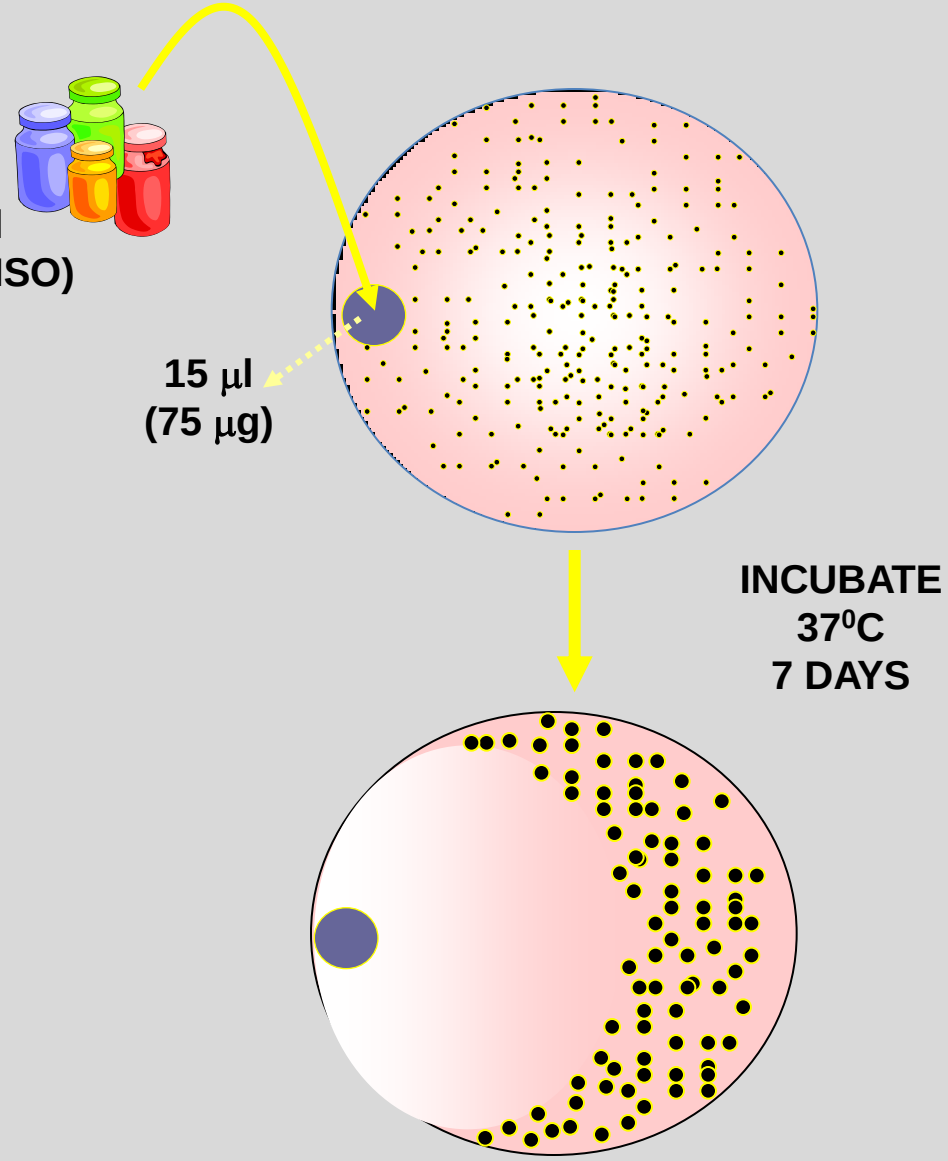
### Step 4
### Clinical trials

- Humans
- What are the side effects?
- Is it effective?
- At what dose?

