

# Integrating Science to Health



## Laboratory Research

- ~110 faculty, ~350 postdocs
- 737 publications in 2009
- \$97.2 million in grants



## Clinical Research

- 214,509 outpatient visits
- 2,754 inpatient admissions
- 402 active clinical trials

Michael A. Dyer, Ph.D.

# Integrating Science to Health



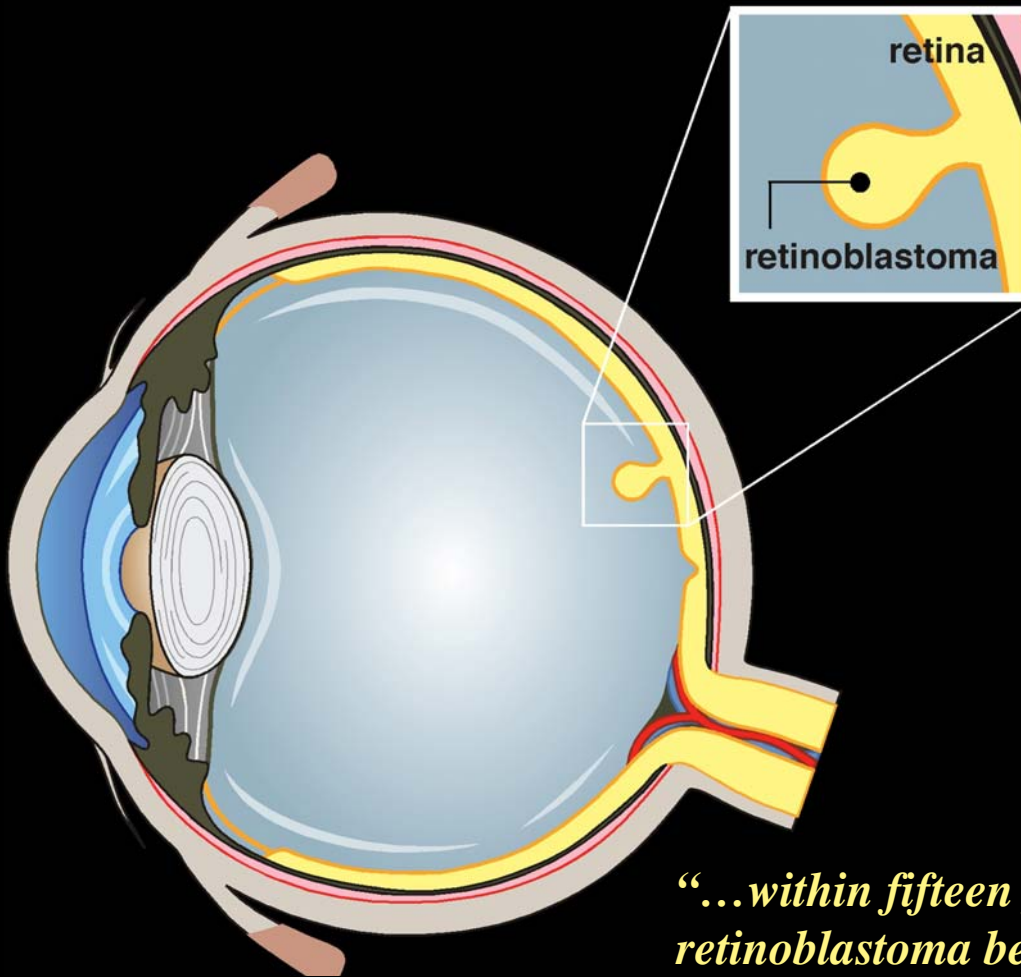
## Education and Outreach

- All discoveries and data made freely available to public
- Results from clinical trials become standard of care around the world
- Educate public about childhood cancer

Michael A. Dyer PhD SDB Education Symposium August 6. 2010 Albuquerque, NM



# Retinoblastoma is the 3rd Most Common Form of Cancer in Infants



- ~5,000 cases/year Worldwide
- 100% Fatal if Untreated
- 10% Survival for Metastatic RBL
- Developmental Tumor
- First Tumor Suppressor Gene

