

# The National Eye Institute: Patient Safety at the CC— Right Path?

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Clinical Center Research Hospital Board

July 20, 2018

Elizabeth Wendell, BSN, MS

Brian P. Brooks, MD, PhD

# Outline

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- Overview of the NEI Clinical Research Program
  - Organization
  - Research
- PDS Closure and the NEI
- Creating an environment of efficiency and safety

# Mission Statement

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Conduct high-quality research on the pathogenesis and treatment of blinding diseases in adults and children, while providing expert clinical care in a safe environment.

# The Clinical Milieu

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- Almost exclusively outpatient
- >9000 visits per year
- Close to 3000 of visits are consultations from other ICs
  - Clinical Care
  - Research collaboration
- Relatively light use of central CC resources (radiology, laboratory, etc.)



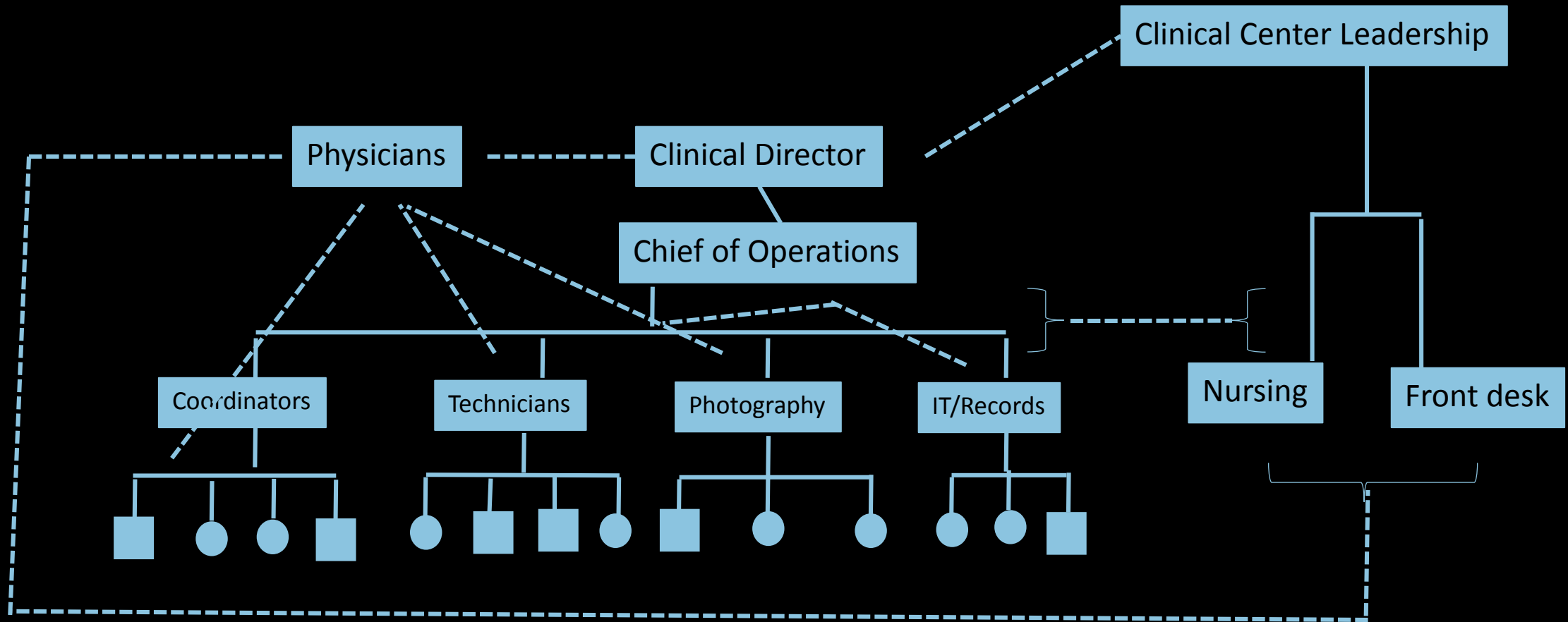
# Who We Are...

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- Six principal investigators (tenure track + tenured)
  - Two new Lasker Scholars
- Seven staff clinicians, one staff scientist
- Major research areas
  - Medical retina
  - Ocular immunology
  - Ophthalmic genetics



# A Matrix Organization



# A Matrix Organization

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- Advantages
  - Allows nimble management of limited resources across multiple investigators in real time
  - Allows for functional redundancy
  - Allows for sub-specialization of support staff
- Disadvantages
  - “Fragmentation of authority and responsibility for clinical operations” as cited as a potential pitfall by the Red Team
  - NEI solutions to this: Betsy Wendell will cover

# Monitoring and Regulatory Affairs

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- Two opportunities for improvement cited in Red Team Report
  - “Insufficient expertise in regulatory affairs”
  - “Insufficient regular monitoring and metrics”
- EMMES Contract Research Organization
  - Relationship established by Scott Whitcup, MD, previous Clinical Director
  - Protocols assigned appropriate levels of regulatory guidance and monitoring at time of scientific review
  - NEI-wide “Activation Meeting” for all intervention protocols; CC staff invited, participate
  - Clinical Center nursing invited to monitoring visits
- Data Safety and Monitoring
  - External DSMB for monitoring “large” interventional trials
  - Internal SAE Review Committee for quarterly group review of NEI SAEs