# 5000 Samples/Year Network

Collaborators: Location ● Collection Sites: ●

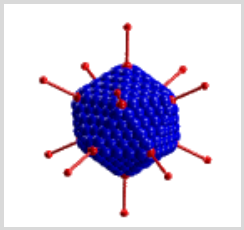
# Disk Diffusion Assay



# Treatment of Prostate & Pancreatic Cancer

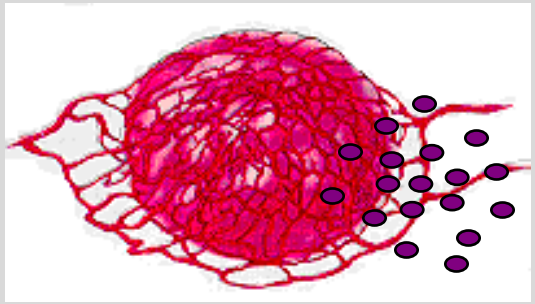
**Svend Freytag, Ph.D.**

**A Novel Three-Pronged Approach**

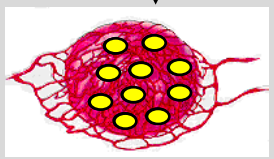


RC adenovirus containing
2 therapeutic genes

Cytosine deaminase /
HSV-Thymidine kinase

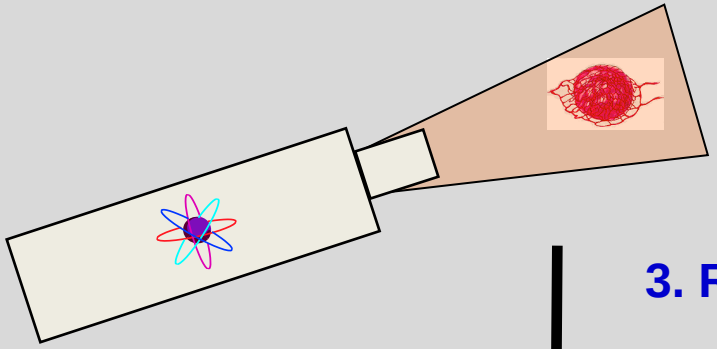


**1. Oncolytic Viral Therapy**



**5-FC + vGCV** → **5-FU + vGCV-MP**

**2. Suicide Gene Therapy**



**3. Radiotherapy**

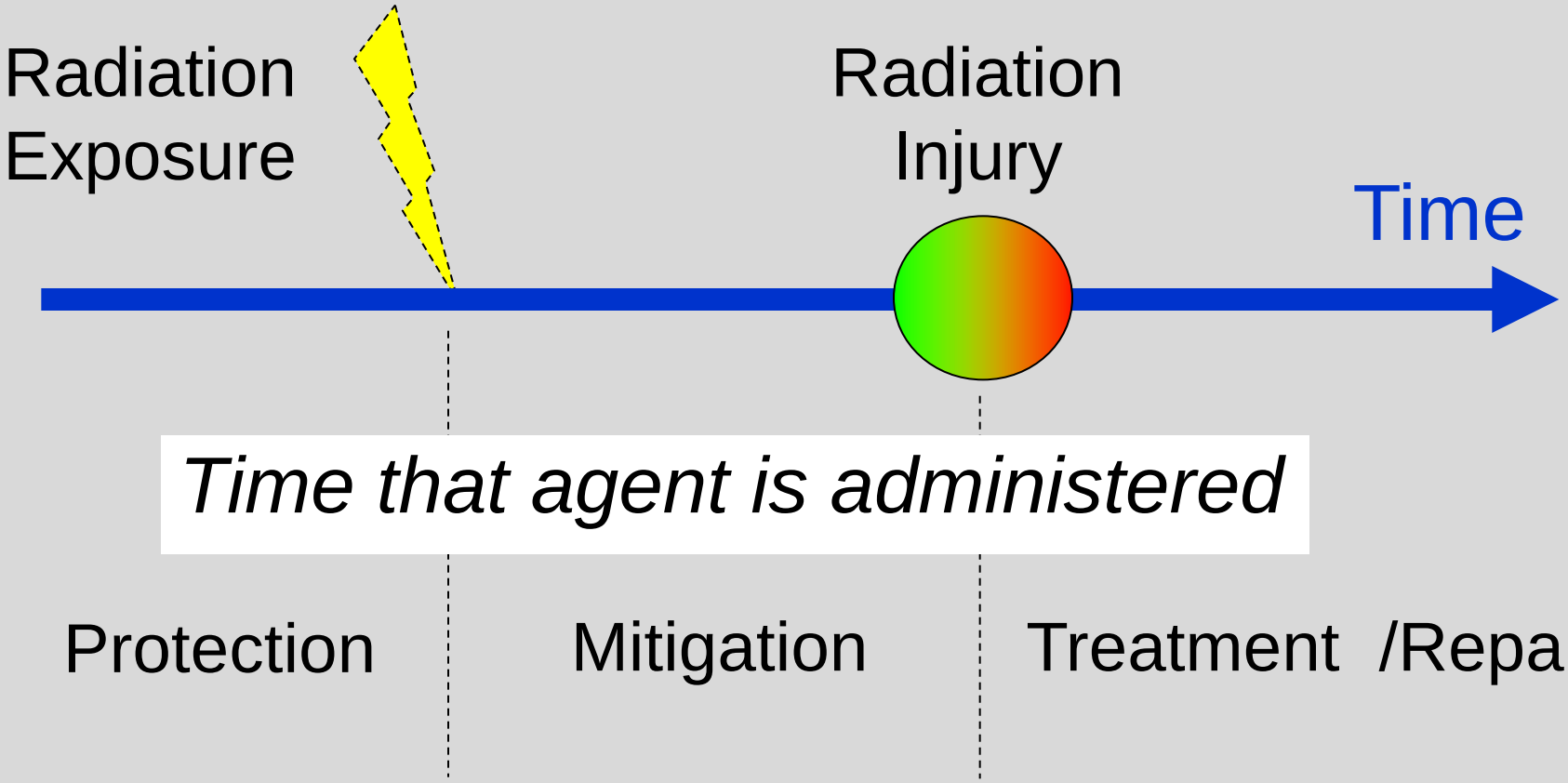
**Tumor Control**

5-FC- 5-Fluorocytosine
5 FU- 5-Fluorouracil
vGCV-ganciclovir monophosphate

# Protection of Normal Tissue from Radiation Therapy

**Stephen Brown, Ph.D.**

Classification of Agents that Reduce Radiation Injury based on Time of Administration



# Urologic Oncology Program

Vattikuti Urology Institute

Public Health Sciences

Hematologic Oncology

Surgery

# Urologic Oncology Program

## Laboratory Members:

Evelyn Barrack, Ph.D.
Mireya Diaz, Ph.D.
**Subhash Gautam, Ph.D.**
**Jagadananda Ghosh, Ph.D.**
Sahn Ho Kim, Ph.D.
**Christine Neslund-Dudas, Ph.D.**
**Prem-Veer Reddy, Ph.D.**
**Ben Rybicki, Ph.D.**