*“...within fifteen years, at the outside, we’ll be able to stop retinoblastoma before it begins. I’m so sure of that that I’ve already given the drug a name. I call it retino-revert.”*

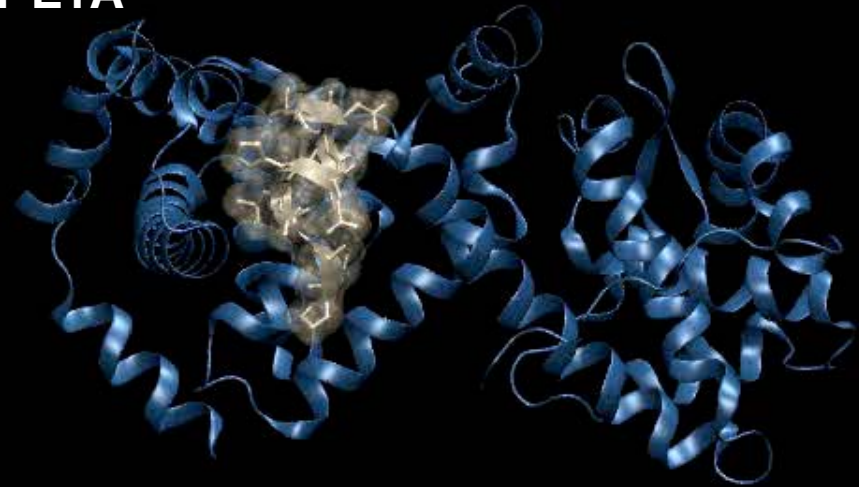
**Dr. David Abramson, 1986**

# 24 years Later: Bridging the Gap Between Clinical & Laboratory Research



*Dr. Matthew Wilson*

**RB1-E1A**



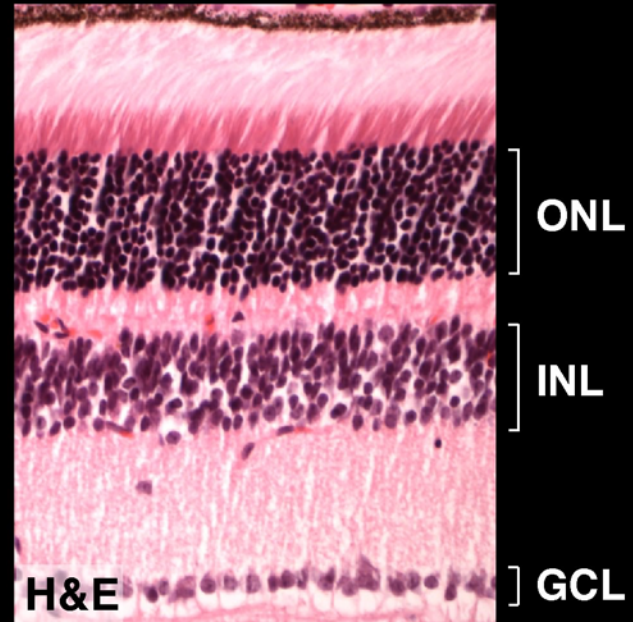
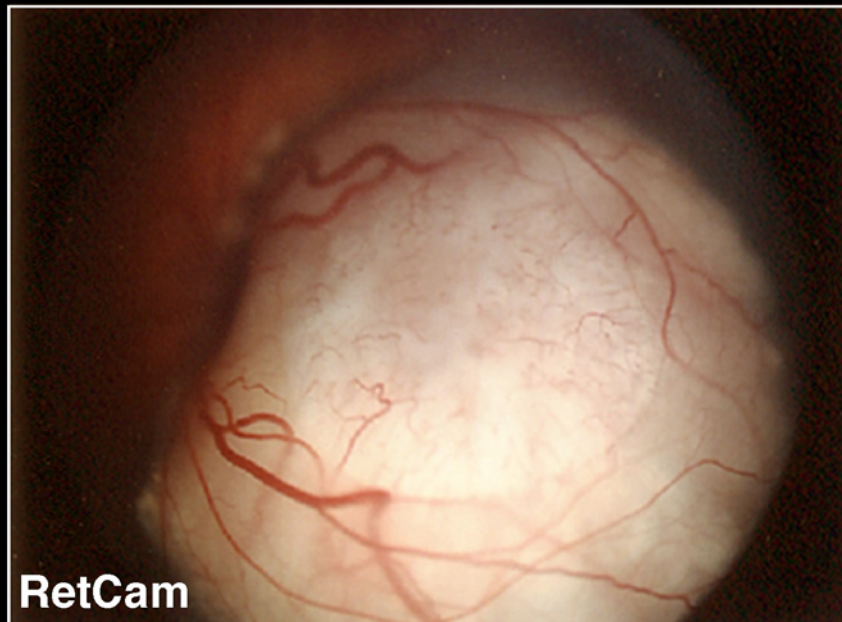
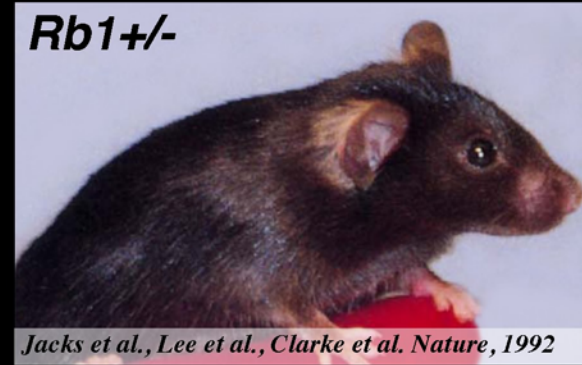
## **CLINICAL RESEARCH**

