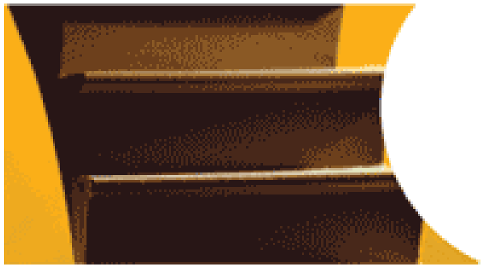

RDCRN

# 3rd Conference on Clinical Research for Rare Diseases

October 2, 2012 Rockville, MD

rdcrn.org/conference

Rare Diseases Clinical Research Network
Funded by the National Institutes of Health

NCATS
National Center for Advancing Translational Sciences
Catalyzing Innovation

CTSA
Clinical & Translational® Science Awards

RARE DISEASES CLINICAL RESEARCH NETWORK
Funded by the National Institutes of Health

CTSA
Clinical & Translational®
Science Awards

# Welcome and Introduction

**Peter A. Merkel, MD, MPH**
**University of Pennsylvania**

**Stephen C. Groft, PharmD**
**Director, NIH Office of Rare Diseases Research**

NCATS
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES
Catalyzing Innovation

Office of Rare Diseases Research
National Institutes of Health

# CCRRD Sponsors

- This conference is a combined program of
  - ➢ The Rare Diseases Clinical Research Network (RDCRN)

    &

  - ➢ The Clinical & Translational Science Awards Program (CTSA)

RARE CLINICAL DISEASES RESEARCH NETWORK
Funded by the National Institutes of Health

CTSA Clinical & Translational® Science Awards

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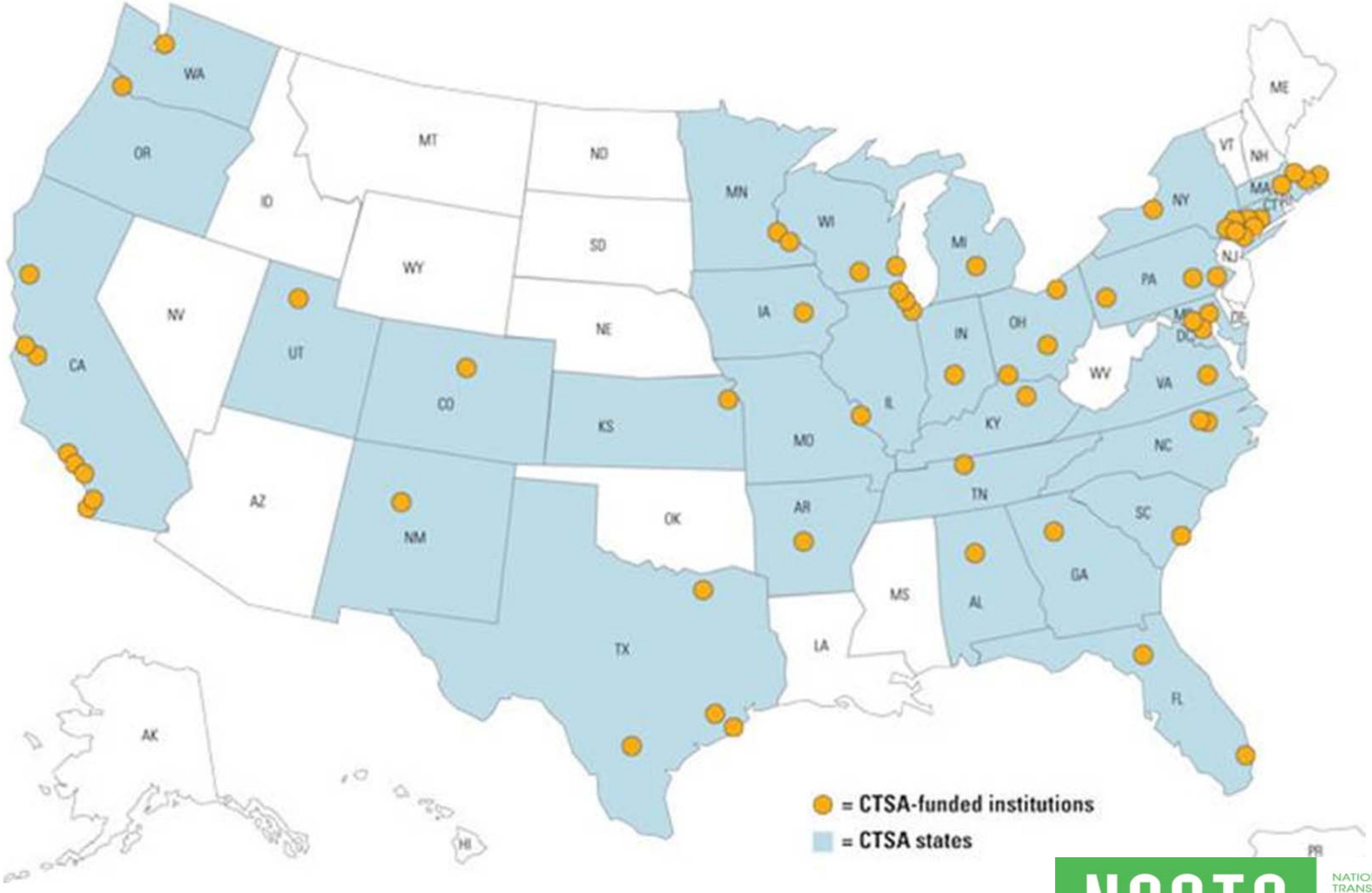
Catalyzing Innovation