## Clinical Members:

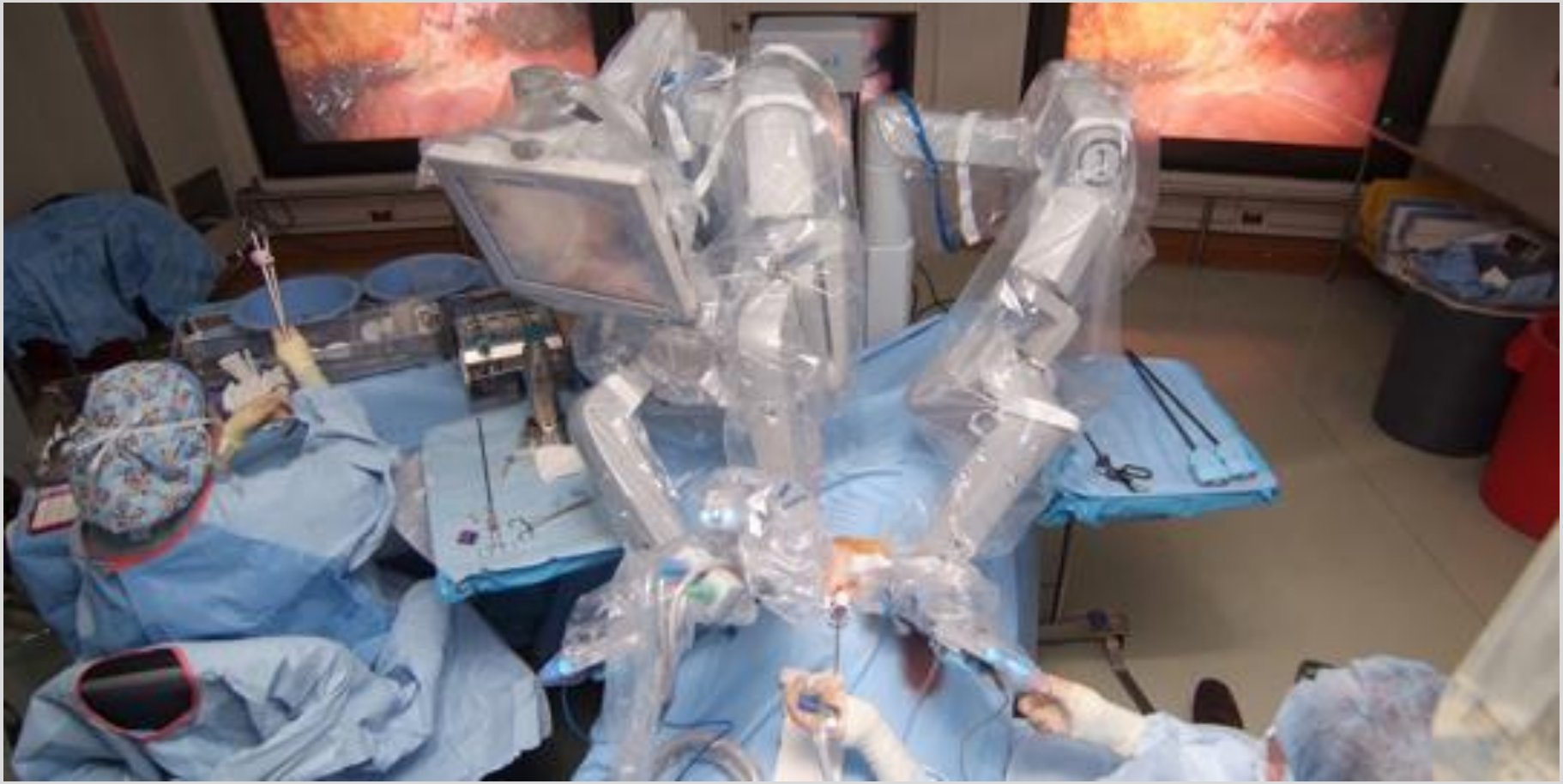
Mani Menon, M.D.
Clara Hwang, M.D.
Craig Rogers, M.D.

**Bold**- Members with KCI membership

# Urologic Oncology Research Program

## Vattikuti Urology Institute

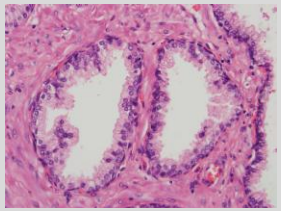
Chair: Mani Menon, M.D.



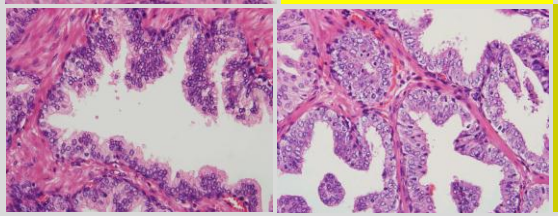
**Robotic Prostate Surgery**

# Prostate Cancer Progression

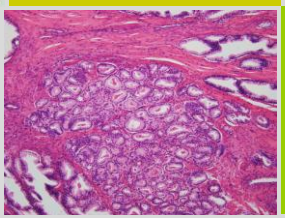
What is different between the normal tissue and the cancer tissue?