- radiation
- chemotherapy
- surgery
- focal therapy

## **LABORATORY RESEARCH**

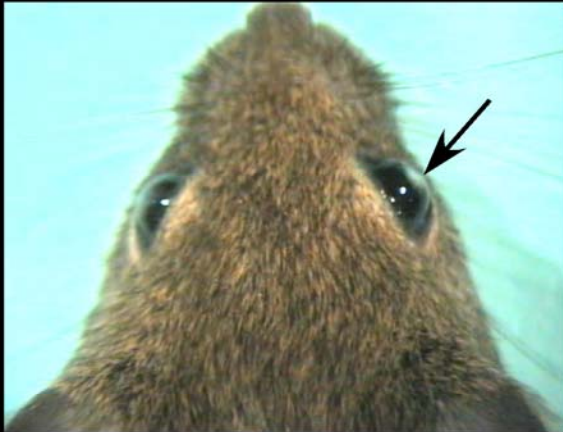
- 2-hit hypothesis
- 1<sup>st</sup> tumor suppressor
- knockout mice
- pathway analysis

# ***RB1* Gene Inactivation Leads to Retinoblastoma in Humans but not Mice**



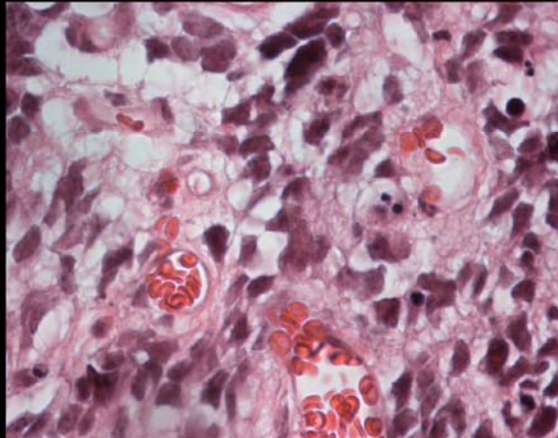


# The First Knockout Mouse Model of Retinoblastoma



2004: Zhang et al. The First Knockout Mouse Model of Retinoblastoma. (*Cell Cycle*)

