



NIH NATIONAL CANCER INSTITUTE

CENTER TO REDUCE  
CANCER HEALTH DISPARITIES

# Professional Development and Mock Review Workshop

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*Training for Independence: Academic Job Search Success*

**Graduate Student Special Session**  
**NCI Intramural Investigator Flash Talk Presentations**

# Yamini Dalal, PhD

## Center for Cancer Research

Laboratory of Receptor Biology and Gene Expression

Senior Investigator

Group Director, Chromatin Structure and Epigenetic Mechanisms Group

United We Stand, Divided We Fall: Mitosis and Disease  
in Human Cells

**Poster Number 2**

# Udayan Guha, MD, PhD

**Center for Cancer Research**

Thoracic and GI Malignancies Branch

Investigator

Head, Cancer Signaling Networks Section

Tumor Heterogeneity and Targeted Therapy Resistance

**Poster Number 5**

# Most common EGFR mutations and EGFR-tyrosine kinase inhibitors (TKIs)

## EGFR TKIs

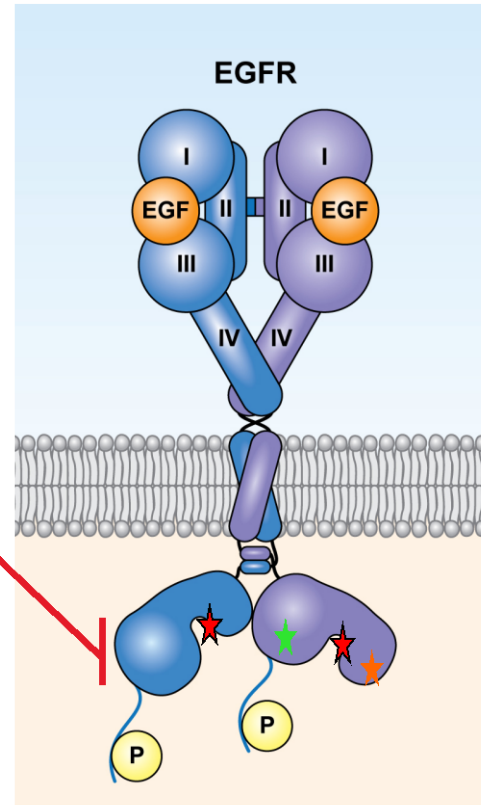
1<sup>st</sup> generation:  
gefitinib  
erlotinib

2<sup>nd</sup> generation:  
afatinib  
dacomitinib

3<sup>rd</sup> generation:  
osimertinib  
BI 1482694

rociletinib

★ C797S  
L718Q, L844V



- EGFR TKI-sensitizing mutations

★ L858R

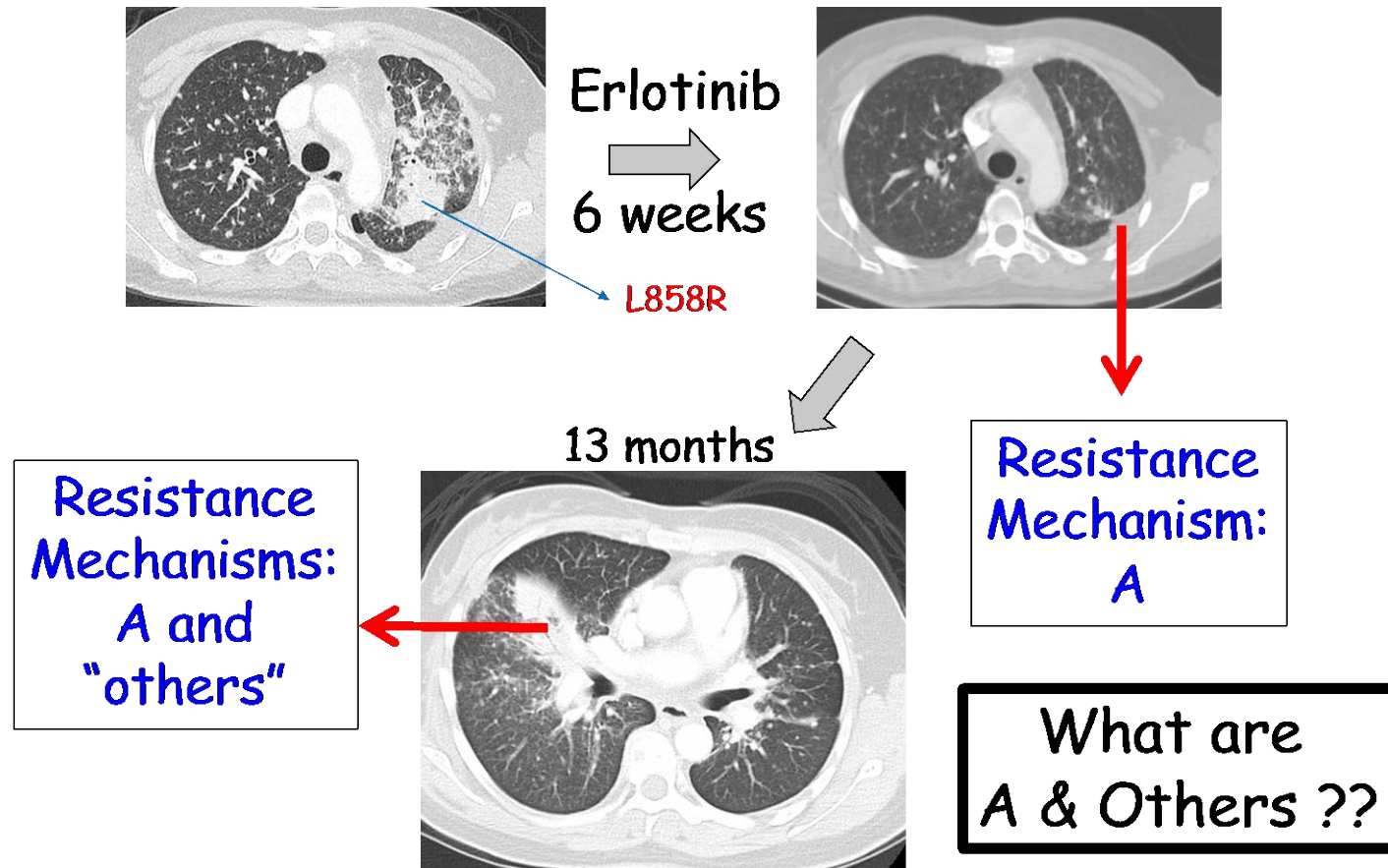
★ Del EGFR

(85%)