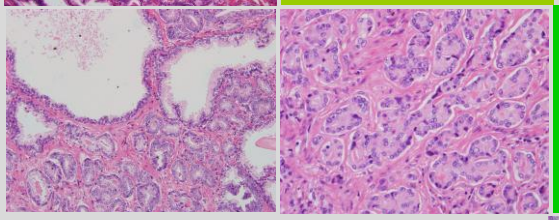
Normal prostate epithelium



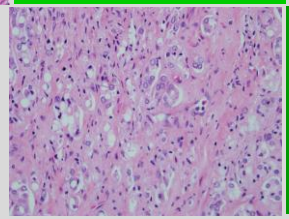
Prostatic intraepithelial neoplasia



Localized prostate cancer



Metastatic prostate cancer



Hormone-refractory cancer

① Etiology & Outcome Prediction:

*Dr. Evelyn Barrack*

② Early detection:

*Drs. Prem Reddy, Craig Rogers & Mani Menon*

③ Treatment:

*Drs. Prem Reddy, Jagat Ghosh, Sahn-ho Kim & Mani Menon Subhash Gautam*

*Prem Veer Reddy, Ph.D.*
Vattikuti Urology Institute

# Neuro-Oncology Program

Hermelin Brain Tumor Center

Radiation Oncology

Imaging

Neurology

Public Health Sciences

# Neuro-Oncology Program

## Members:

Arbab Ali, M.D., Ph.D.
**Chaya Brodie, Ph.D.**
Stephen Brown,Ph.D.
Michael Chopp, Ph.D.
James Ewing, Ph.D.
**Svend Freytag, Ph.D.**
Feng Jiang, Ph.D.
Steven Kalkanis, M.D.
Norman Lehman, M.D.
Ali Messer, Ph.D.
**Tom Mikkelsen, M.D.**
Laila Poisson, Ph.D.
**Sandra Rempel, Ph.D.**

## Clinical Members:

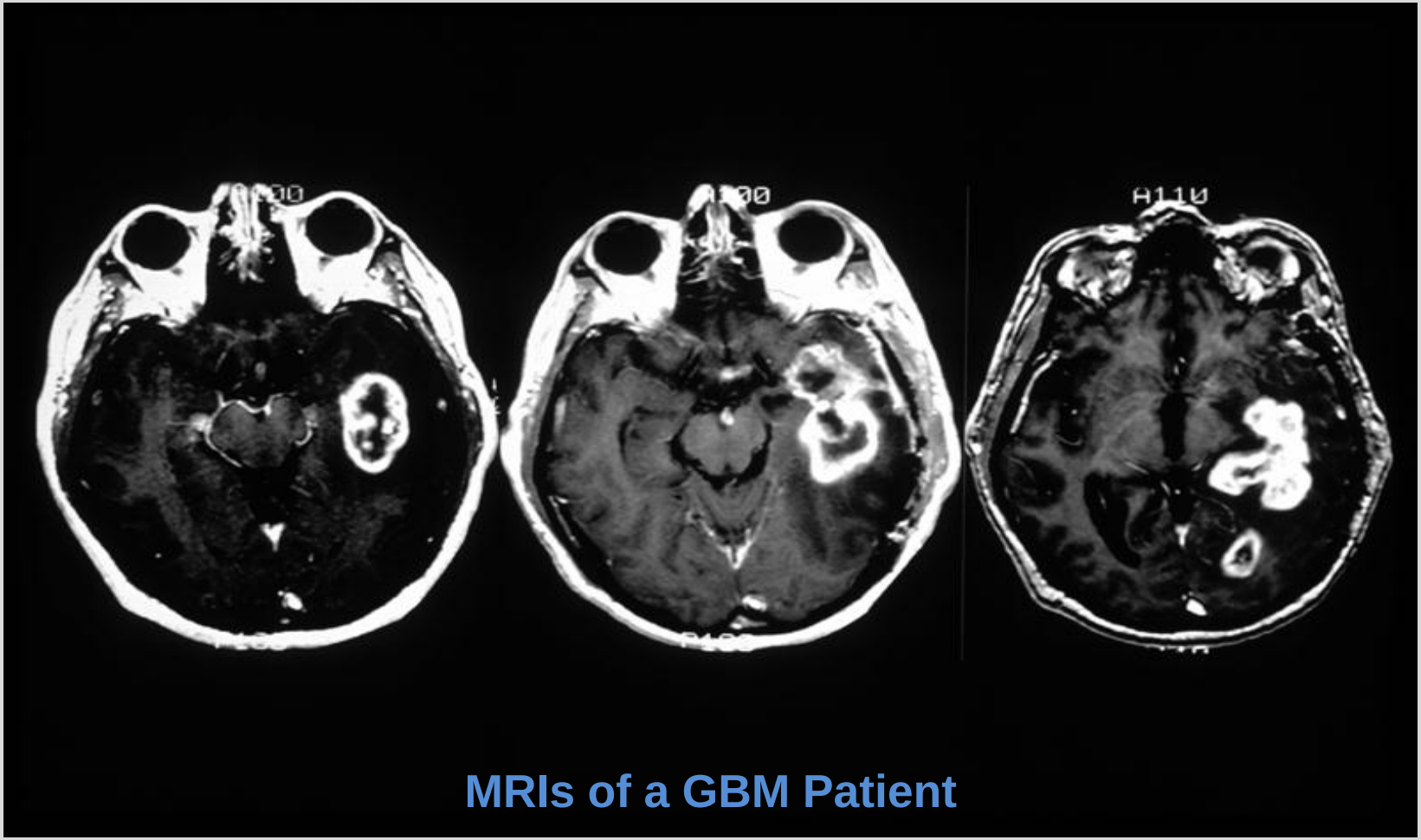
Mani Brown, M.D.
Jorge Gutiérrez, M.D.
Rajan Jain, M.D.
Steven Kalkanis, M.D.
Norman Lehman, M.D.
**Tom Mikkelsen, M.D.**
Jack Rock, M.D.
Mark Rosenblum, M.D.
Tobias Walbert, M.D.