# CTSA Sites October 2012



NCATS
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES
Catalyzing Innovation

# Thanks to Our Financial Supporters

## NIH

- National Institute of Neurological Disorders and Stroke (NINDS)
- Office of Rare Diseases Research (ORDR)
- National Center for Advancing Translational Sciences (NCATS)
- National Institute of Allergy and Infectious Diseases (NIAID)

# Thanks to Our Financial Supporters

## Multiple Patient Advocacy Groups

- Adenoid Cystic Carcinoma Research Foundation
- Churg-Strauss Syndrome Association
- National Mucopolysaccharidoses (MPS) Society
- Primary Ciliary Dyskinesia (PCD) Foundation
- Sturge Weber Foundation
- United Mitochondrial Disease Foundation

# Thanks to many folks

- **Organizing Committee**
  - **Peter A. Merkel, MD, MPH, *Chair***
  - **Mark Batshaw, MD**
  - **Debbie Gipson, MS, MD**
  - **Nancy Green, MD**
  - **Robert Griggs, MD**
  - **Hyder Jinnah, MD, PhD**
  - **Jeffrey P. Krischer, PhD**
  - **Carol McAlear, MA**
  - **Dawn Milliner, MD**
  - **Robert Steiner, MD**

# Thanks to many folks

- **NIH Liaisons**
  - **Stephen Groft, PharmD**
  - **Randall Stewart, PhD**
  - **Mary Prurucker, MD**

- **Data Management Coordinating Center (DMCC)**
  - **Jeffrey P. Krischer, PhD,**
  - **Heather Guillette, MS**
  - **Jennifer Harris, MSPH, *CRA***
  - **Joseph L. Gomes**
  - **Jennifer Lloyd**

- **Kathleen Ryan**

# Housekeeping Items

- You MUST register (and pay)

- Extra program material to obtain:
  - Wendler syllabus

- Meals
  - Breakfast—now
  - Lunch–in the plaza and around corner
  - Caffeine, fluids, snacks–-continuous!
  - Breaks–-exist

PLEASE put your cell phones and pagers on vibration or silent modes

Better yet, turn them off and actually enjoy the meeting!

# Travel Awards

- **Travel award recipients _MUST_ be sure to receive reimbursement forms and instructions from registration desk-*do not leave without one***
- **Follow the directions completely**
- **Tuesday, October 16, 2012: Strict deadline for returning reimbursement form and all necessary documents; *we are not kidding*!**

# Today's Program

- Target audience:
  - Trainees and junior faculty engaged in clinical investigation into rare diseases
  - Any others engaged in research in rare diseases
  - List of attendees included in the binder
- Lectures/Panels:
  - Save up questions (write them down)
  - Goal is to have interchange
- Poster session
- Workshops
- Reception

# *“Challenges and solutions to conducting clinical research in rare diseases”*

**Peter A. Merkel, MD, MPH**
*University of Pennsylvania*

# *“Clinical trial design issues and options for study of rare diseases”*

**Jeffrey Krischer, PhD**
*University of South Florida*

# *“Ethical issues, conflicts of interest, and privacy issues unique to rare diseases research”*

**David S. Wendler, PhD**

***National Institutes of Health***

# *“From the lab to labeling: clinical drug to development for rare diseases. Investigator, industry, and regulatory perspectives”*