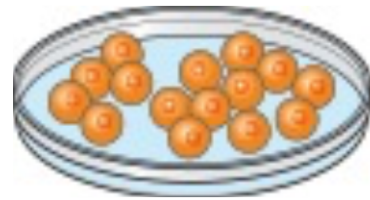
- EGFR TKI-resistant mutation

★ T790M (60% of resistance)

# Influence of tumor heterogeneity on targeted therapy resistance



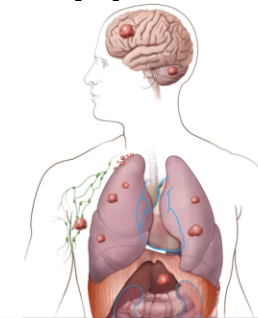
# A multipronged approach from the bench to bedside- multi-"omics" approach and disease modeling to study targeted therapy resistance



Lung adenocarcinoma cells in culture



Mouse models *in vivo* (GEM and orthotopic)

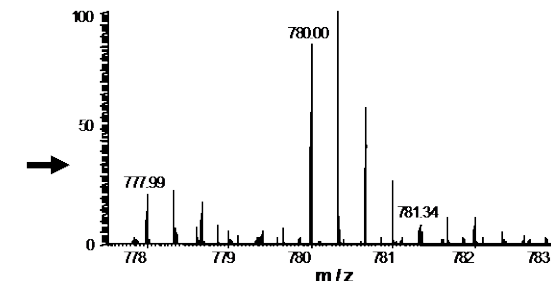
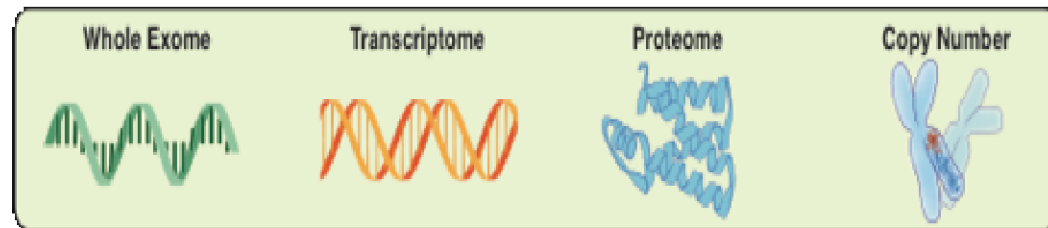


Human tissues-biopsy, surgery and rapid autopsy



Genomics

Quantitative mass spectrometry-based proteomics



# **Christian S. Hinrichs, MD**

**Center for Cancer Research**

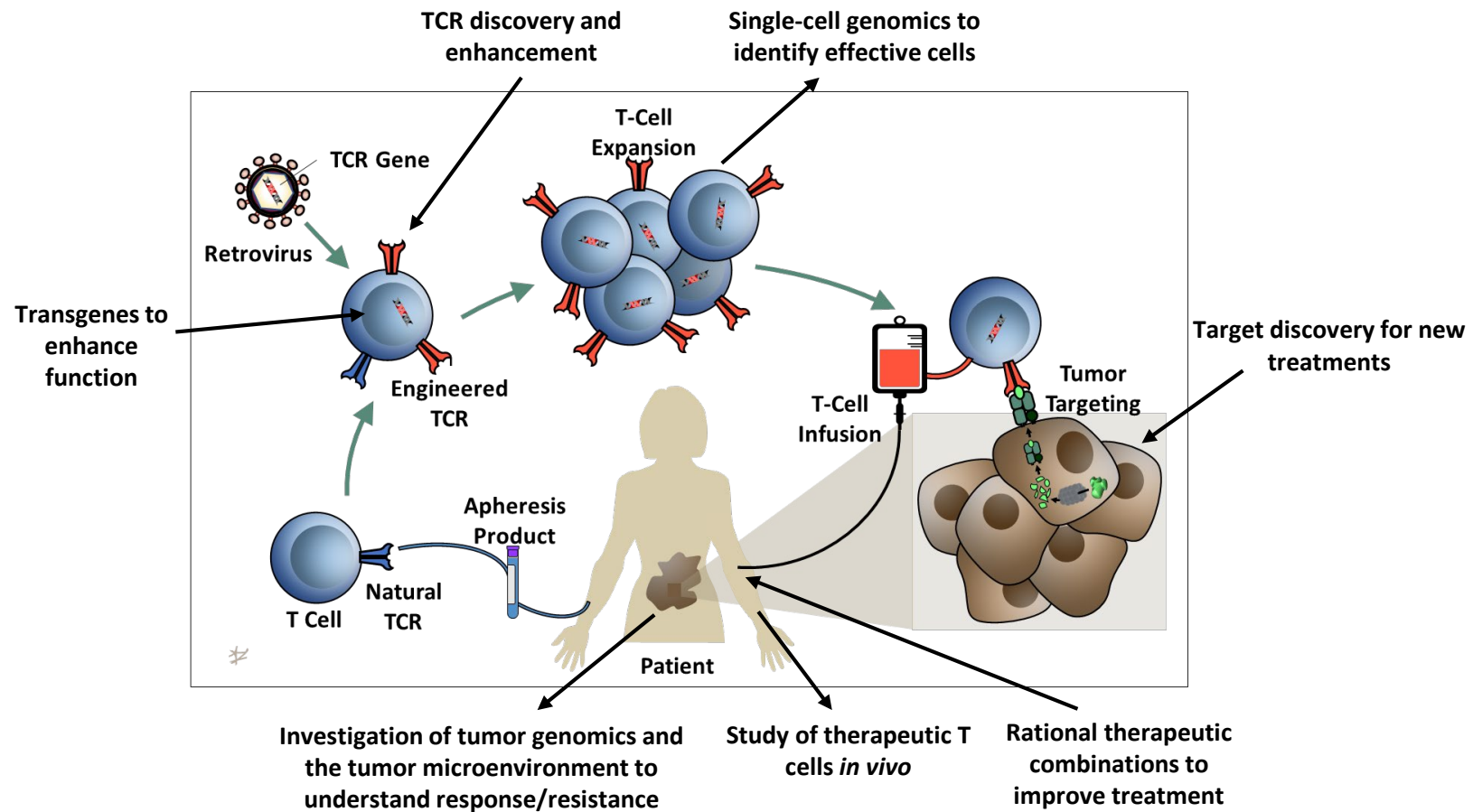
Experimental Transplantation and Immunology Branch