# Outline

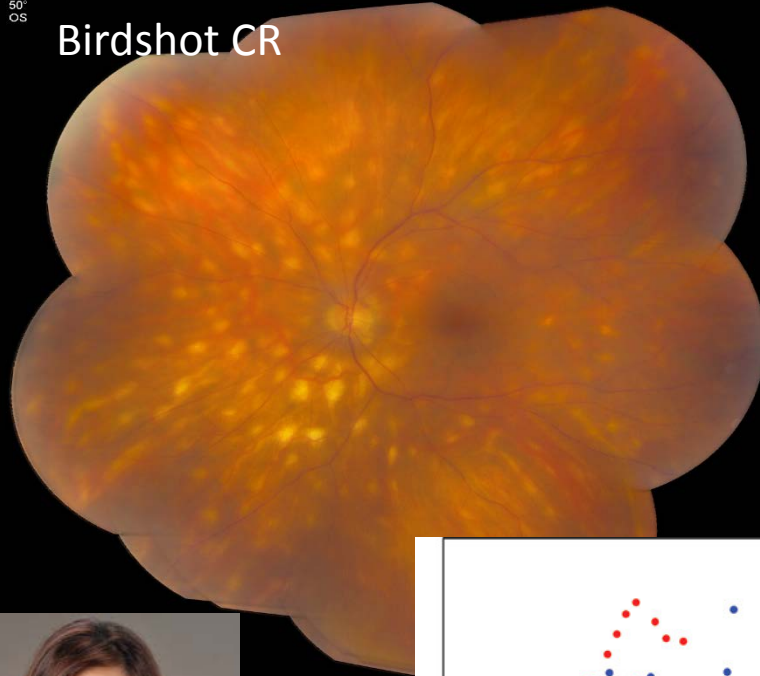
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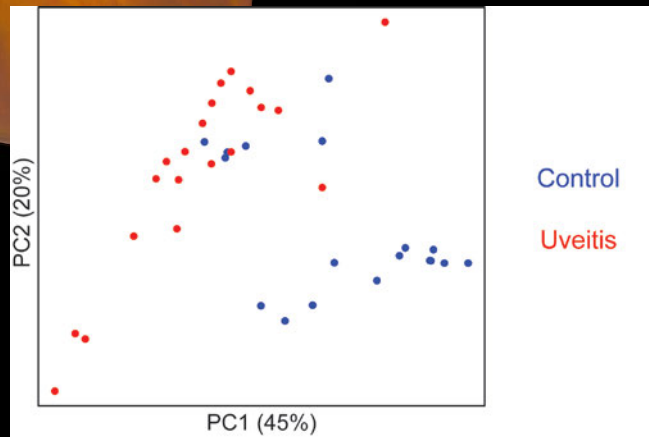
# Human Microbiome In Uveitis

50°  
OS

Birdshot CR



H. Nida Sen, MD

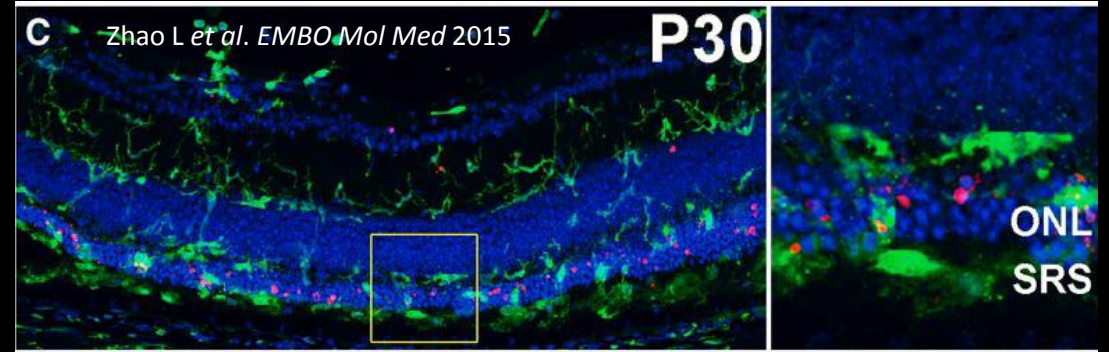


- The pathogenesis of most forms of non-infectious uveitis remains a mystery
- Role for microbiome
  - Pathogenesis of autoinflammatory disorders (e.g., rheumatoid arthritis)
  - Data from animal models

*Scatter plot showing a difference in the microbiome of Controls vs. Patients with Uveitis*

# Phase I/II study of oral minocycline in the treatment of GA associated with AMD

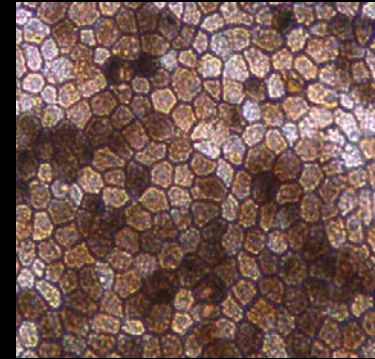
- Geographic atrophy (GA)
  - Leading cause of untreatable blindness in the developed world
  - Immune cells (microglia) implicated in pathogenesis
- Microglial activation modified by minocycline
  - Translation directly from Wong lab's work showing microglial activation worsens retina degeneration
- Repurposes an approved oral medication
  - Unlikely to have been pursued by Pharma