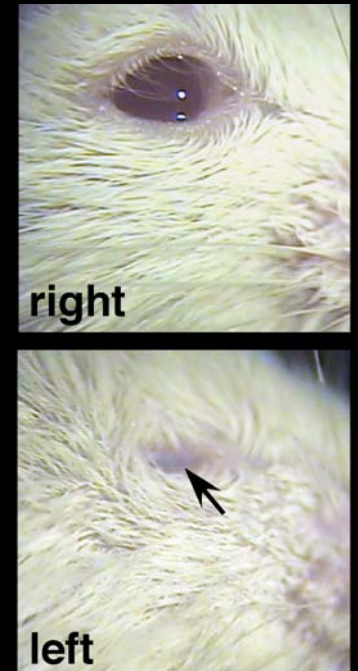
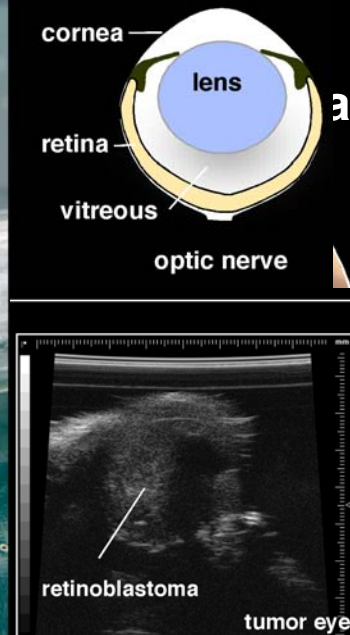
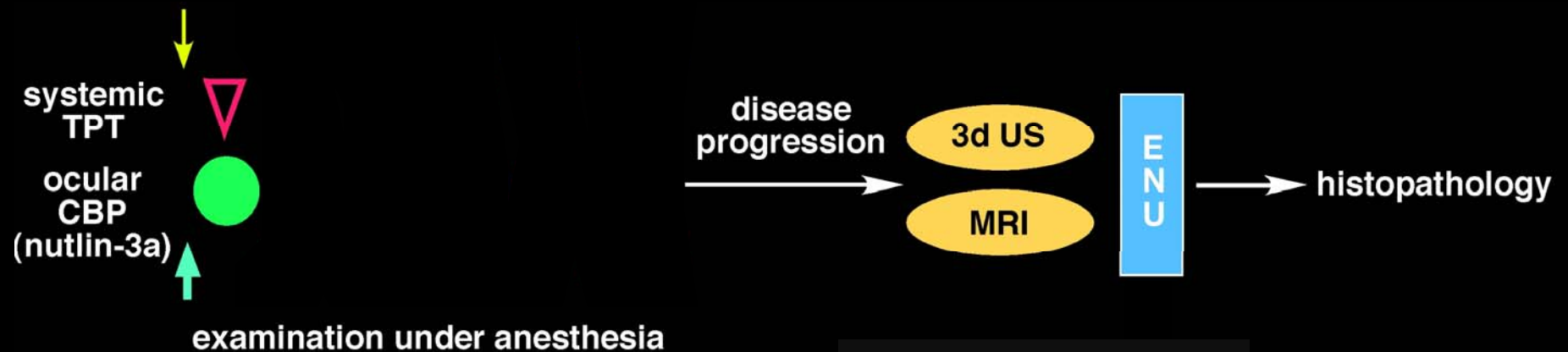
2004: MacPherson et al. Cell Type Specific Effect of Rb Deletion in the Murine Retina. (*Genes & Development*)



2004: Chen et al. Cell Specific Effects of Rb or Rb/p107 Loss On Retinal Development. (*Cancer Cell*)