**Bonnie W. Ramsey, MD**
*Seattle Children’s Research Institute*

**Eric Olson, PhD**
*Vertex Pharmaceuticals, Inc.*

# *“Energizing and engaging patient advocate groups to partner in rare diseases research”*

**Janet Hieshetter**
**Hyder Jinnah, MD, PhD**
*Emory University*
**Barbara Wedehase, MSW**
**Chester Whitely, PhD, MD**
*University of Minnesota*

# *“Award winning abstracts”*

**Rivka Ayalon, MD**
**Leigh Anne Daniels, MD, MPH**
**M. Chiara Manzini, PhD**
**Semone Myrie, PhD**

# Poster Session (and Lunch)

- Set up time: last night, now (breaks)
- Poster-board number—see list
- Poster session
  - Please grab some food and stand by your poster for most of the session
  - Take down poster at end of night or the poster will be discarded
  - Can also view posters during breaks
- Senior investigators and NIH program staff will be viewing your posters—good time for feedback, etc.

# Afternoon Breakout Sessions

- Parallel small-group breakouts
- 2 sessions for each of 2 breakouts
- Each breakout will be repeated so that all attendees will take part in a breakout on both topics

# Breakout 1: Career Development and Mentoring

- Panel discussions by senior faculty mentors and trainees/junior faculty
- Focus on issues related to trainees studying rare diseases

# Breakout 2: Logistics of conducting rare disease research

- Short presentations by principal investigators and subsequent discussion
- Focus on examples of successful approaches and unexpected challenges to conducting research in rare diseases

# Evaluation Forms

- Please complete after each talk
- Your comments are quite important and will help determine content of future conferences
- Please return the completed forms to the basket on the registration desk (or we will collect them last session)

# Wine and cheese reception

- Informal setting for networking
- All attendees encouraged to join the reception

# *“Challenges and solutions to conducting clinical research in rare diseases”*

**Peter A. Merkel, MD, MPH**

**University of Pennsylvania**

# Peter A. Merkel, M.D., M.P.H.
# Financial Disclosures

***Dr. Merkel has current or has had recent financial support for research, consultation, and/or educational activities from the following sources:***

- **Actelion**
- **Bristol-Myers Squibb**
- **Celgene**
- **Genentech**
- **Genzyme**
- **Human Genome Science**
- **Nordic Group**
- **American College of Rheumatology**
- **European League Against Rheumatism**
- **National Institutes of Health**
  **NCATS • NIAMS • NINDS • NHLBI**
  **NIAID • NCRR • ORDR**
- **The Patient Centered Outcome Research Institute (PCORI)**
- **US Food and Drug Administration**
- **The Vasculitis Foundation**

# Rare Diseases

- What is a rare disease?
  - A disease with a prevalence of <200,000 persons in USA
    - Estimated to be ~7000 rare diseases
    - US estimate: 25-30 million people with a rare disease (8-12% of US population)

- Increasing awareness of rare diseases by public via media, internet, advocacy/support groups
- Many major scientific breakthroughs have arisen stemming from investigation of rare diseases that often have impact on common disorders

- Rare disorders have fascinated physicians and non-physicians for centuries

# Why do we do rare diseases research?

- **When you are the patient with a rare disease, the disease is no longer rare**
- **When you have a patient with a rare disease, your ignorance will not help: become expert or refer**
- **People are drawn to rare disease research for the some of the same reasons others choose a research focus**
  - **Fascination with subject**
  - **Opportunity**
  - **Inspiration by patient/teacher**

# Inspiration and motivation comes from many places

# Some Joys & *Challenges* of Rare Disease Care and Research

- Nice to be an expert about things most people don’t know about
- *Nobody really knows what on earth you study or see clinically*