**Bold**- Members with KCI membership

# Neuro-Oncology Research Program

## Hermelin Brain Tumor Center

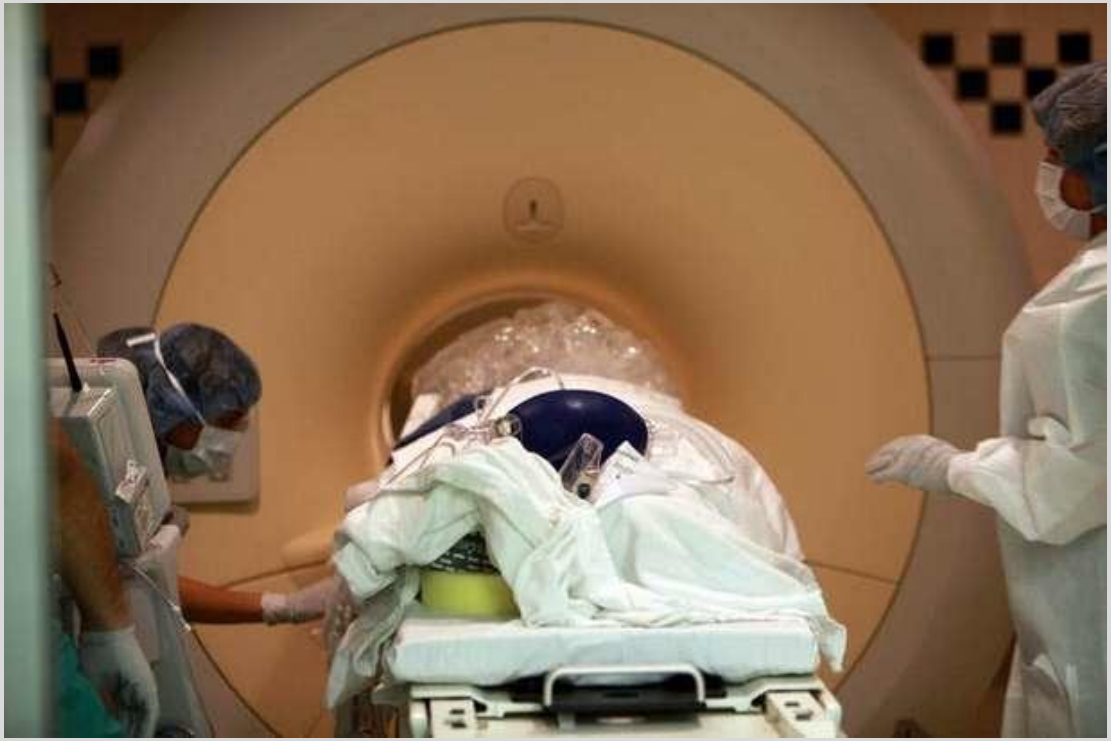
Chair: Mark L. Rosenblum, M.D.




**MRIs of a GBM Patient**

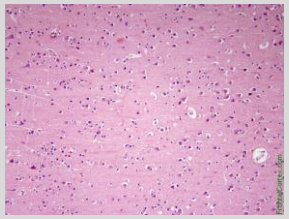
# Neuro-Oncology Research Program

Intra-operative MRI



# Astrocytoma Tumor Progression

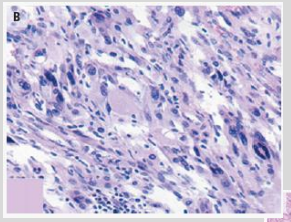
What is different between the normal tissue and the cancer tissue?



Normal Brain

① Etiology & Outcome Prediction:

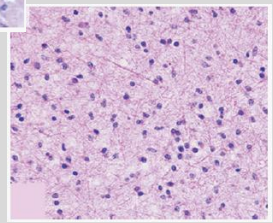
*Drs. Tom Mikkelsen, Steven Kalkanis, Chaya Brodie, Sandra Rempel*



Grade I

② Early Detection, Progression, and Tumor Biology:

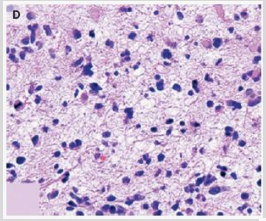
*Drs. Tom Mikkelsen, Steven Kalkanis, Chaya Brodie, Sandra Rempel*



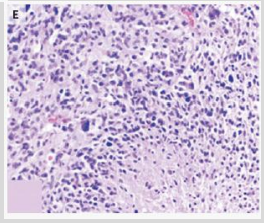
Grade II

③ Treatment:

*Drs. Tom Mikkelsen, Steven Kalkanis, Chaya Brodie, Sandra Rempel*



Grade III



Grade IV

Adapted from Sanai N, et al., N Engl J Med 2005;353:811-22.