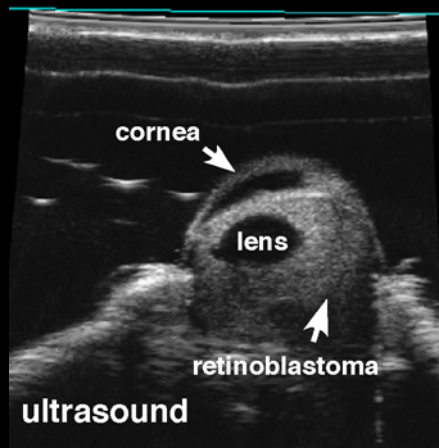
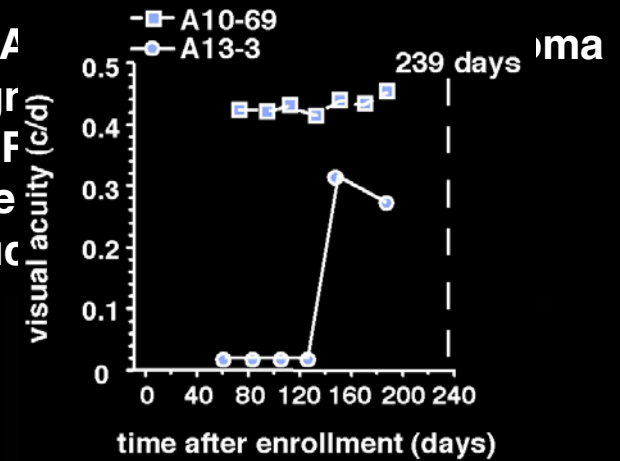
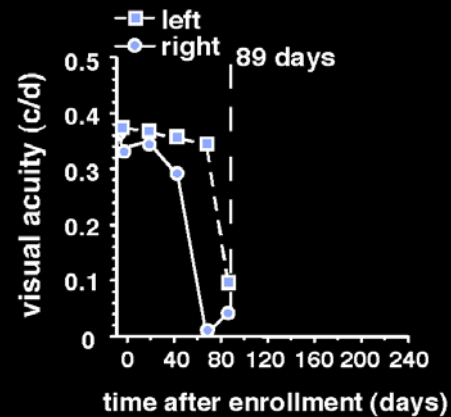
2006: Donovan et al. Compensation By Tumor Suppressor Genes During Retinal Development. (*BMC Biology*)

# Retinoblastoma Preclinical Trial with 212 Mice Enrolled to Date on 3 Trials

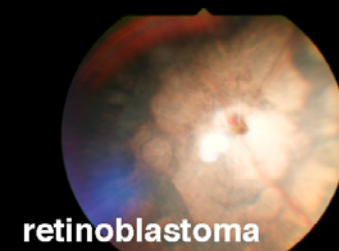
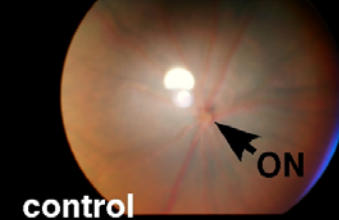


# TPT/CBP Response in Humans and Mice

Diagnosis: A  
Age at Diagn: 69  
Treatment: F  
Current Age: 133  
Vision: Enucleated



retinal camera



Left

Representative example from ongoing study: DSMB Approved 11/17/09



# Retinoblastoma Translational Research Team

## Chemical Biology

Drs. Kip Guy, Anang Shelat, David Smithson,  
Fangyi Zhu, Ying Shen

## Structural Biology

Drs. Brenda Schulman, Don Bashford, Tony Ferreira  
and Richard Kriwacki  
**Dr. Wuyuan Lu**

## Pharmacology and Toxicity

Drs. Clinton Stewart and Michael Tagen  
**Dr. Henry Edelhauser**

## Pathology and Toxicity

Drs. David Ellison and Matt Wilson

## Diagnostic Imaging

Drs. Robert Ogg and Beth McCarville

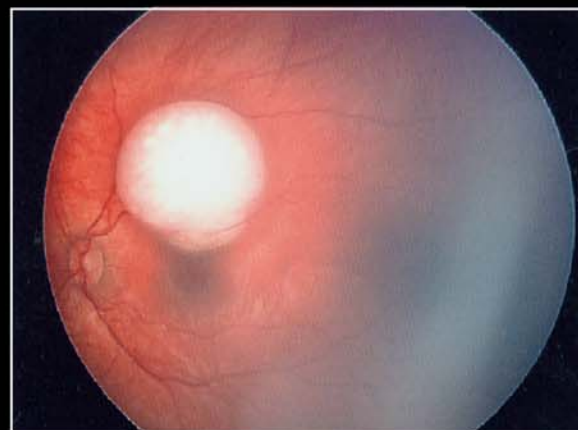
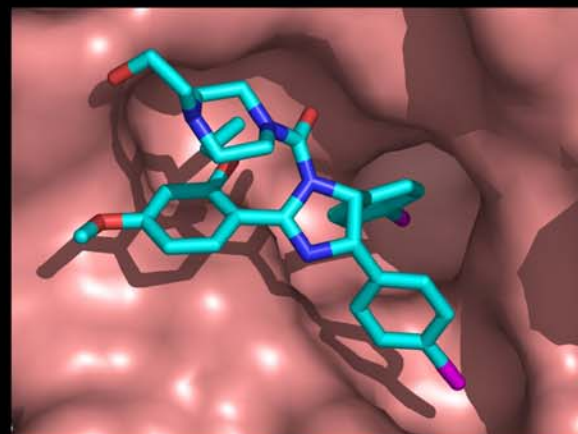
## Neurobiology and Cancer Biology