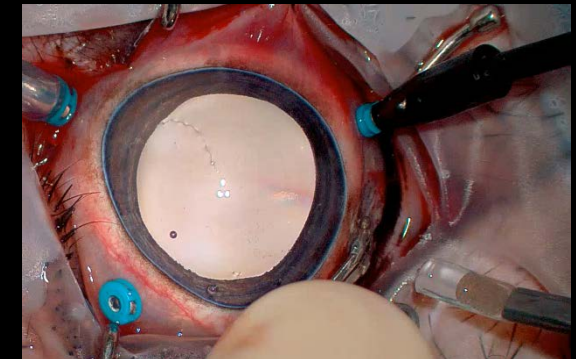
Wai T. Wong MD PhD  
UNGIRD (PI)

# iPS cell-derived RPE for AMD

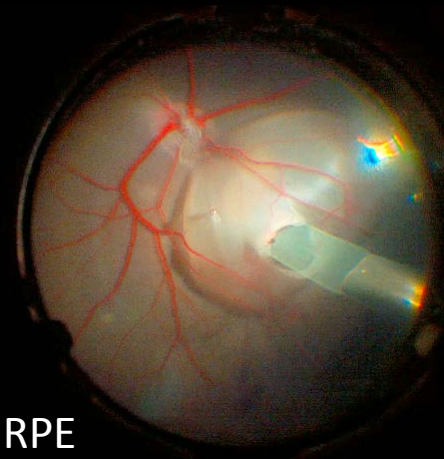
- Authentic, autologous retinal pigment epithelium (RPE) derived from induced pluripotent stem cells (iPSCs)
- Developed transplantation technique in house
- IND Submission September 2018
- Made possible by CC Cell Processing Unit
  - David Stroncek, MD and Harvey Klein, MD



RPE cells



Pig eye surgery



Insertion of RPE  
under the retina



*Kapil Bharti, PhD*

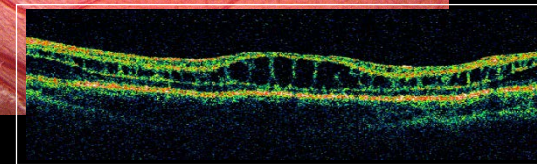
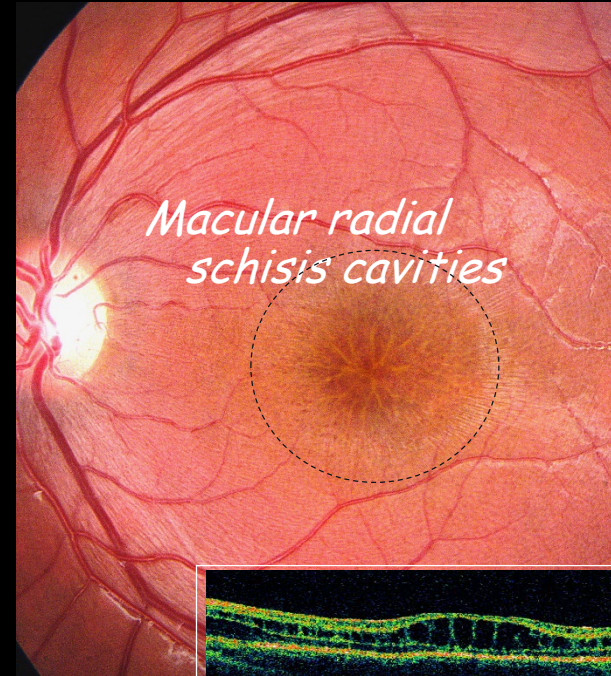


*Henry Wiley, MD*

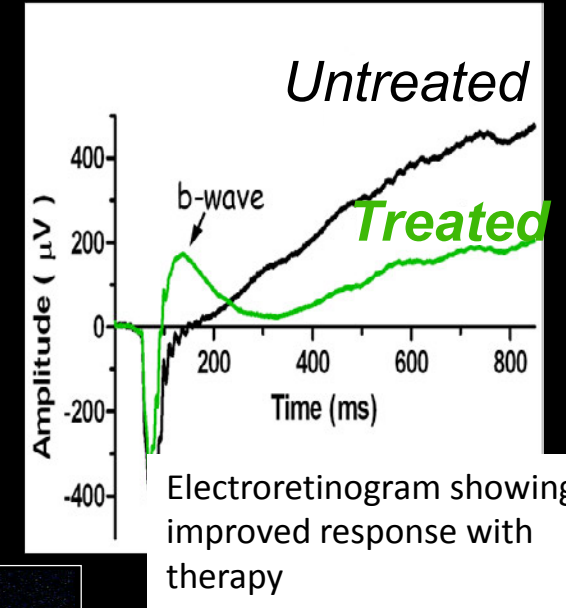


# X-linked retinoschisis (XLRS) gene replacement therapy

- Affected boys develop schisis cavities in the neural retina
  - Acuity ~20/50-20/200
  - Macular atrophy by middle age
- scAAV8-hRS1/IRBP-hRS1 clinical vector
  - Preclinical efficacy in mouse model
  - Intravitreal injection
  - Phase I/IIa dose escalation