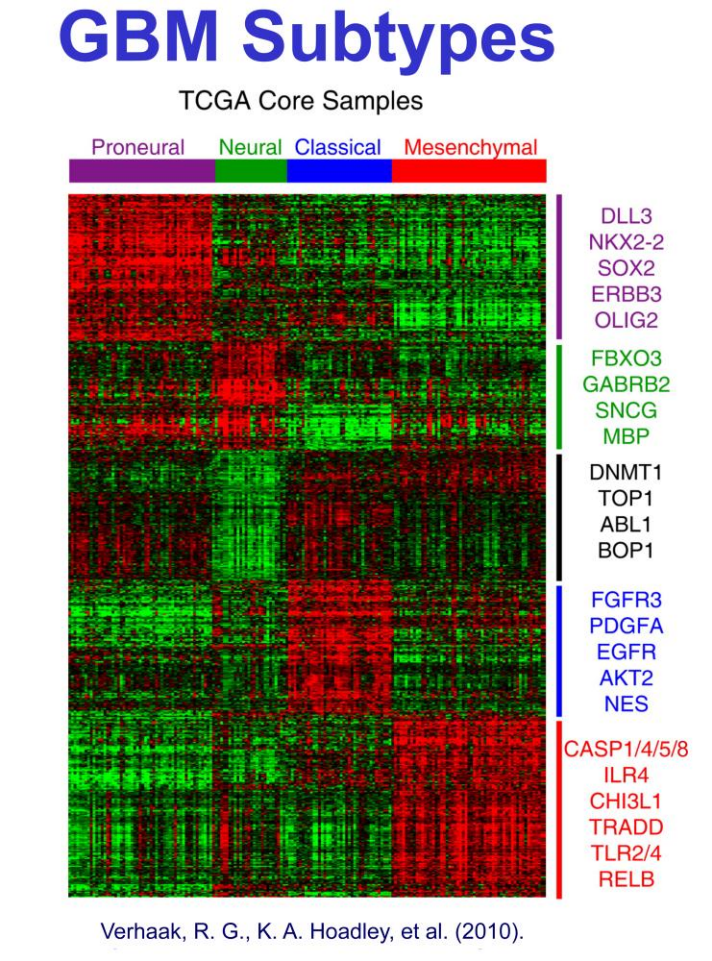
gliageek

# Tumor Biology- cDNA Arrays

## TCGA

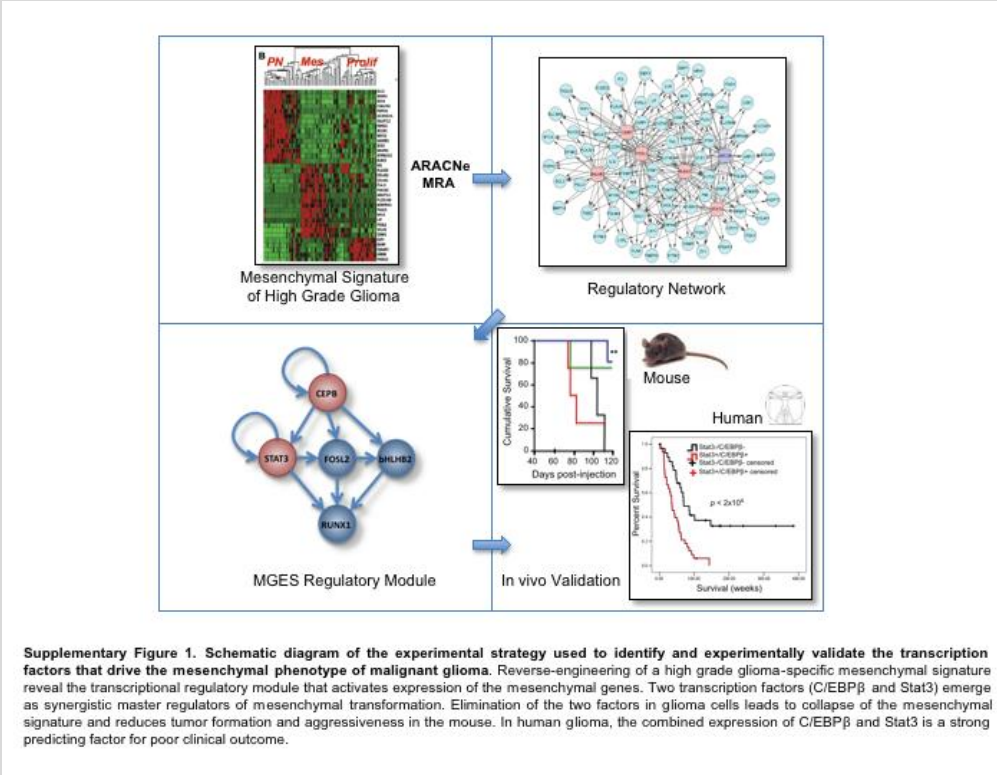
What is different between the normal tissue and the cancer tissue?

cDNA Array Data




Verhaak, R. G., K. A. Hoadley, et al. (2010).

(Califano & Iavarone, Nature 2009)




**Supplementary Figure 1. Schematic diagram of the experimental strategy used to identify and experimentally validate the transcription factors that drive the mesenchymal phenotype of malignant glioma.** Reverse-engineering of a high grade glioma-specific mesenchymal signature reveal the transcriptional regulatory module that activates expression of the mesenchymal genes. Two transcription factors (C/EBPβ and Stat3) emerge as synergistic master regulators of mesenchymal transformation. Elimination of the two factors in glioma cells leads to collapse of the mesenchymal signature and reduces tumor formation and aggressiveness in the mouse. In human glioma, the combined expression of C/EBPβ and Stat3 is a strong predicting factor for poor clinical outcome.

# Cancer Imaging Program

Radiology

Neurology

# Cancer Imaging Program

## Laboratory Members:

Arbab Ali, M.D., Ph.D.
James Ewing, Ph.D.
Meser Ali, Ph.D.