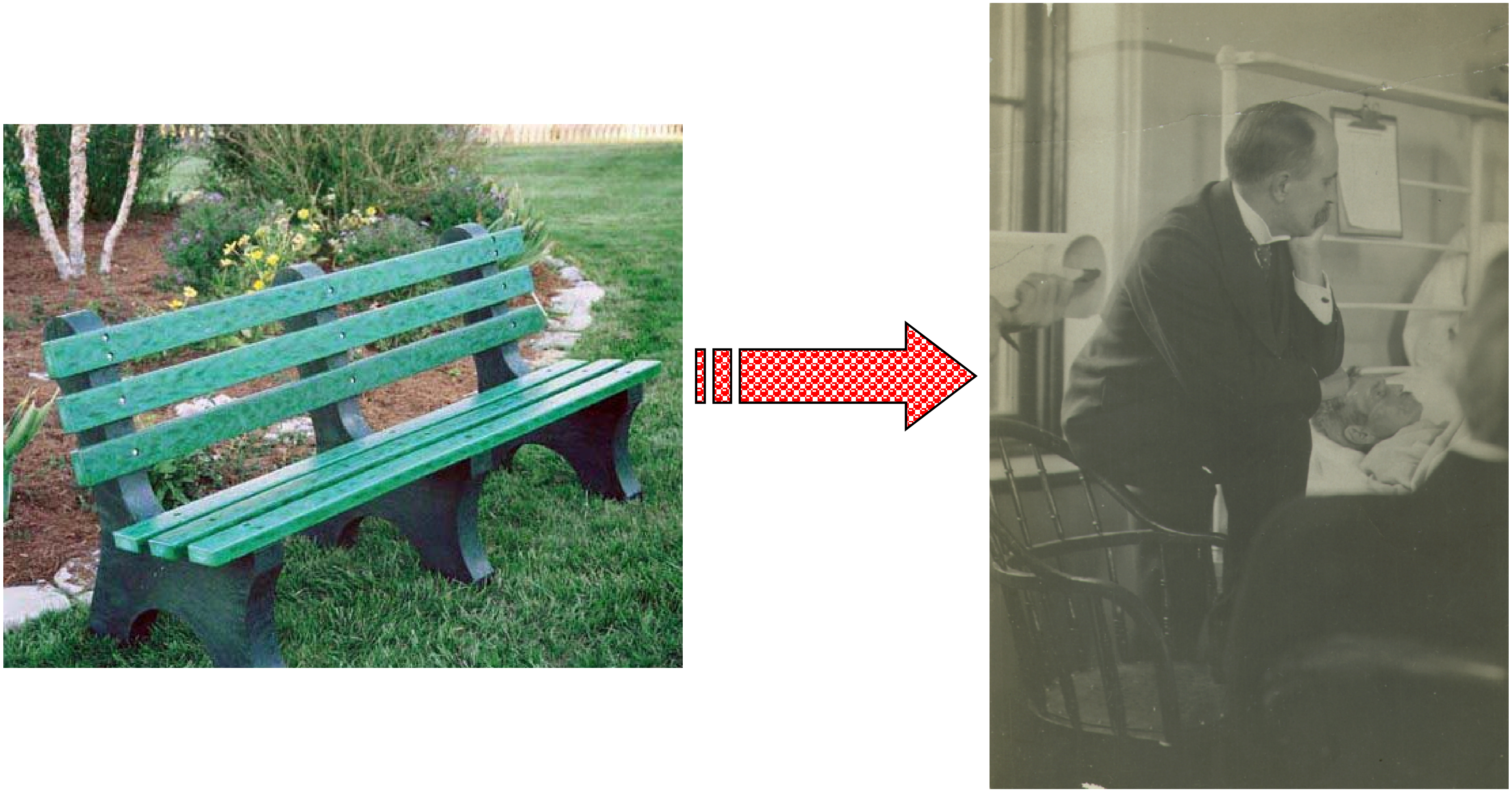
- There are HUGE unanswered questions for rare diseases
- *There are HUGE unanswered questions for rare diseases*

- You can carve out your own niche when studying a rare disease
- *You must carve out your own niche when studying a rare disease*

- Often need to work in collaborative, multi-center research groups
- Markedly increased complexities with multi-center studies