*Optical Coherence Tomography*

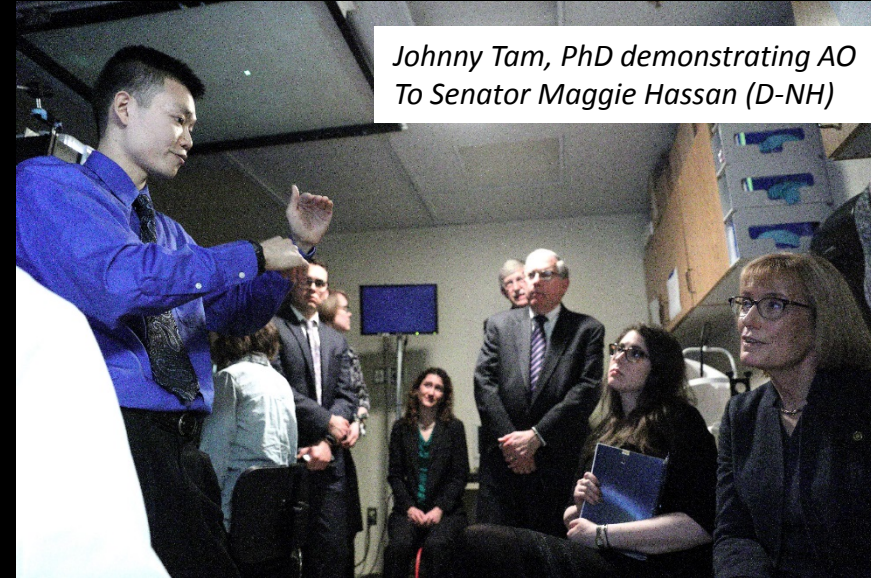


*Catherine A Cukras, MD, PhD*

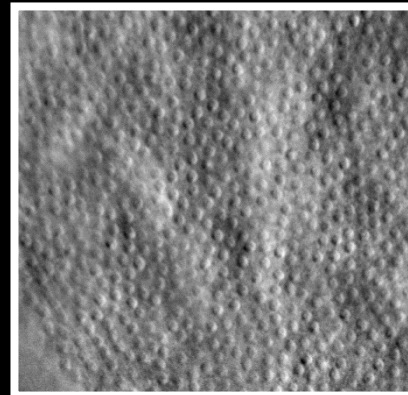
# Adaptive optics

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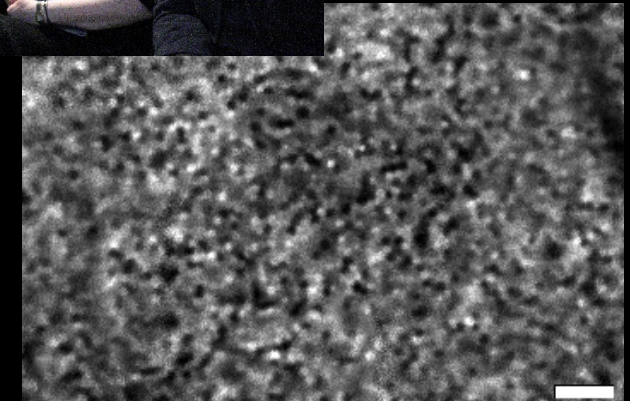
- Allows for imaging of individual cells (rods, cones, RPE) in the living human subject
  - Longitudinal
  - Health and disease
- Clinical outcome variable at cellular resolution
- Understanding pathogenesis of disease (structure + function)



Cone  
photoreceptors



RPE imaged after ICG injection





# Effects of the PDS Closure on NEI Clinical Research

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- Randomized placebo-controlled study of minocycline for geographic atrophy (AMD)
  - No placebo
  - Protocol redesigned to be open-label with run-in following the natural growth of GA
  - Delay 11 months to initiation

