

BME 695L Engineering Nanomedical Systems

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**Lecture 19: In vivo model systems to study  
nanomedical approaches  
to cancer detection and intervention**

# Translational Cancer Research “Bench to Bedside”

In vitro work → Animal studies → Human trials

# In Vivo Studies

- Three dimensional environment
- Microenvironment
- Blood supply
- Immune system
- Other intact body processes

# In Vivo Studies

- Route of administration
- Biodistribution / pharmacokinetics
- Toxicity
- Efficacy

# Types of Animal Models

- Tumors induced by chemicals, irritants, light/radiation
- Syngeneic models
- Immunocompromised animals with “foreign xenografts”
- Transgenic models
- Naturally-occurring animal models

# Naturally-Occurring Canine Cancer

- Models of human cancer
  - Invasive urinary bladder cancer
  - Primary bone cancer
  - Prostate cancer
  - Others



# Translational Cancer Research

Bench Research,  
Laboratory Animal Research



Human Clinical  
Trials



# Translational Cancer Research

Bench Research,  
Laboratory Animal Research



Naturally-Occurring  
Canine Cancer



Human Clinical  
Trials



# Why Study Pet Dogs With Naturally-Occurring Cancer?

- Specific forms of naturally-occurring canine cancer closely mimic the human condition
- Dogs develop heterogeneous, drug-resistant cancer
- Dogs and humans share environment

# Why Study Pet Dogs With Naturally-Occurring Cancer?

- Dogs are large enough for medical procedures
- Pet owners allow their dogs to participate in clinical trials
- Compressed life span of dogs allows timely study of the entire cancer process from initial development until death

# Why Study Pet Dogs With Naturally-Occurring Cancer?

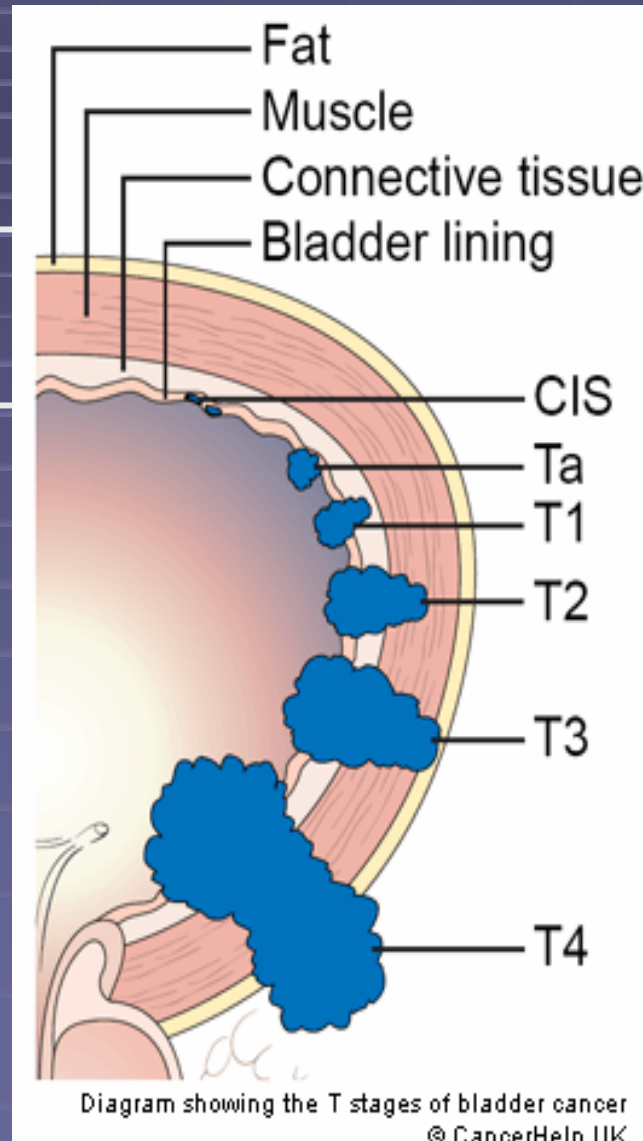
- Naturally-occurring canine cancer models complement other animal models, i.e. experimentally-induced rodent cancer models