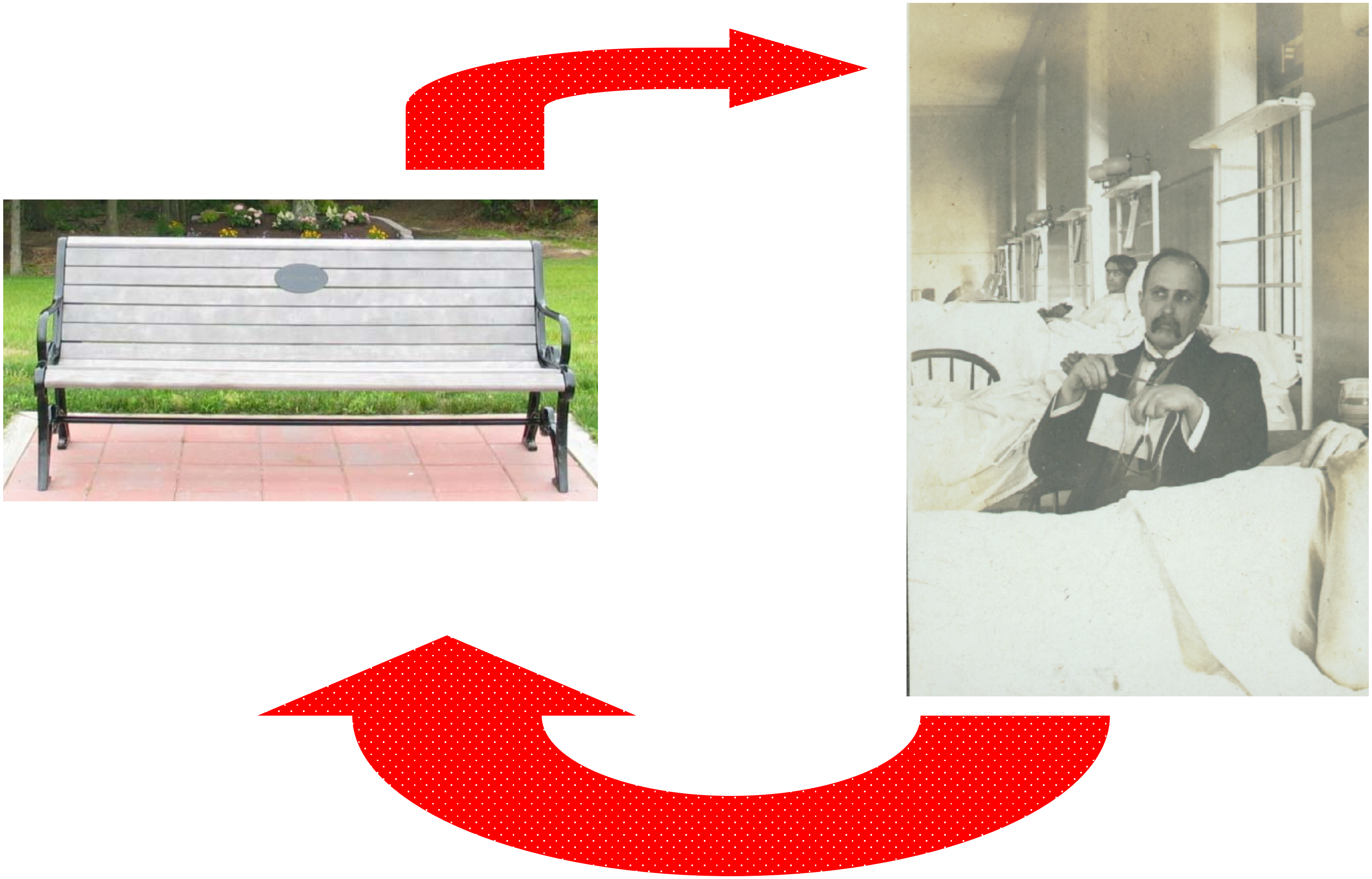
- Face interesting and unique issues in dealing with rare diseases
- Still face the same challenges as studying common disorders

# Bench to Bedside is a nice model…



# Bedside to Bench is likely more productive and common (esp. for rare disease)

# Bedside ↔ Bench is really a bidirectional process, especially for rare diseases



# Example: Eprodisate for AA Amyloidosis

- *Bedside:* Observation of AA Amyloidosis
- *Bench:*
  - Discovery of SAA protein
  - Understanding role of GAGs in amyloidogenesis
  - Development of anti-amyloid agents that interfere with interaction b/w amyloidogenic proteins + GAGs
- *Bedside:* Design and conduct of trial
  - Collaboration with industry
  - Work with FDA
  - Design for small numbers
  - Create collaborative research network
  - Recruit via centers known for amyloidosis