## Clinical Members:

Mani Brown, M.D.
Rajan Jain, M.D.

## Imaging Capabilities

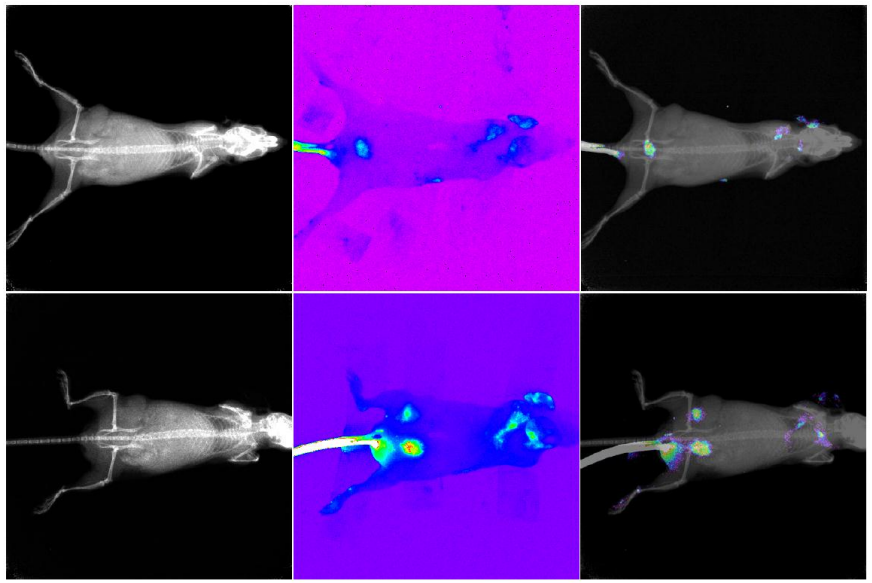
**Arbab Ali, M.D., Ph.D.** SPECT, Optical Imaging (Fluorescence, bioluminescence, x-ray, radioisotope), IVIS

**James Ewing, Ph.D.** - MRI

**Meser Ali, Ph.D**.- Imaging agents, Nanoparticles

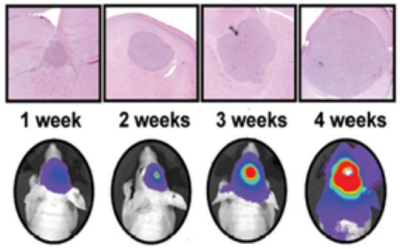
# Animal Models and Cancer Imaging

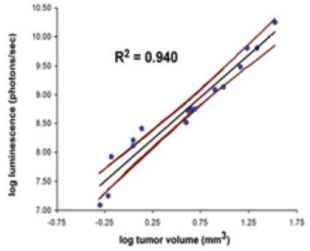
**Fluorescent and X-ray**



Caliper LifeSciences

## Real time monitoring of glioblastoma




**Monitoring Xenograft models of glioblastoma using BLI and IVIS:**

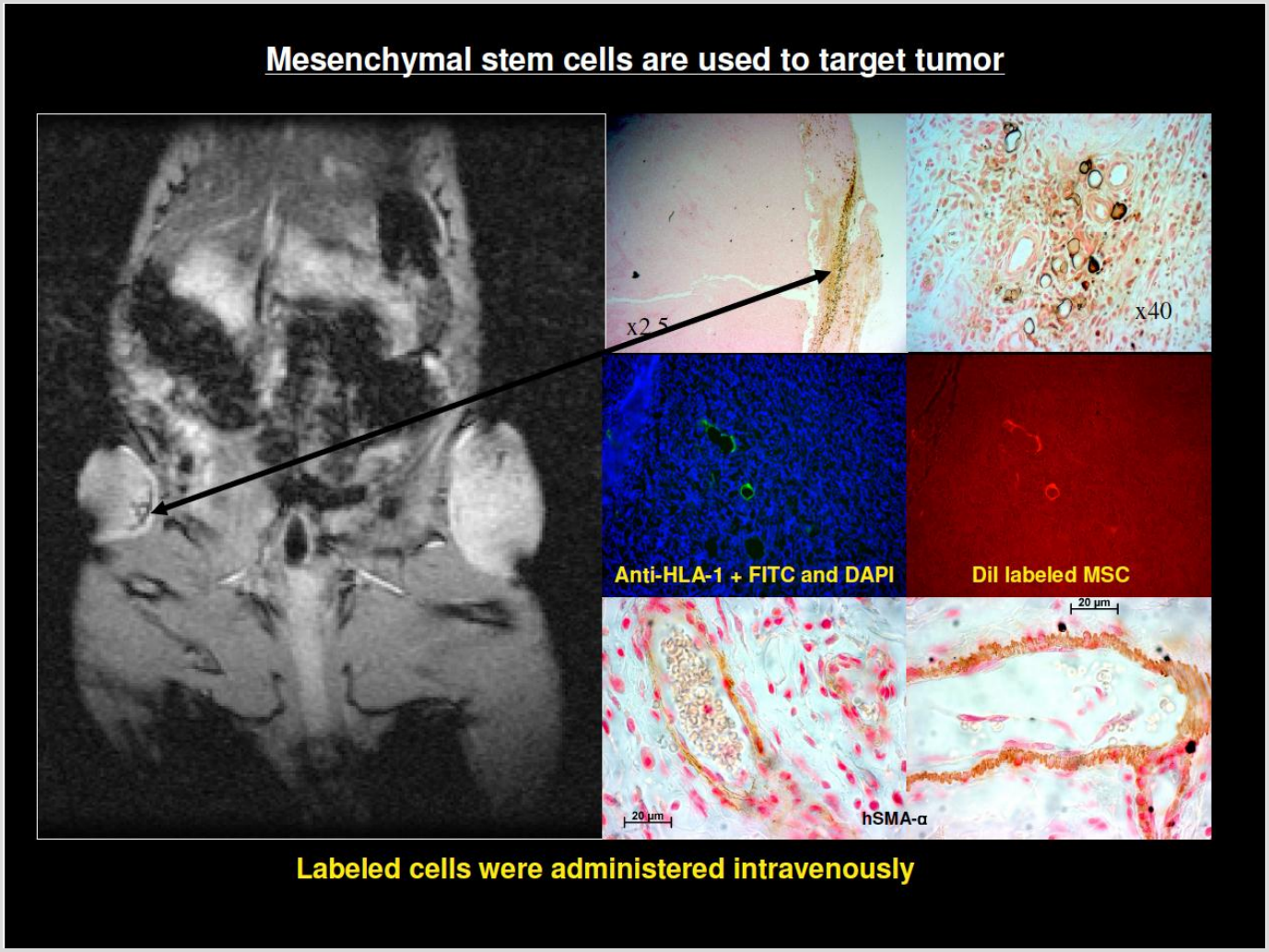
- Correlates with tumor volume measured by histopathological morphometry
- Provides appropriate micro-environment for tumor growth and development
- Allows salvage/secondary therapy efficacy against recurrent tumors
- Effectively predicts survival in a glioblastoma model