Dr. Dianna Johnson  
**Drs. Connie Cepko, Karen Vousden, Aart Jochemsen**

## Patient Care and Clinical Trials

Drs. Matthew Wilson, Carlos Rodriguez-Galindo, Barrett Haik  
**Dr. David Abramson**

## From Bench to Bedside



# Missed Opportunities in Translational Research

**The New York Times**  
*Sunday, June 27<sup>th</sup>, 2009*

Grant System Leads Cancer Researchers to Play it Safe



“The cancer institute has spent \$105 billion since President Nixon declared war on the disease in 1971.

Yet the fight against cancer is going slower than most had hoped.”

**We need to build interdisciplinary teams made up of doctors and researchers to efficiently translate research discoveries into new treatments for childhood cancer.**



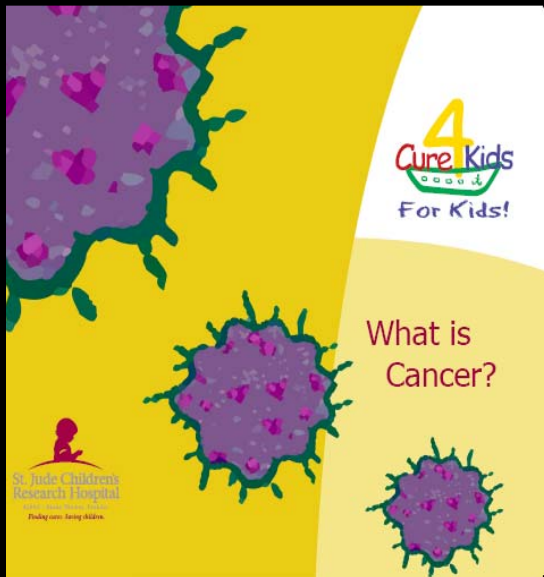
# St. Jude Cancer Education Outreach Program (“Cure4Kids for Kids”)



- Started in 2006 as part of Comprehensive Cancer Center outreach initiative
- Housed in International Outreach Program
- School-based education program
- Educate students, parents, teachers about:
  - Cancer and dispel misconceptions
  - Healthy living practices to reduce the risk of cancer in adulthood
  - Inspire science and health-related careers

# Accomplishments

- 1,800 students
- 150 teachers
- 20+ St. Jude departments
- 3 experts developed children's books





# Format



- St. Jude experts visit local schools
- Give interactive, engaging presentations
- Lead hands-on, discovery-based activities

# Career Talks at Local Schools

- Highlight Careers
  - Clinical care
  - Basic science
  - Computing
  - Administration
  - Writing
  - Etc.





# Career and Research Day

- Hosted in conjunction with St. Jude Postdoctoral Association
- 20 students and 2 teachers from local high schools visit campus
  - “Career tour”
  - Mentoring luncheon
  - Hands-on lab experiment in GFP genotyping and electrophoresis



# Teacher Training

- Three events in 2 years for local teachers
- St. Jude doctors, scientists, teachers participated as presenters
- Website with teacher



Cure4Kids for Kids  
Professional Development Conference  
June 8, 2010 Memphis, TN