# Example: Urinary Bladder Cancer

- Transitional cell carcinoma (TCC)
- >500,000 people living with TCC in North America
- >65,000 new cases diagnosed yearly
- >14,000 deaths yearly
  
- 2 broad forms of TCC: (1) lower grade superficial, (2) higher grade invasive

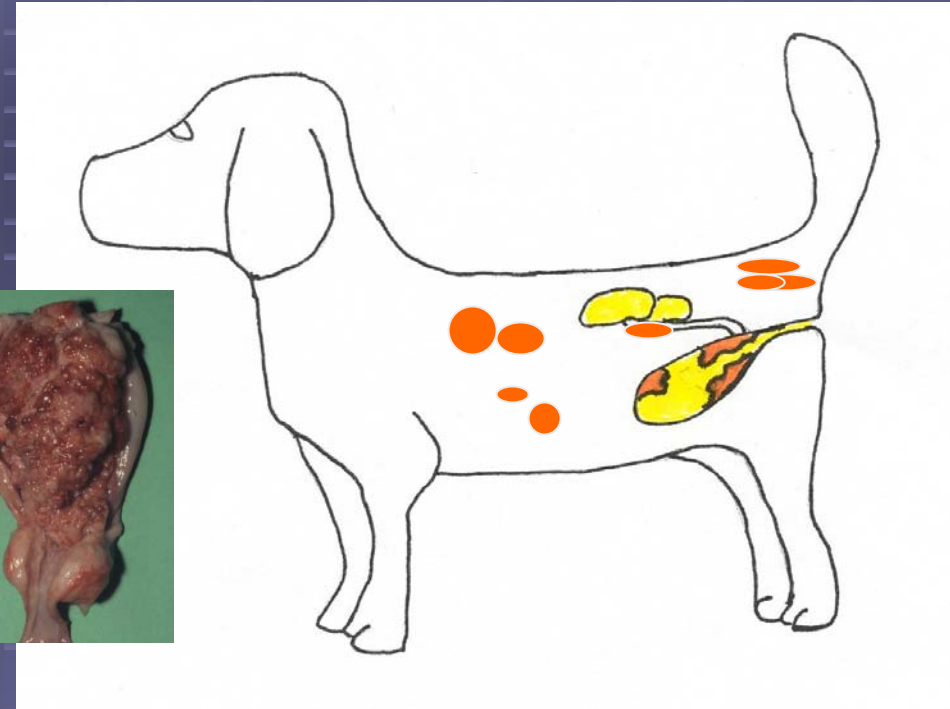
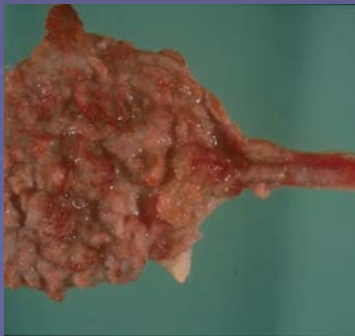
# Stages of Urinary Bladder Cancer

Urinary Bladder Wall

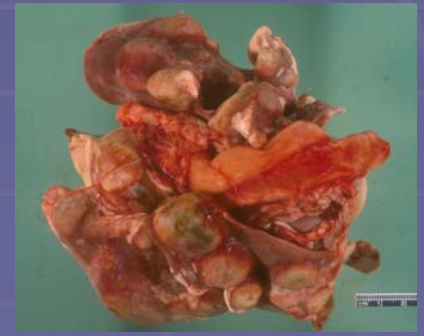
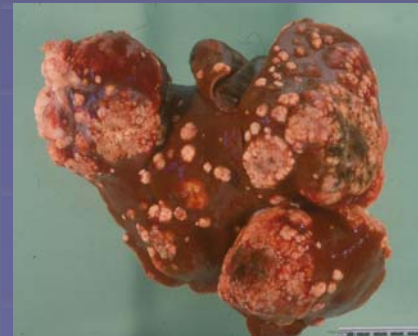