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 7, 2007 VOL. 356 NO. 23

# Eprodisate for the Treatment of Renal Disease in AA Amyloidosis

Laura M. Dember, M.D., Philip N. Hawkins, F.Med.Sci., Bouke P.C. Hazenberg, M.D., Peter D. Gorevic, M.D., Giampaolo Merlini, M.D., Irena Butrimiene, M.D., Avi Livneh, M.D., Olga Lesnyak, M.D., Xavier Puéchal, M.D., Ph.D., Helen J. Lachmann, M.D., Laura Obici, M.D., Robert Balshaw, Ph.D., Denis Garceau, Ph.D., Wendy Hauck, Ph.D., and Martha Skinner, M.D., for the Eprodisate for AA Amyloidosis Trial Group*

# Eprodisate for AA Amyloidosis

- Funded by industry
- Conducted by a collaborative group of international centers (183 patients at 27 centers)
- Aided by patient advocacy groups and internet recruitment
- Need for special analyses/outcomes for small numbers
- A confirmatory Phase II randomized controlled trial is ongoing and if “positive” could lead to FDA/EMA labeling

# Eprodisate for AA Amyloidosis

- Funded by industry
- Conducted by a collaborative group of international centers (183 patients at 27 centers)
- Aided by patient advocacy groups and internet recruitment
- Need for special analyses/outcomes for small numbers
- Additional ancillary translational studies also arising from this project
- Approval process challenging
- A confirmatory Phase II randomized controlled trial is ongoing and would, if "positive" could lead to FDA/EMA labeling

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OL. 356 NO. 23

Eprodisate for the isease
in A

Laura M. Dember, M.D., Ph , F , Peter D. Gorevic, M.D.,
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Helen J. Lachmann, M.D., Laura Obici, M.D., R .D., Wendy Hauck, Ph.D.,
and Martha Skinner, M.D., for Group*

# Rare Disease Research: Opportunities

- HUGE unanswered questions for rare diseases
- Potential to make a major impact on a clinically and scientifically underserved population
- The internet is now a key resource for rare disease research
  - Referrals/Recruitment
  - Networking
  - Conduct of research
- Increasing recognition in the scientific community and among funding agencies regarding the importance and benefits of research in rare diseases
- You can carve out your own niche when studying a rare disease

# Rare Disease Research: Challenges

- Sample sizes and recruitment:
  - these *are* <u>rare</u> diseases!
- IRB/HIPPA:
  - must protect privacy
- Funding:
  - these markets are, by definition, small
- Career development
  - mentors/models are harder to find
  - obtain protected time while still a clinical expert
- Still have all the usual challenges of a career in academic medicine...

# Solutions: Clinical Piece

- Don’t forget the patient
  - Listen to your patients-they will teach you
- Master the disease
  - Become a student of the disease
- Join/engage with patient advocacy groups
  - Become a citizen of the disease
- Promote your expertise (if it is real)
- Protect your time and focus (well, try)

# Solutions: Science Piece

- Do good science
  - There is a limit to compromising due to small sample sizes
  - Be realistic

- "Borrow" ideas and approaches from other fields
  - Research approaches for related common diseases may be well-developed and adaptable

- Work collaboratively: Network, international
  - Face the challenges to sharing credit among many people

# Solutions: Funding Piece

- Don’t believe the hype
  - There IS funding for research (in US)
  - The NIH budget doubled in the past 25 years
  - Seek opportunities and leverage resources (not just $)
    - Grants: NIH/FDA/PAGs/Industry/VA/Institutional/Others
    - Clinical Trials
    - Existing Datasets/Repositories
    - Collaborations
    - Core Resources: Institutional, National/International
  - Expand the focus of your inquiry
    - E.g.: not just vasculitis but vascular inflammation in general
  - Keep your eyes open

# Solutions: Funding Piece

- Don’t believe the hype
  - There IS funding for research (in US)
  - The NIH budget doubled in the past 25 years
    - Funding mechanisms shifted to more collaborative and multi-specialty approaches
    - Need to work with the new funding realities
  - Take advantage of opportunities and leverage resources (not just $)
    - Grants: NIH/FDA/PAGs/Industry/VA/Institutional/Others
    - Clinical Trials
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# NIH Numerology, Alphabet Soup, and Nomenclature

- K08
- K12
- K23
- K24
- K30
- T32
- NRSA (F32)

- R01
- R21
- U01
- U5

- Grants
- Contracts
- Cooperative agreements
- Networks
- SBIRs
- ISTs
- RFAs
- RFPs

**Explore them all!**

# Solutions: Career Piece

- Find a good mentor or at least a supporter
- Don’t be afraid of learning new research skills
- Create the right environment for research
  - Ask for the resources you need
- Contribute and receive benefit from collaborations
  - Be a team player but don’t just be a follower