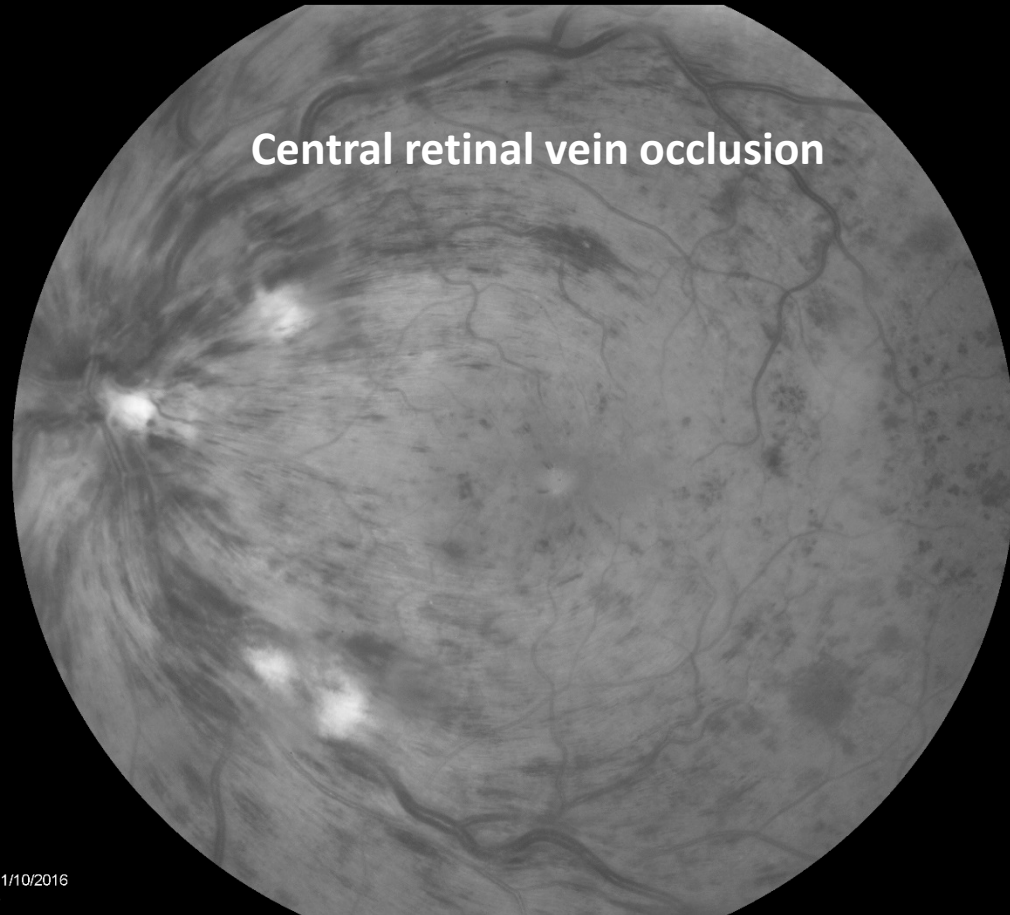
50°  
OD



6/27/2018  
13

# Effects of PDS Closure on NEI Clinical Research

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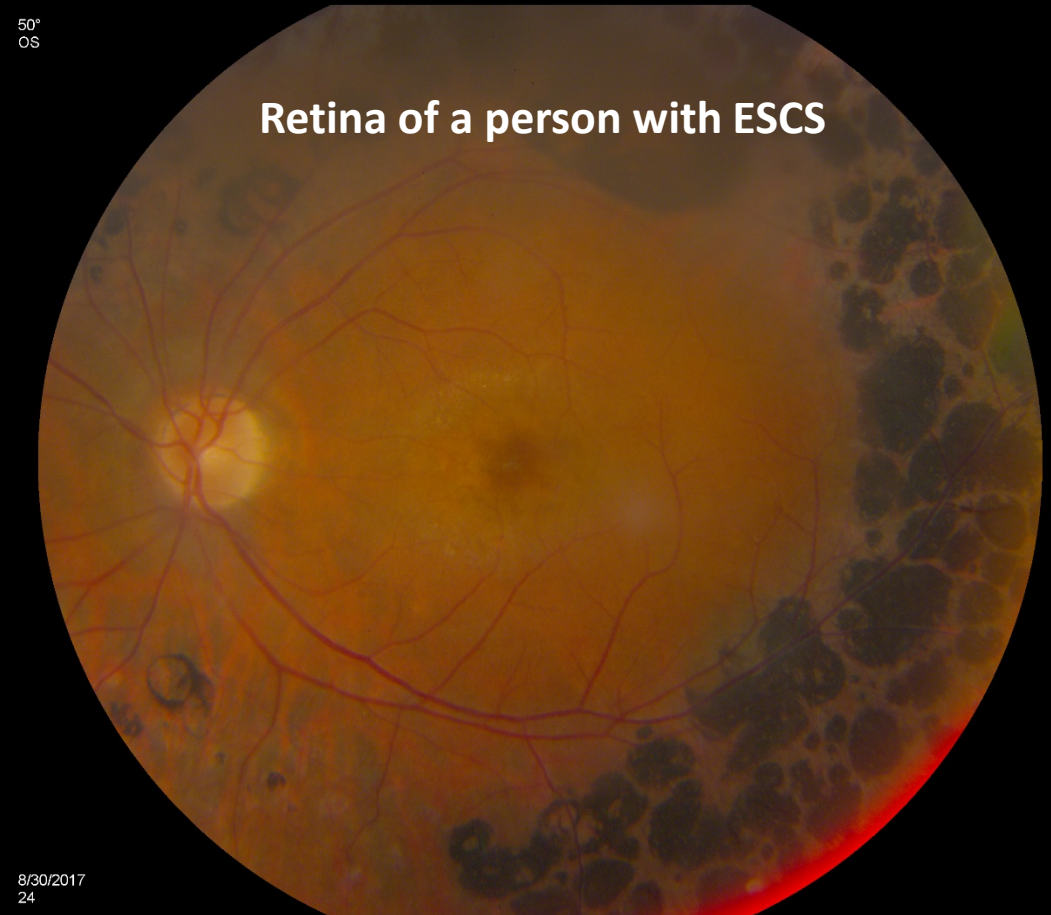
- Randomized, placebo-controlled clinical trial of minocycline in branch- and central retinal vein occlusion
  - No placebo
  - These are acute events, no option for a run-in phase, followed by open label treatment
  - Required outsourcing of placebo from 3<sup>rd</sup> party
  - Delay > 2 years
  - Extra IC cost of >\$30K