Cure4Kids for Kids Teacher  
Summit April 2010

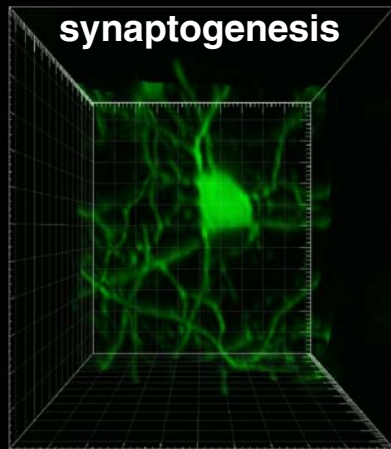
# Educational Website



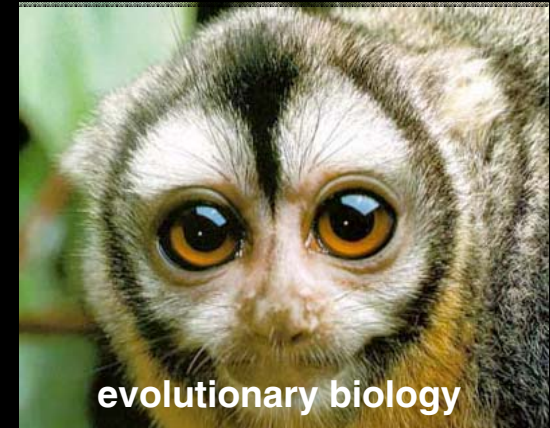
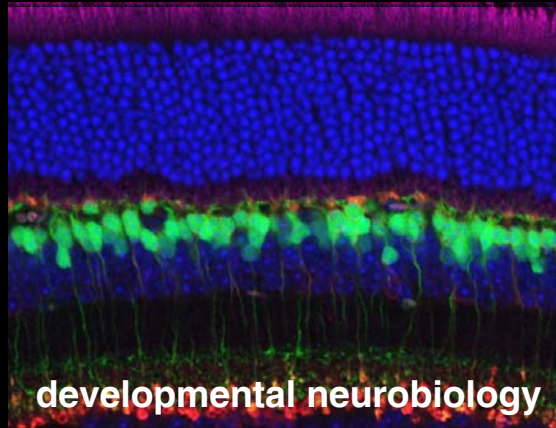
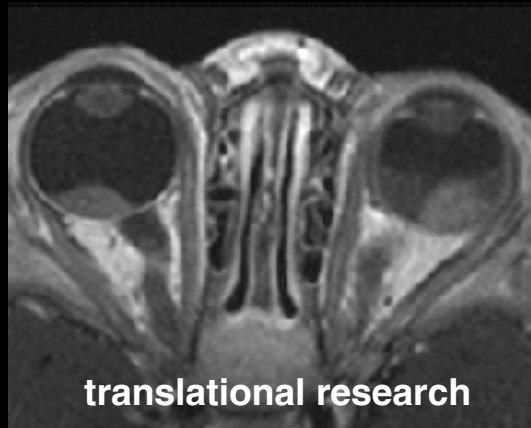
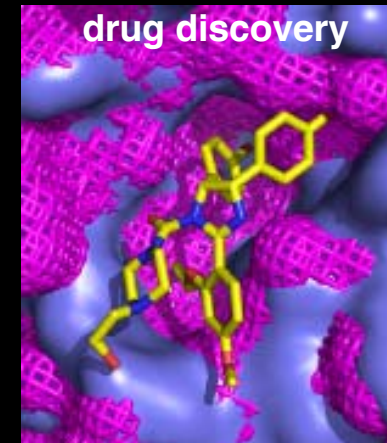
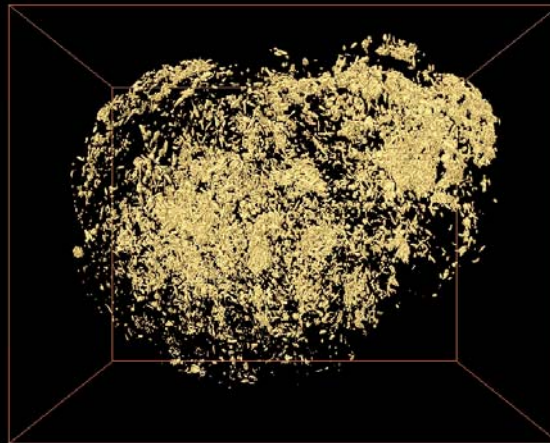
- Electronic access to education materials
- (eg. books, glossary, etc.)
- Extends classroom, increases access and reach
- “Experts” section profiling experts and careers
- [www.Cure4Kids.org/kids](http://www.Cure4Kids.org/kids)