# Successful Rare Disease Research is *Clearly* Possible!

- The >50 posters at this meeting testify to this fact

- As with any type of research, challenges exist but solutions are available

**This is an excellent time to engage in clinical research in rare diseases**

**Multi-center research collaborations are extremely helpful for conducting high-quality, high-impact clinical research in rare diseases**

# Research Networks for Rare Diseases

- ***Pros:***
  - Reduce start-up time/costs-leverage resources
    - Centers, personnel, systems already in place
    - Forms/data entry/CRFs, training, communications
  - Established cohorts and recruitment streams
  - Share workload & credit → *trust*
  - Combine expertise
  - Recycle experience
  - Look good to funding agencies/sponsors

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  - Recycle experience
  - Look good to funding agencies/sponsors

- ***Cons:***
  - **Must maintain infrastructure**
  - **Need to avoid stagnation → add flexibility**
  - **Require work to maintain cohesiveness**
  - **Takes a long time until productive**
  - **Many, many authors share credit-problem for jr. faculty**

Rare Diseases Clinical Research Network

National Institutes of Health

# The Rare Diseases Clinical Research Network (RDCRN)

Office of Rare Diseases Research
National Institutes of Health

RARE DISEASES
CLINICAL RESEARCH
NETWORK
National Institutes of Health

# RDCRN

- Established by the Office of Rare Diseases Research
- Started in 2003--currently in 2nd 5 year cycle
  - 1st cycle (10 Consortia) supported by ORDR, NCRR, NINDS, NIAMS, NICHD, NHLBI, NIDDK
  - 2nd cycle (19 Consortia) supported by ORDR, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIAID, NIDCR, NCI
- Currently involves 164 institutions world-wide
- Collectively studying >200 diseases
- 13640 patients enrolled in studies

Rare Diseases Clinical Research Network
National Institutes of Health

# Goals of the RDCRN

- Facilitate clinical research by:
  - Creation of Consortia focused on related diseases
  - Cost-sharing research infrastructures
  - Establishing uniform protocols for data collection
  - Making meaningful large-scale studies possible
    - Longitudinal cohorts, pilot projects, and randomized trials
- Directly engage patients and their advocates
- Train new investigators in rare diseases research

***DHHS-NIH***

***ORDR, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIDCR, NIAID, NCI***

**RARE DISEASES CLINICAL RESEARCH NETWORK**

Funded by the National Institutes of Health

- **Collaborative Clinical Research**
- **Centralized Data Coordination and Technology Development**
- **Public Resources and Education**
- **Training**