Investigator

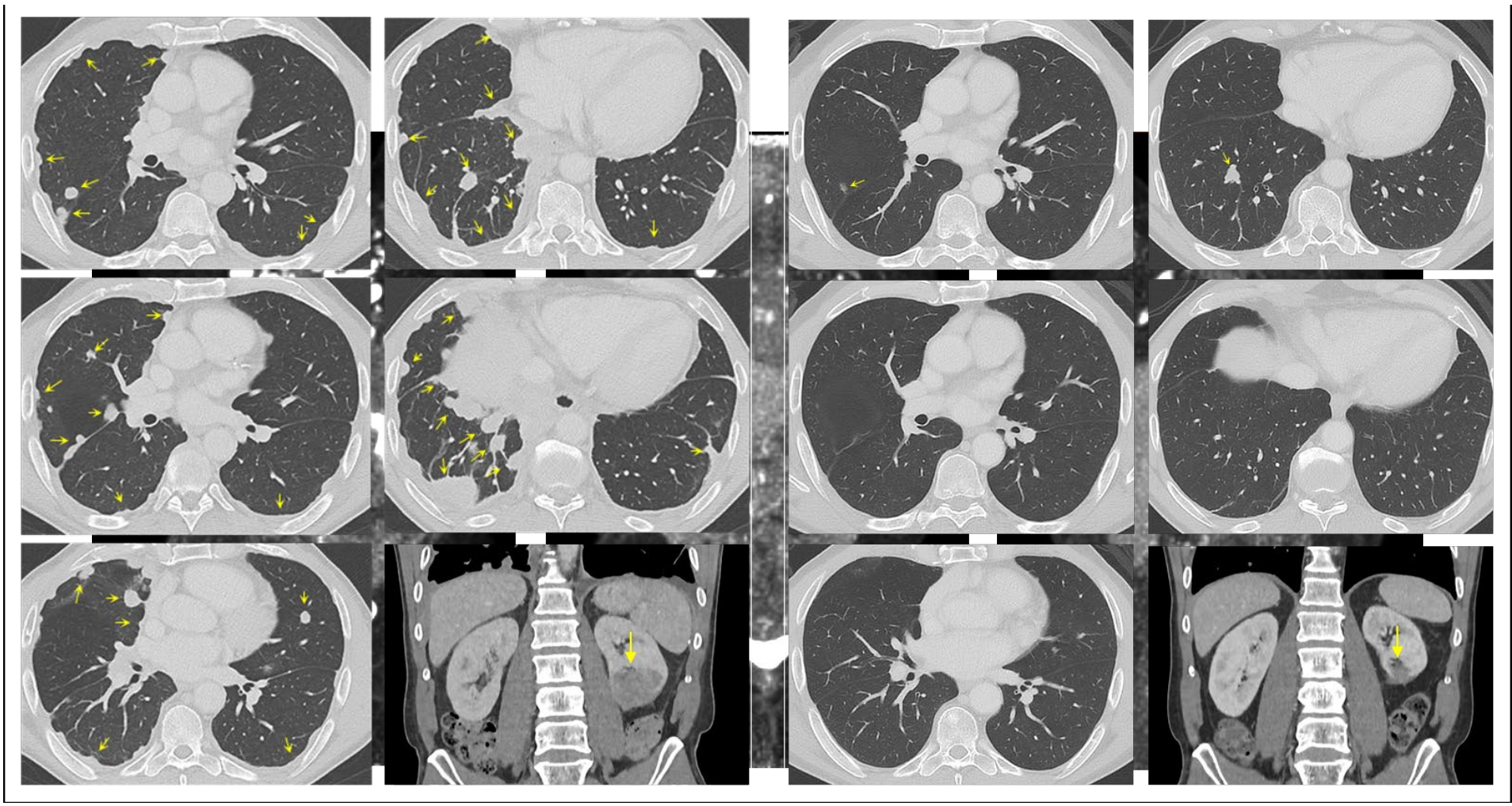
Lasker Clinical Research Scholar

**Adoptive T Cell Therapy for Cancer**

**Poster Number 6**







# Jing Huang, PhD

## Center for Cancer Research

Laboratory of Cancer Biology and Genetics

Senior Investigator

Head, Cancer and Stem Cell Epigenetics Section

p53 in Mesenchymal Stem Cells and Osteosarcoma

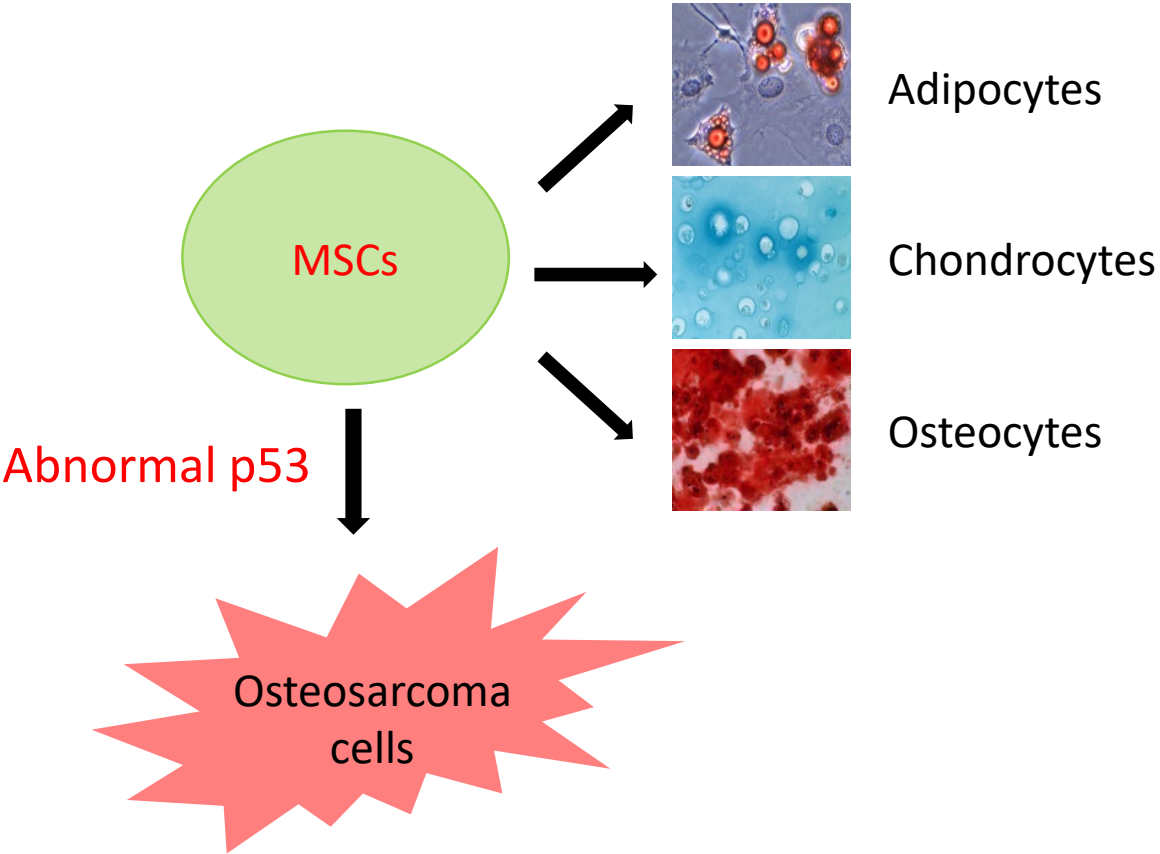
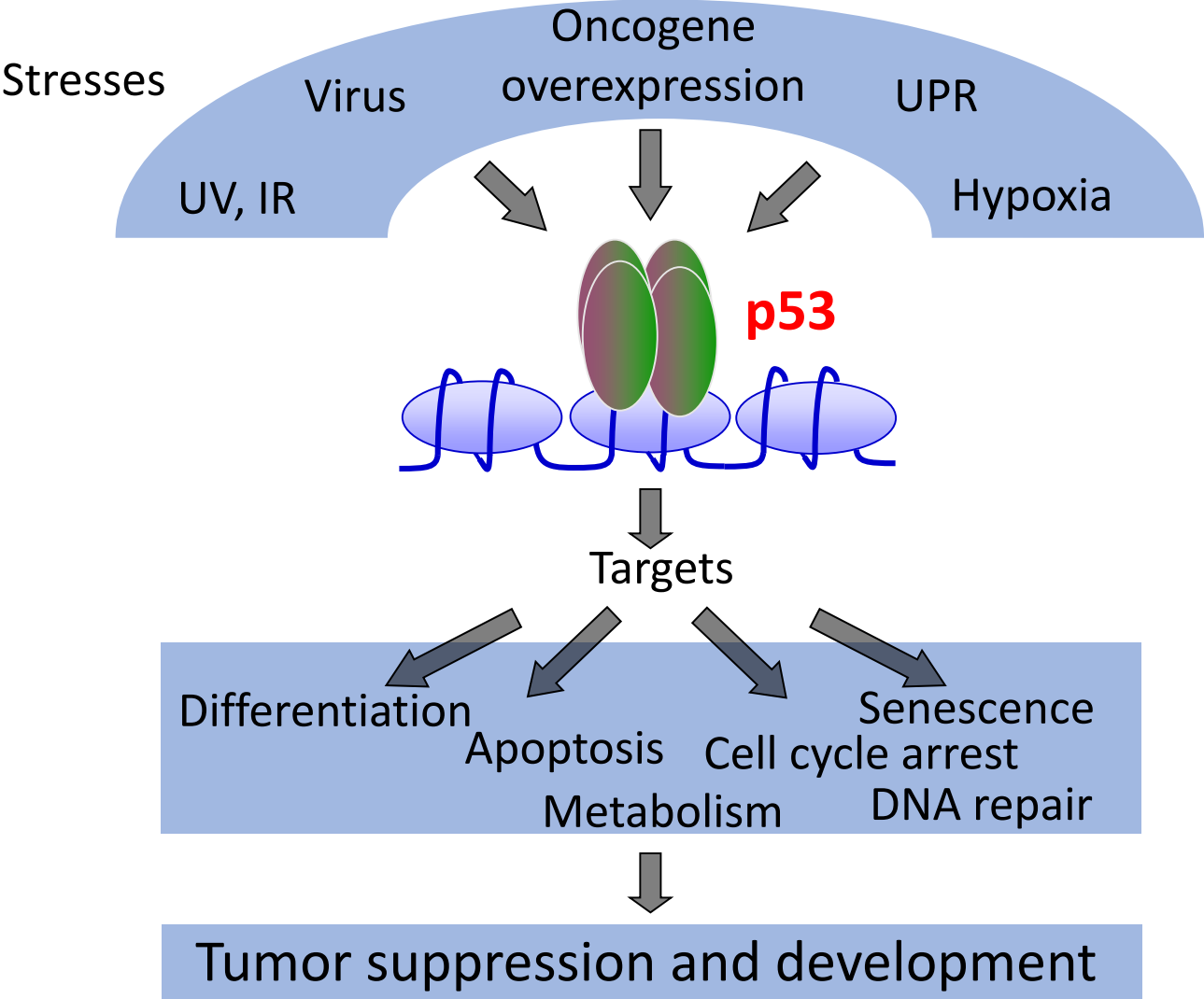
**Poster Number 7**

# Osteosarcoma Is a Devastating Cancer for Children and Young Adults

- Osteosarcoma (OS) is one of the leading causes of cancer-related death in pediatric patients.
- **Challenges of OS treatment**
  - 1) **No FDA-approved targeted therapy.**
  - 2) **Current standard of care is the same as 30 years ago.**
  - 3) **Metastasis decreases 5-year survival to around 25%.**
  - 4) **Current immune checkpoint inhibitors are not effective.**
- Osteosarcoma is included in the Rare Tumor Initiative at CCR in NCI.



