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
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
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.

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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.

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

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

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

Fred Valeriote, Ph.D.

Drug Discovery and Development Paradigm
5000 Samples/Year Network

Collaborators: Location 🟥 Collection Sites: 🟢
Disk Diffusion Assay

5 mg/ml (0.25 ml DMSO)

15 μl (75 μg)

INCUBATE
37°C
7 DAYS
**Treatment of Prostate & Pancreatic Cancer**

Svend Freytag, Ph.D.

A Novel Three-Pronged Approach

- **1. Oncolytic Viral Therapy**
- **2. Suicide Gene Therapy**
- **3. Radiotherapy**

**RC adenovirus containing 2 therapeutic genes**

Cytosine deaminase / HSV-Thymidine kinase

- **5-FC** + vGCV
- **5-FU** + vGCV-MP

**5-FC** - 5-Fluorocytosine
5 FU - 5-Fluouracil
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

- Radiation Exposure
- Radiation Injury

Time

Time that agent is administered

Protection  Mitigation  Treatment /Repair
Urologic Oncology Program

Vattikuti Urology Institute
Public Health Sciences
Hematologic Oncology
Surgery
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?

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

Normal prostate epithelium

Prostatic intraepithelial neoplasia

Localized prostate cancer

Metastatic prostate cancer

Hormone-refractory cancer
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?

① Etiology & Outcome Prediction:
Drs. Tom Mikkelsen, Steven Kalkanis, Chaya Brodie, Sandra Rempel

② Early Detection, Progression, and Tumor Biology:
Drs. Tom Mikkelsen, Steven Kalkanis, Chaya Brodie, Sandra Rempel

③ Treatment:
Drs. Tom Mikkelsen, Steven Kalkanis, Chaya Brodie, Sandra Rempel

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

**cDNA Array Data**

**GBM Subtypes**

*TCGA Core Samples*

- Proneural
- Neural
- Classical
- Mesenchymal

**cDNA Array Data**

**Tumor Biology- cDNA Arrays**

**TCGA**


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 reveals the transcriptional regulatory module that activates expression of the mesenchymal genes. Two transcription factors (C/EBPβ and Snail) originate an synergistic master regulator 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 CEBPβ and Snail is a strong predictor for poor clinical outcome.)

*(Califano & Iavarone, Nature 2009)*
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
**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

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*Dinca et al., J Neurosurgery 107: 610-616, 2007*
Mesenchymal stem cells are used to target tumor

Labeled cells were administered intravenously
## Clinical Trials - Ultimate Test

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