# Urinary Bladder Cancer

Experimentally-induced, low grade, superficial tumors



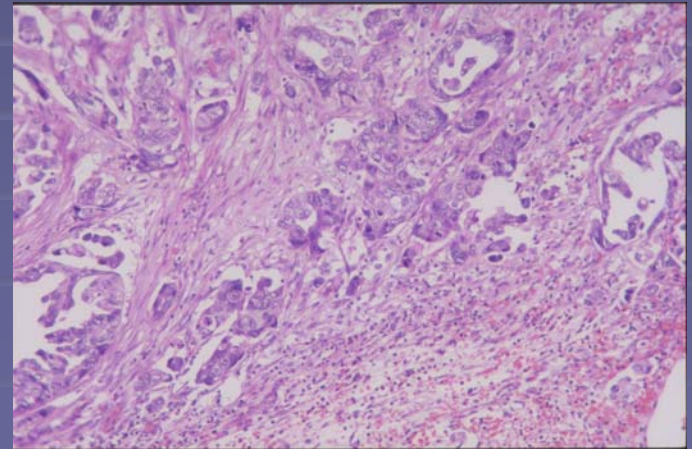
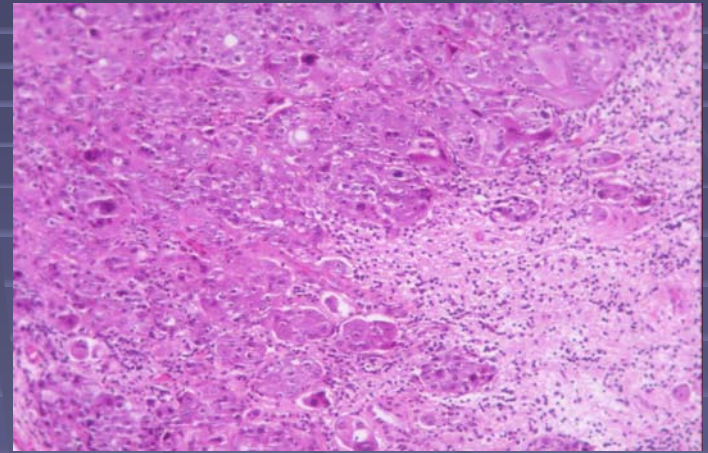
Naturally-occurring, high grade invasive TCC

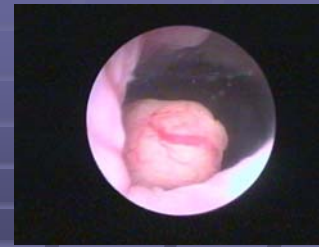


# Urinary Bladder Cancer

## Invasive TCC: “Dog = Human”

- Histopathology
- Cellular features
- Biologic behavior
- Prognostic factors
- Response to chemotherapy