# Study p53 in Mesenchymal Stem Cells to Understand Osteosarcoma



# Jennifer C. Jones, MD, PhD

**Center for Cancer Research**

Laboratory of Pathology

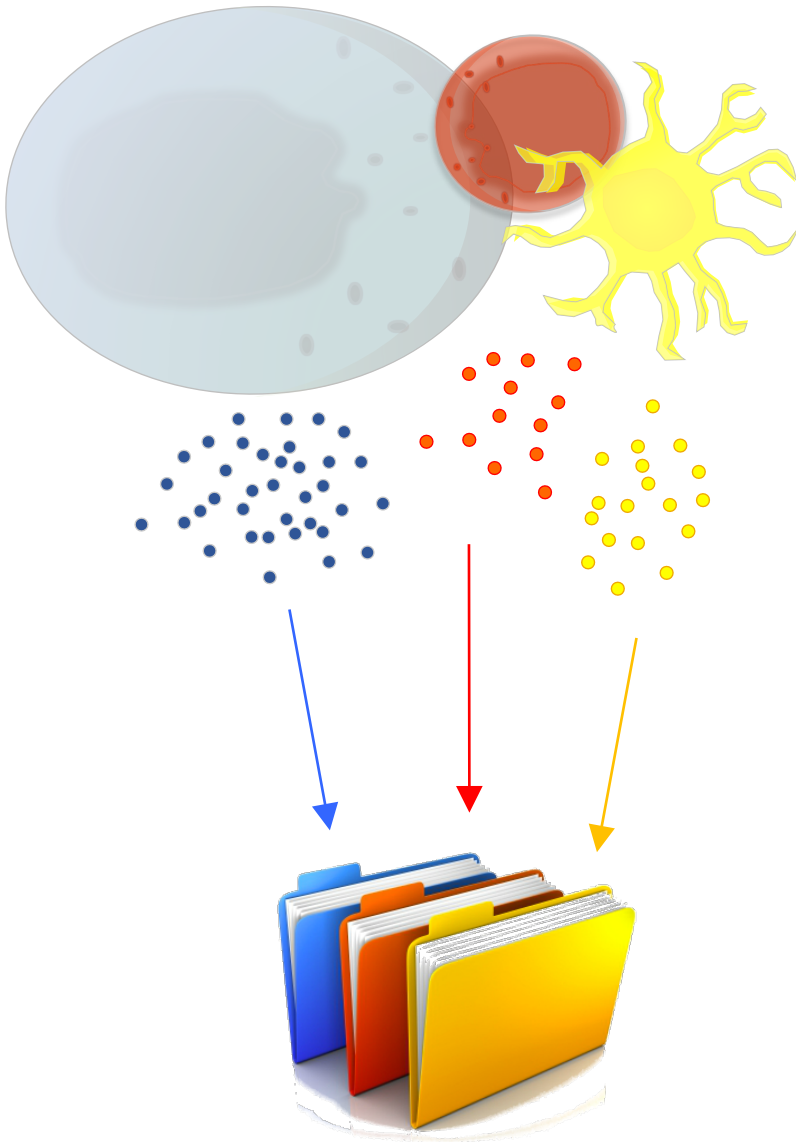
NIH Earl Stadtman Investigator (Pending)

Extracellular Vesicles for Precision Medicine: A New Frontier, New Challenges, and Revolutionary Potential

**Poster Number 8**

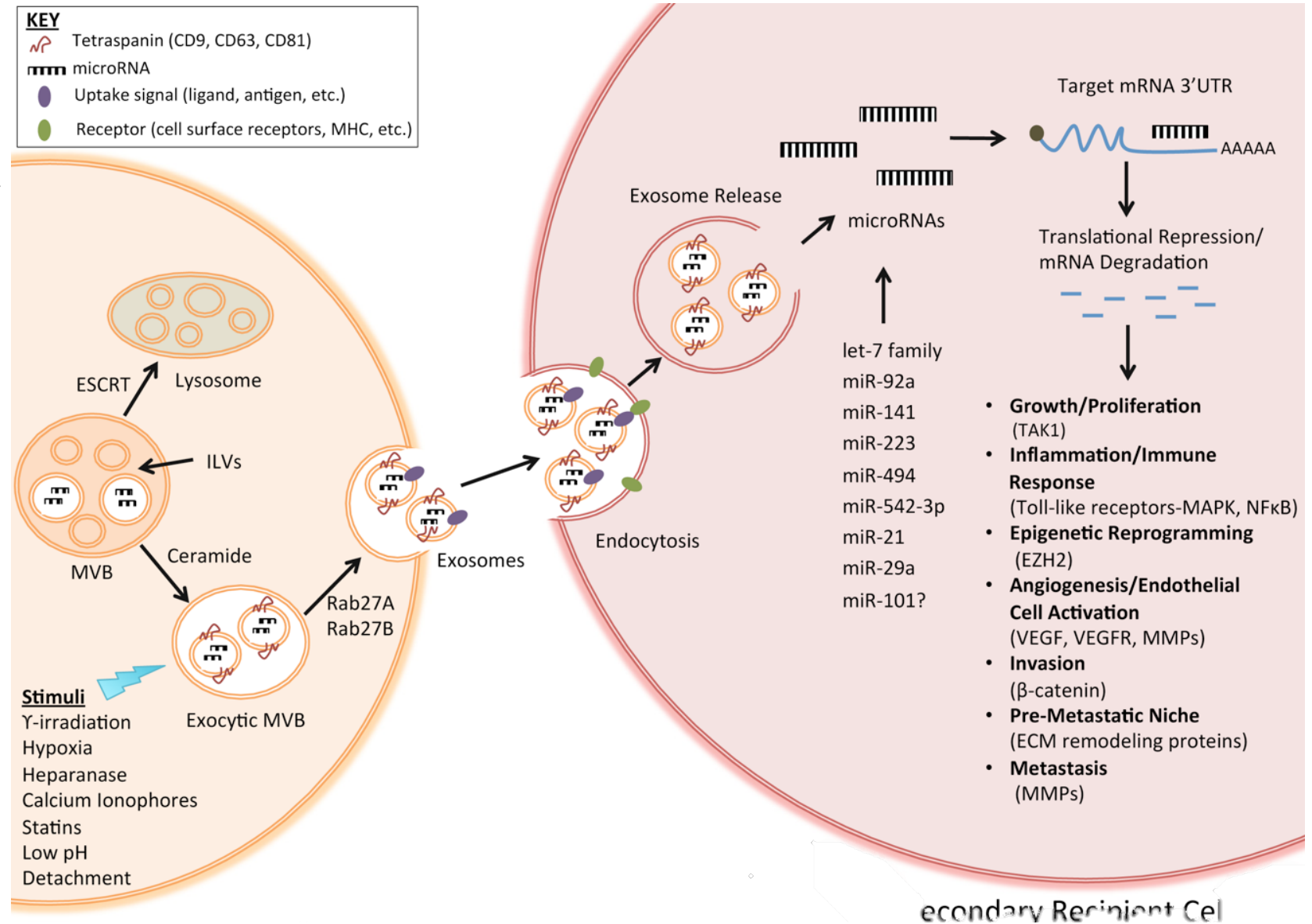


# Extracellular Vesicles (EVs): Multidimensional Packets



**KEY**

	Tetraspanin (CD9, CD63, CD81)
	microRNA
	Uptake signal (ligand, antigen, etc.)
	Receptor (cell surface receptors, MHC, etc.)