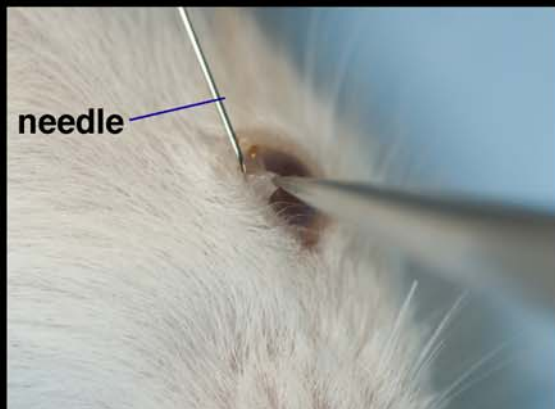
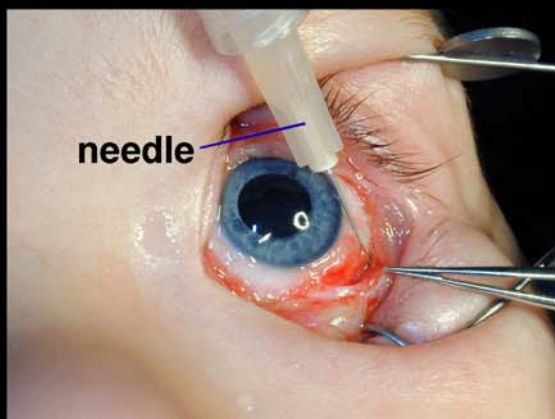
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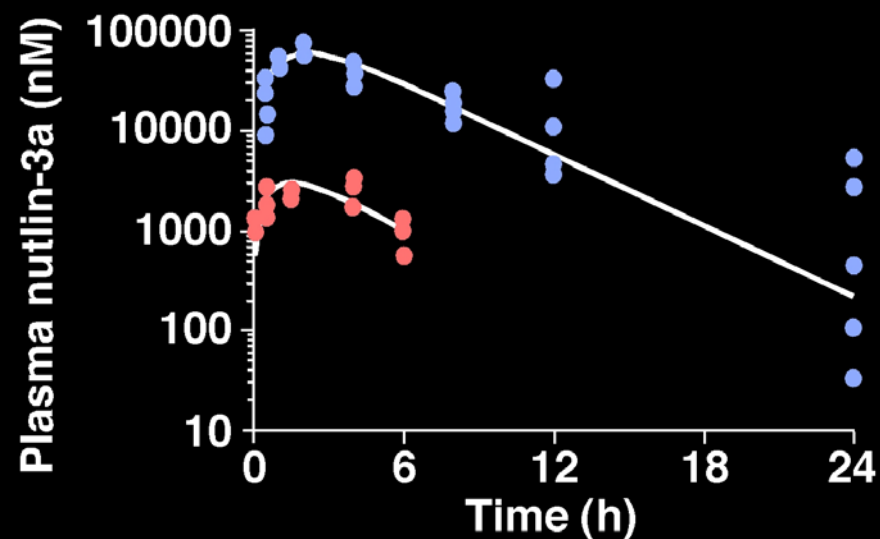
**stem/iPS cells & reprogramming**



# Pharmacokinetics of an Ocular Formulation of Nutlin-3a



*oral (200 mg/kg)*  
*subconjunctival (25 mM)*



Ocular Formulation of Nutlin-3a  
15% polypropylene glycol  
10% propylene glycol  
5% Cremophor EL  
in PBS



# Identification and Characterization of the First MDMX Inhibitor



296,488

4,363

1,152



13 Chemotypes

*Damon Reed, Ying Shen and Kip Guy*