# Effects of PDS Closure on NEI Clinical Research

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- Gamma-interferon for macular edema in enhanced S-cone syndrome (ESCS)
  - Aliquoting investigational product into dropperettes
  - Difficulties in having a workable beyond-use-date
  - Outsourcing cost-prohibitive
  - Study suspended indefinitely



# Effects of PDS Closure on NEI Clinical Research

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- Likely several projects never pursued because no clear path forward without a viable PDS
  - Effect on morale
- The Good News
  - Leadership of Dr. Majid Tanas, greatly improved communication
  - Monthly operations meeting between pharmacy staff and the NEI staff, CRO
- A path forward?
  - If one service previously offered by the PDS could be restarted, having the ability to create a matched oral placebo in house would be a tremendous positive step for the NEI clinical research program

# Creating an environment of efficiency and safety

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Elizabeth (Betsy) Wendell, BSN, MS

# Clinical Operations Planning Meeting

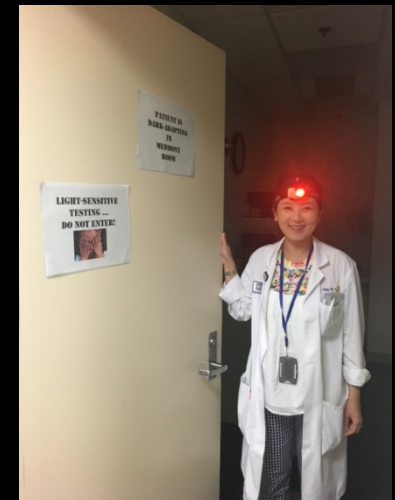
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- Established and overseen by William O'Donnell, Chief, Clinical Operations
- Weekly meetings to evaluate the clinical and research activities within the OP 10 and Op 11 clinics.
- Interdisciplinary membership represent all facets of the Institute and Clinical Center
- Goals
  - Escalate quality and safety concerns quickly
  - Communication across disciplines
  - Check-in with each discipline
  - Facilitates group decision making
  - Forum for rapid cycle change
  - Build consensus surrounding mission

Management  
Support for Patient  
Safety



2017 Culture of  
Safety Survey



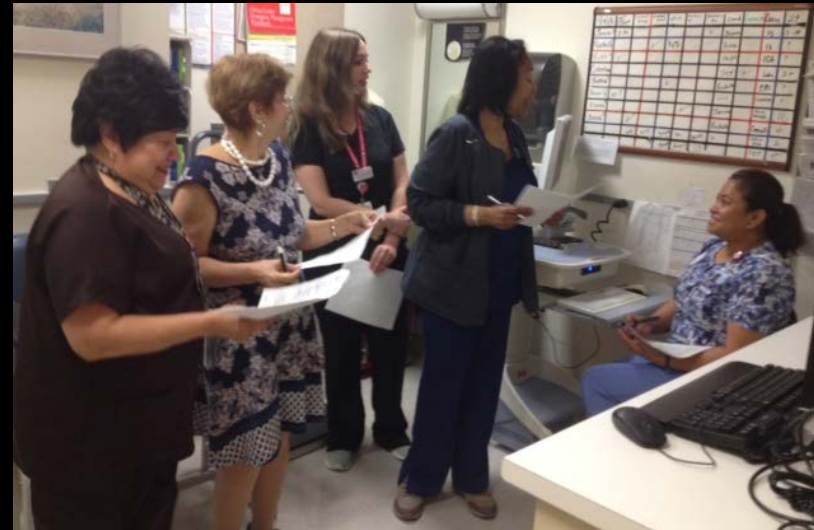
Xueyang (Sharon) Yin, COA  
Entering room to perform ERG

# Daily Nursing Huddles

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- Daily nursing huddles focused on daily clinical and research activities

- Staff led
- Review plan for high risk patients
- Resource utilization
- Just in time education
- Announcements
- Morale



OP10 Nursing Team discussing at huddle

- Safety and quality concerns with the goal of quick escalation.

# Mini-360 : The Reasons Why...

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- Perceived by senior NEI OCD leadership. Developed and implemented by Dr. Elizabeth C. Murphy Dep. Chief, Clinical Operations
- Knowledge is power
- Hard data are the starting point for recognizing strengths and weaknesses
- Knowledge and self-awareness are themselves sometimes agents of positive change
- Provides a metric for tracking progress
- The processes of both can be modified based on experience
- Nursing experience