# Translational Exosome, EVs Analysis Pipeline



A. Sample

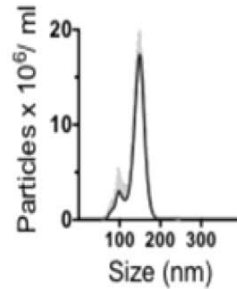


B. Isolation

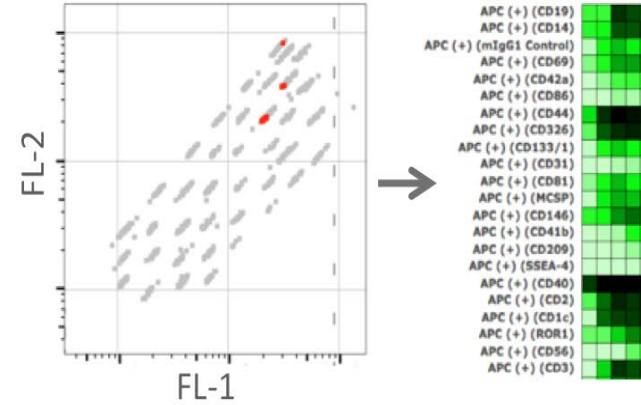


C. General EV Size, Concentration, and Cargo Assays

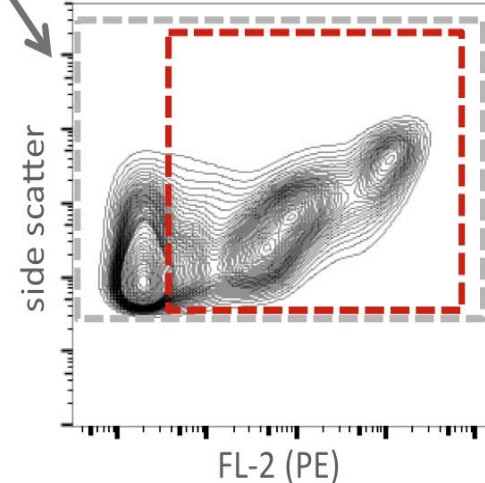
Protein Concentration  
Western Blot (Tsg101, Alix)  
Nanoparticle Tracking Analysis



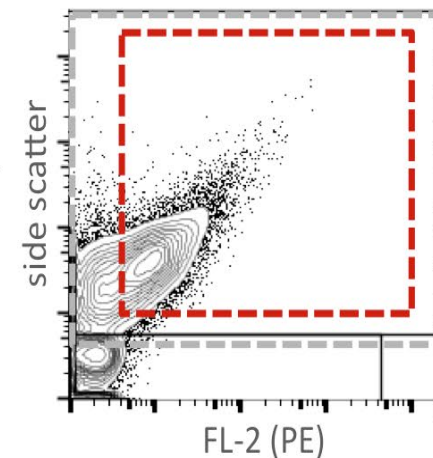
D. Multiplex EV Assay: > 20 Epitope Survey



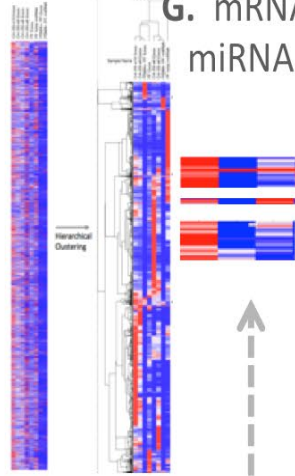
E. High Resolution EV Analysis



F. nanoFACS Sorting



G. mRNA, miRNA



# **Daniel W. McVicar, PhD**

## **Center for Cancer Research**

Deputy Director for Basic Science, Cancer and Inflammation Program

Head, Leukocyte Signaling Section

CCR Deputy Director

Identification of Macrophage Irg-1 as Possible Target in  
Ovarian Cancer

**Poster Number 9**



# Sharon Savage, MD

**Division of Cancer Epidemiology and Genetics**

Chief, Clinical Genetics Branch

Senior Investigator

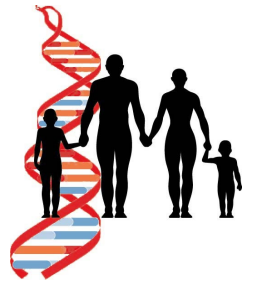
DCEG Clinical Director

Research Opportunities in Clinical Cancer Genetics

**Poster Number 11**

# The Clinical Genetics Branch

“Saving lives & improving quality of life for individuals at increased genetic risk of cancer”



## Discovery in High Risk Individuals

- Clinical
- Genetic
- Epidemiology



## Clinical Translation to Different Populations

- High-Risk Individuals
- General Population



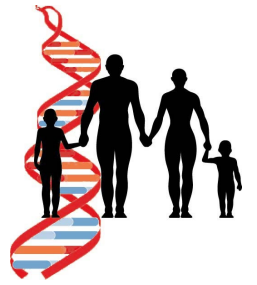
## Direct Application to Clinical Care

- Clinical Care
- Clinical Guidelines

Cross-Cutting Collaborations

# The Clinical Genetics Branch

“Saving lives & improving quality of life for individuals at increased genetic risk of cancer”



## Family Studies

- Inherited Bone Marrow Failure Syndromes
- *DICER1*-related Pleuropulmonary Blastoma Cancer Predisposition Syndrome
- Li-Fraumeni Syndrome
- Familial Testicular Cancer
- Neurofibromatosis Type 1
- Familial Melanoma
- Lymphoproliferative Diseases
- Familial Chordoma
- Psychosocial studies across all syndromes

## Molecular Epidemiology

- Transplant outcomes in aplastic anemia and leukemia
- Pediatric cancer genetic susceptibility
- Upper gastrointestinal malignancies
- Myotonic dystrophy and cancer susceptibility
- Rare tumors
- Viral genomics

[savagesh@mail.nih.gov](mailto:savagesh@mail.nih.gov)