*Dinca et al.*, J Neurosurgery 107: 610-616, 2007

# Cancer Imaging Research Program

## Combining Delivery Vehicles/Agents with Imaging

Arbab Ali, M.D., Ph.D. Radiology

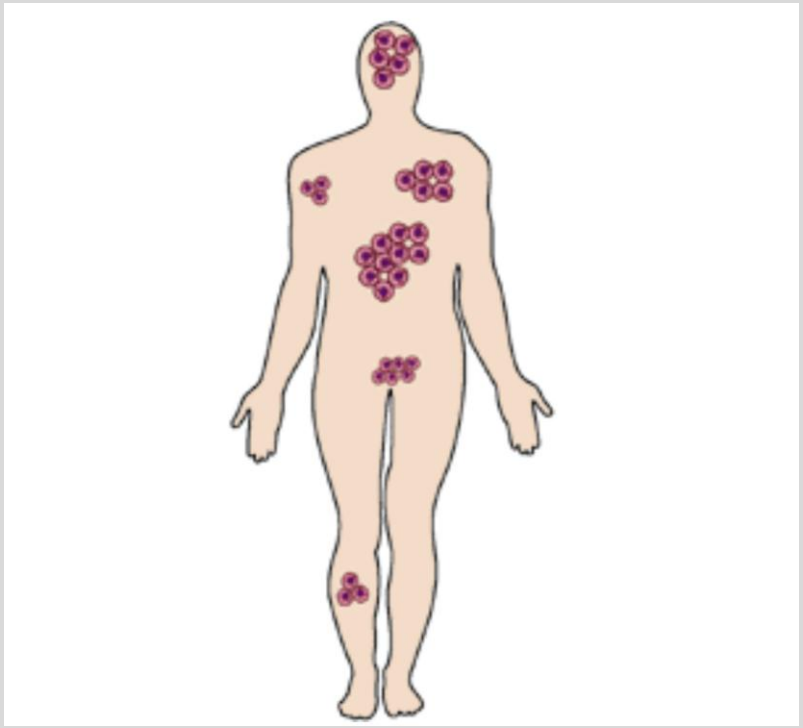


# Clinical Trials- Ultimate Test

| Cancer type | # trials | # patients |
|---|---|---|
| Breast (Radiology) | 1 | 365 |
| Prostate (JFCC + Rad Onc) | 8 | 100 |
| Breast (JFCC) | 13 | 79 |
| Bone mets | 3 | 44 |
| Brain | 16 | 43 |
| Mets | 5 | 27 |
| Melanoma | 1 | 20 |
| Lung | 12 | 17 |
| Blood disorders | 9 | 17 |
| Thyroid | 2 | 9 |
| Pancreatic Adenocarcinoma | 2 | 9 |
| Bladder Cancer | 5 | 5 |
| Spine | 1 | 4 |
| Renal | 1 | 3 |
| Unresect. Hilar Cholangiocarcinoma | 1 | 2 |
| Colorectal | 2 | 1 |
| GI stromal | 1 | 1 |
| Esophageal | 1 | 1 |
| Ovarian | 1 | 1 |
| Hepatocellular carcinoma | 1 | 1 |
| Gastric | 1 | 1 |
| Endometrial cancer | 1 | 0 |
| **Total** | **88** | **749** |

# Eventual Goal

## Individualized Cancer Treatment



DNA Sequence,
cDNA and protein arrays

↓

Genotype-specific cancer profile

↓

Treatment based on your specific cancer

# Summary

## ❑ Five JFCC Cancer Research Programs

- Study many types of cancer

## ❑ Study the Molecular Basis of Cancer

- Markers for prognosis and diagnosis
- Tumor biology- target tumor growth, blood vessel formation (angiogenesis) and invasion and metastases
- Identify novel therapeutic targets

## ❑ Translational Studies

- Animal models

## ❑ Clinical Trials

- Human studies

## ❑ Personalized Treatment