# Mini-360 continued...

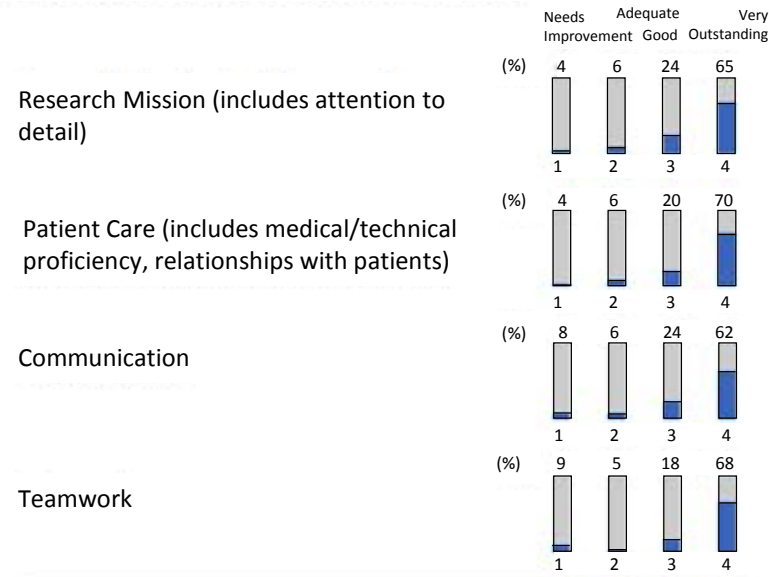
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- Dropdown menu of personnel
- Four axes
  - Research mission (includes attention to detail)
  - Patient care (includes medical/technical proficiencies, relationships with patients)
  - Communications
  - Teamwork
- Four “grades”: Outstanding, Very Good, Adequate, Needs Improvement
- Free text

# Results

- Total 650 responses

2. Rate the individual on a scale of Needs Improvement, Adequate, Very Good, or Outstanding in the following areas. Please provide details in Comments for any area rated "Needs Improvement".



Total: 650



# Thoughts

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- This was an experiment
- Provides baseline
- Single negative comments should be taken as simply that; patterns are more important
- Plan
  - Repeat around Thanksgiving with closure around Christmas
  - Given to supervisors as one datum for performance assessments in January 2019

# Ongoing and Future Directions

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- **Research**

- Interdisciplinary planning with new protocols
- Increased ongoing participation at the activation meetings
- Interdisciplinary monitoring visit-ongoing

- **Patient Care**

- Revisions of standards of care of procedures performed in clinic
- Use of primary nursing
- Joint education days for patient care (NEI/CC staff)
- Pharmacy collaborative

- **Communication**

- NEI Town Hall Meetings
- Dissemination of information

- **Team work**

- Clinic Redesign
- Monthly morale boosters
- Daily planning



OP10 Team

# Improving patient quality and safety: Intravitreal Injection

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- Interdisciplinary planning
- Revision of standards of practice
- Focus on infection control
  - Centralization of sterilization
  - Review of procedures
- Focus on comfort during procedures
  - Equipment
  - Medications
  - Primary nursing

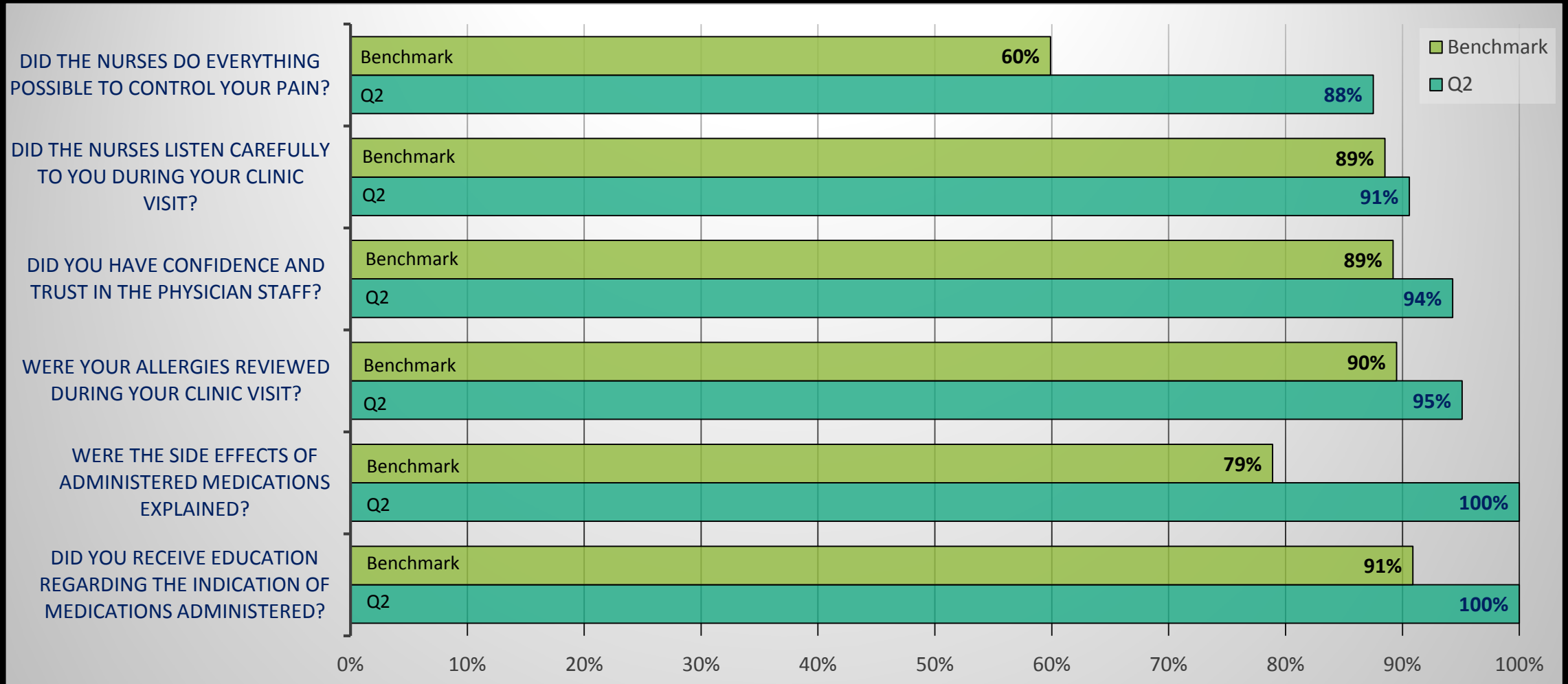


Rochelle Woodard, BSN, RN  
Senior Clinical Research Nurse  
Retina Protocol Coordinator