# Allan M. Weissman, MD

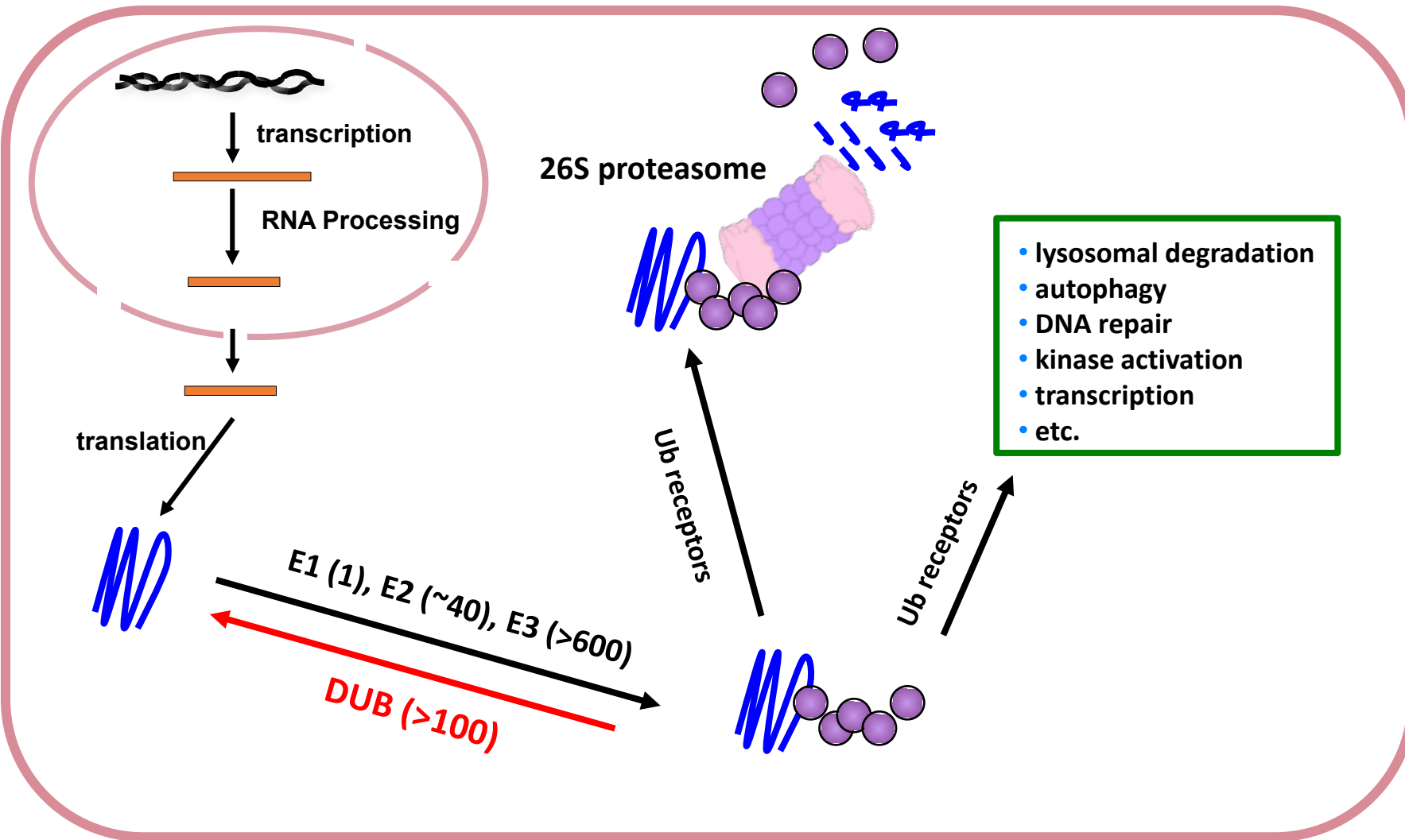
**Center for Cancer Research**

Chief, Laboratory of Protein Dynamics and Signaling  
Senior Investigator

Functions of the Ubiquitin-Proteasome System in Health  
and Disease

**Poster Number 13**

# Ubiquitin-Proteasome System (UPS)



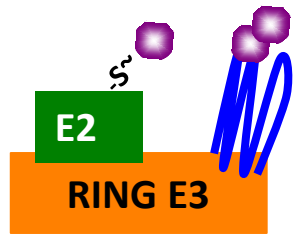
- Tumor suppressors
- Proto-oncogenes
- Cell cycle regulators
- Receptors
- Transporters
- Channels
- Transcription factors
- Kinases
- Histones

**All of the basic UPS components represent potential therapeutic targets!**

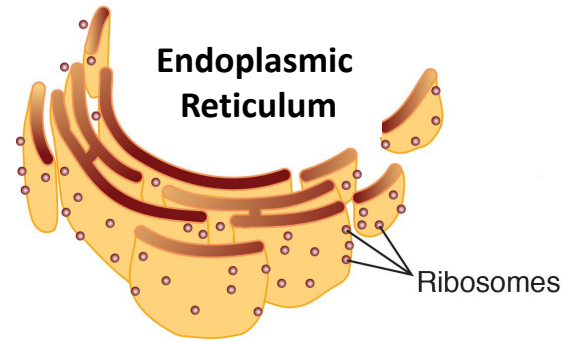
E1: ubiquitin-activating enzyme; E2: ubiquitin-conjugating enzyme; E3: ubiquitin ligase; DUB: deubiquitinating enzyme