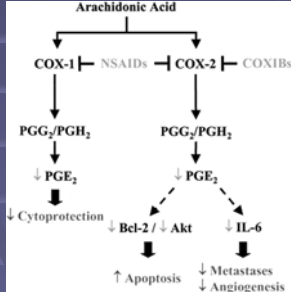


**Prevention -  
Define genetic and  
environmental causes**

**Improved detection / staging -  
NIFR imaging studies  
Proteomics, metabolomics**



# Urinary Bladder Cancer – Transitional Cell Carcinoma



**Human clinical trials –  
Cox inhibitor trials, etc.**

**Better use of existing drugs -  
Cox inhibitors and chemo  
Metronomic chemo**

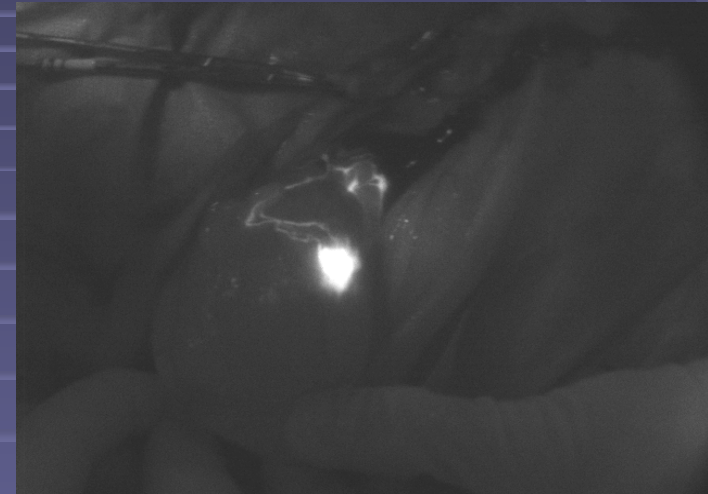
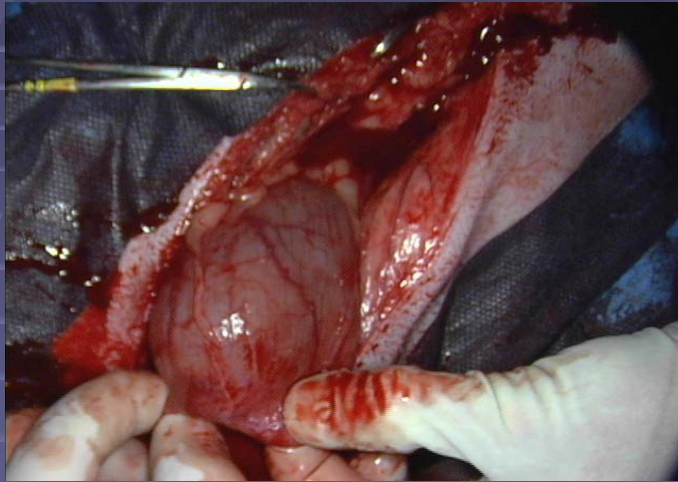


**Novel therapy -  
MCC  
EphA2  
Nanomedicine**



# Bladder Cancer Staging

## Real Time NIRF Imaging to Map Lymph Node Drainage

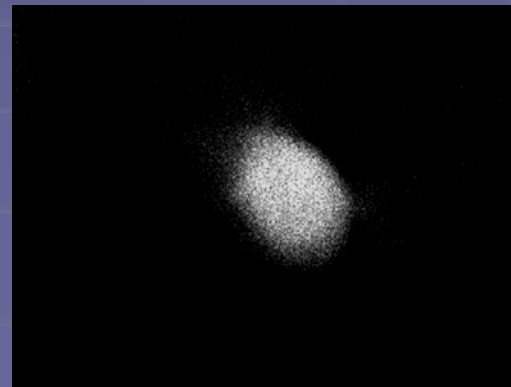


Ex Vivo

Color Video



NIR Fluorescence



Color-NIR Merge



# Clinical Challenges in InvTCC

## Areas to Apply Nanomedicine

- Prevention
- Earlier detection
- More accurate staging
- Predict cancer behavior
- Bladder sparing therapy
- Treatment of metastatic disease

# Bladder Cancer and Nanoparticle Research Investigators, Staff, and Collaborators

## Knapp Lab and Med. Oncology Clinics

D Knapp                      D Dhawan  
M Lucroy                    A Abbo  
J Stewart                    M Childress  
R Zheng                     P Bonney  
A deGortari                L Fourez

## National Institutes of Health

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C Khanna

## Harvard University

J Frangioni

## University of Missouri

C Henry

## Indiana University Collab

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N Hahn                     D Jones

## SVM/Purdue Collab

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N Glickman                B Craig  
J Ramos-Vara             J Leary  
D Bergstrom              S Orcun  
A Murphy                   P Snyder  
W Widmer                   C Stauffacher  
S Mohammed              S Hooser  
D Raftery

## Michigan State University

E McNeil

# Questions & Answers

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