# NRC Picker Data: Patients' Experience and Indicators

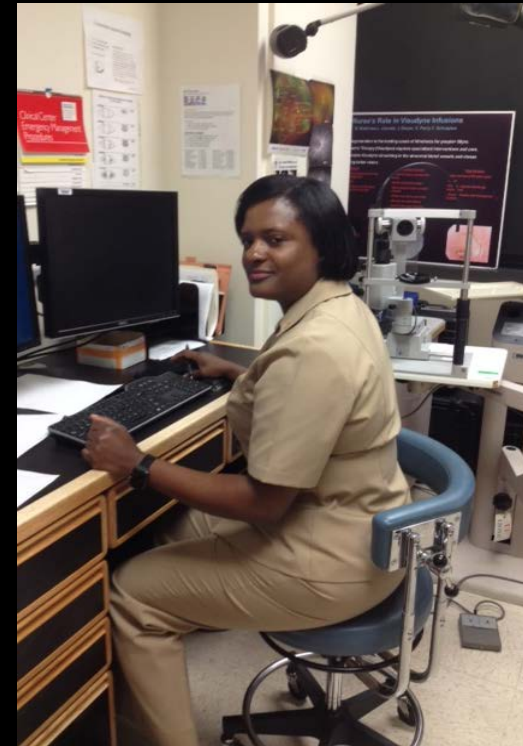
## Data for OP10: Q2-2018



# Consult Services: Quality and Safety

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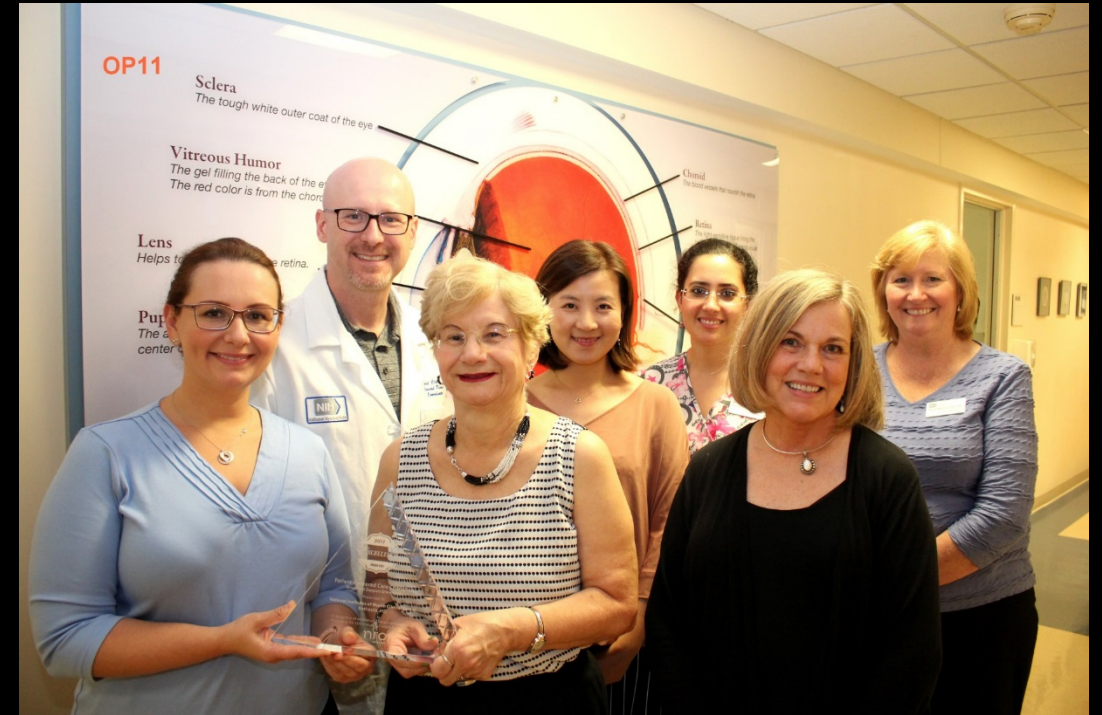
- We care for close to 3,000 consult patients per year
- Many patients are high risk
- Collaboration and communication
- Addition of 1.0 FTE for a consult primary nurse



Celestina Igbinosun, BSN, RN  
Lieutenant, United States Public Health  
Consult Nurse



# Celebration of Our Team



NIH Clinical Center won an excellence award in 2017 from the NRC Picker Institute for providing extraordinary high level of emotional support to our patients.

## Thank You