# Weissman Lab: Areas of Focus in the Ubiquitin-Proteasome System

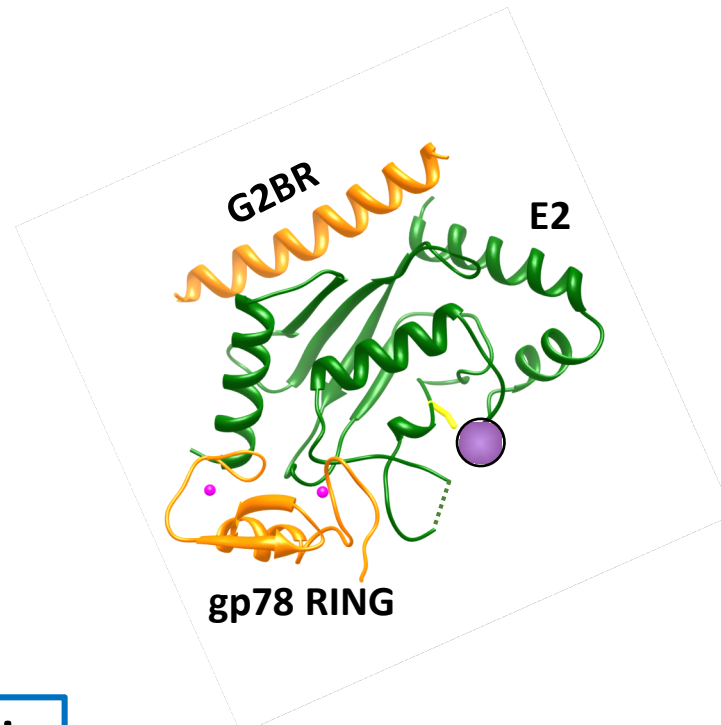
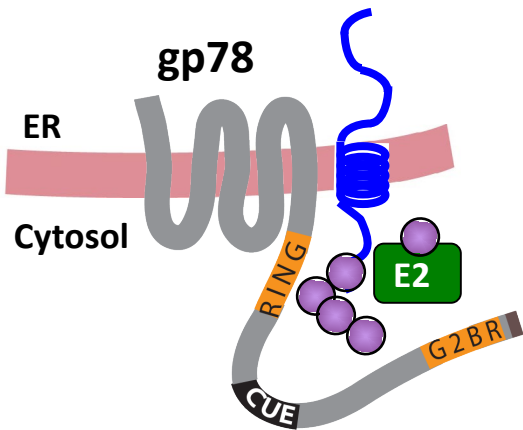
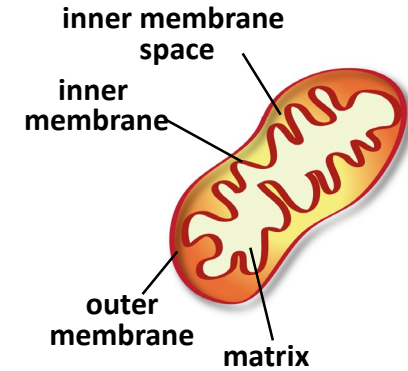
## E2-E3 structure-function relationships



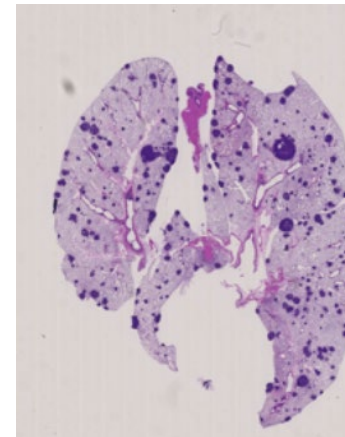
## ER-associated degradation (ERAD)



## Mitochondria-associated degradation (MAD)



## gp78 tg<sup>+</sup> lung with mammary tumor metastasis



## High gp78 levels in breast cancer....

Characteristic	Significance (p value)
Race (Black>White)	.013
Low 3 yr. survival	<.001
Lymph node positive	<.050
Triple negative	<.001

# Nicolas Wentzensen, MD, PhD, MS

**Division of Cancer Epidemiology and Genetics**

Deputy Chief, Clinical Genetics Branch

Senior Investigator

Head, Clinical Epidemiology Unit

Clinical Epidemiology: Translating Etiologic Discoveries  
to Clinical and Public Health Applications

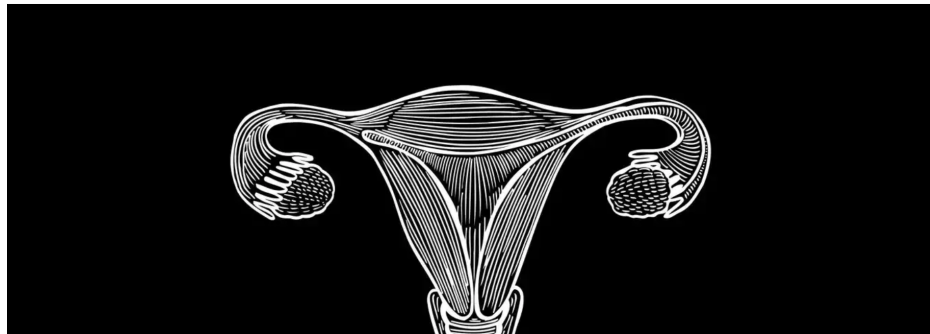
**Poster Number 14**

# Translating evidence to clinical practice

EDITOR'S PICKS **TheJily**   

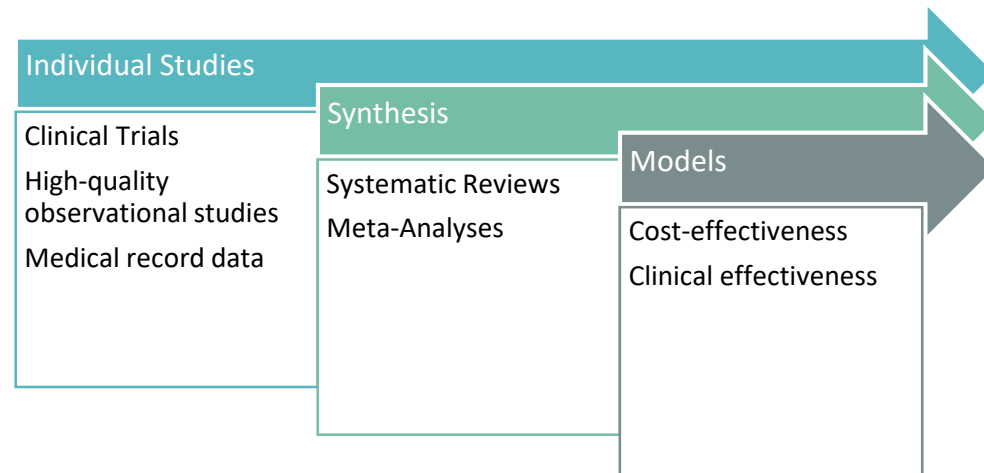
Modified Pap smears could revolutionize cancer screening

Early detection for two deadly gynecologic cancers



- Translating evidence to clinical practice is a long process, most discoveries do not make it
- Careful assessment of clinical implications is necessary before implementation of public health and clinical guidelines
- Areas of work:
  - Biomarker discovery and translation
  - Risk prediction
  - Big data from epidemiologic studies and electronic health records
  - Methods development
  - Development of clinical guidelines

**Identify key questions**



**Implementation**



# A Clinical Epidemiology Framework

Component	Important Considerations
Public health burden	<ul style="list-style-type: none"><li>- Prevalence, incidence and mortality rates and trends</li><li>- Demographics</li></ul>

# **Bríd M. Ryan, PhD, MPH**

**Center for Cancer Research**

Laboratory of Human Carcinogenesis

Investigator

NIH Earl Stadtman Investigator

**Integrative and Translational Epidemiological Studies of  
Lung Cancer Health Disparities**