**Dystonia Coalition**

**Coalition of Patient Advocacy Groups (CPAG)**

**Chronic Graft Versus Host Disease Consortium**

**North America Mitochondrial Diseases Consortium**

**Primary Immune Deficiency Treatment Consortium**

**The Data Management and Coordinating Center**

**Rare Kidney Stone Consortium**

**Nephrotic Syndrome Rare Disease Clinical Research Network**

**Angelman, Rett and Prader-Willi Syndromes Consortium**

**Spinocerebellar Ataxia – Clinical Research Consortium**

**Brain Vascular Malformation Consortium**

**Autonomic Rare Diseases Clinical Research Consortium**

**Sterol and Isoprenoid Diseases Consortium**

**Molecular and Epidemiologic Characterization of Salivary Gland Carcinomas Consortium**

**Urea Cycle Disorders Consortium**

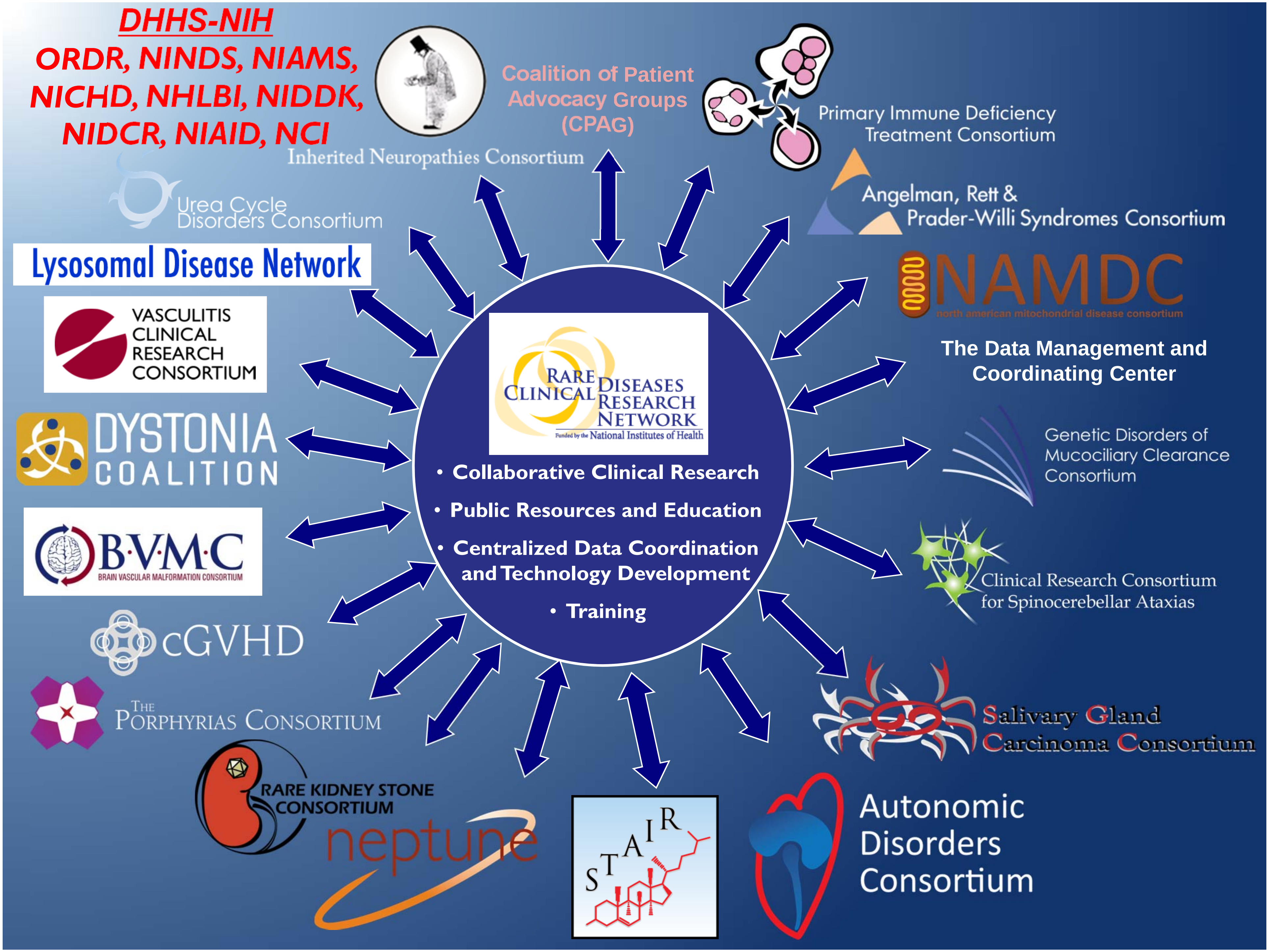
**Inherited Neuropathies Consortium**

**Lysosomal Disease Network**

**Vasculitis Clinical Research Consortium**

**Porphyria Rare Disease Clinical Research Consortium**

**Genetic Disorders of Mucociliary Clearance Consortium**



**DHHS-NIH**

**ORDR, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIDCR, NIAID, NCI**

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NAMDC
north american mitochondrial disease consortium

**The Data Management and Coordinating Center**

Genetic Disorders of Mucociliary Clearance Consortium

Clinical Research Consortium for Spinocerebellar Ataxias

Salivary Gland Carcinoma Consortium

Autonomic Disorders Consortium

STAIR

RARE KIDNEY STONE CONSORTIUM

neptune

The Porphyrias Consortium

cGVHD

B·V·M·C
BRAIN VASCULAR MALFORMATION CONSORTIUM

DYSTONIA COALITION

VASCULITIS CLINICAL RESEARCH CONSORTIUM

Lysosomal Disease Network

Urea Cycle Disorders Consortium

RARE DISEASES CLINICAL RESEARCH NETWORK
Funded by the National Institutes of Health

- **Collaborative Clinical Research**
- **Public Resources and Education**
- **Centralized Data Coordination and Technology Development**
- **Training**

VASCULITIS
CLINICAL
RESEARCH
CONSORTIUM

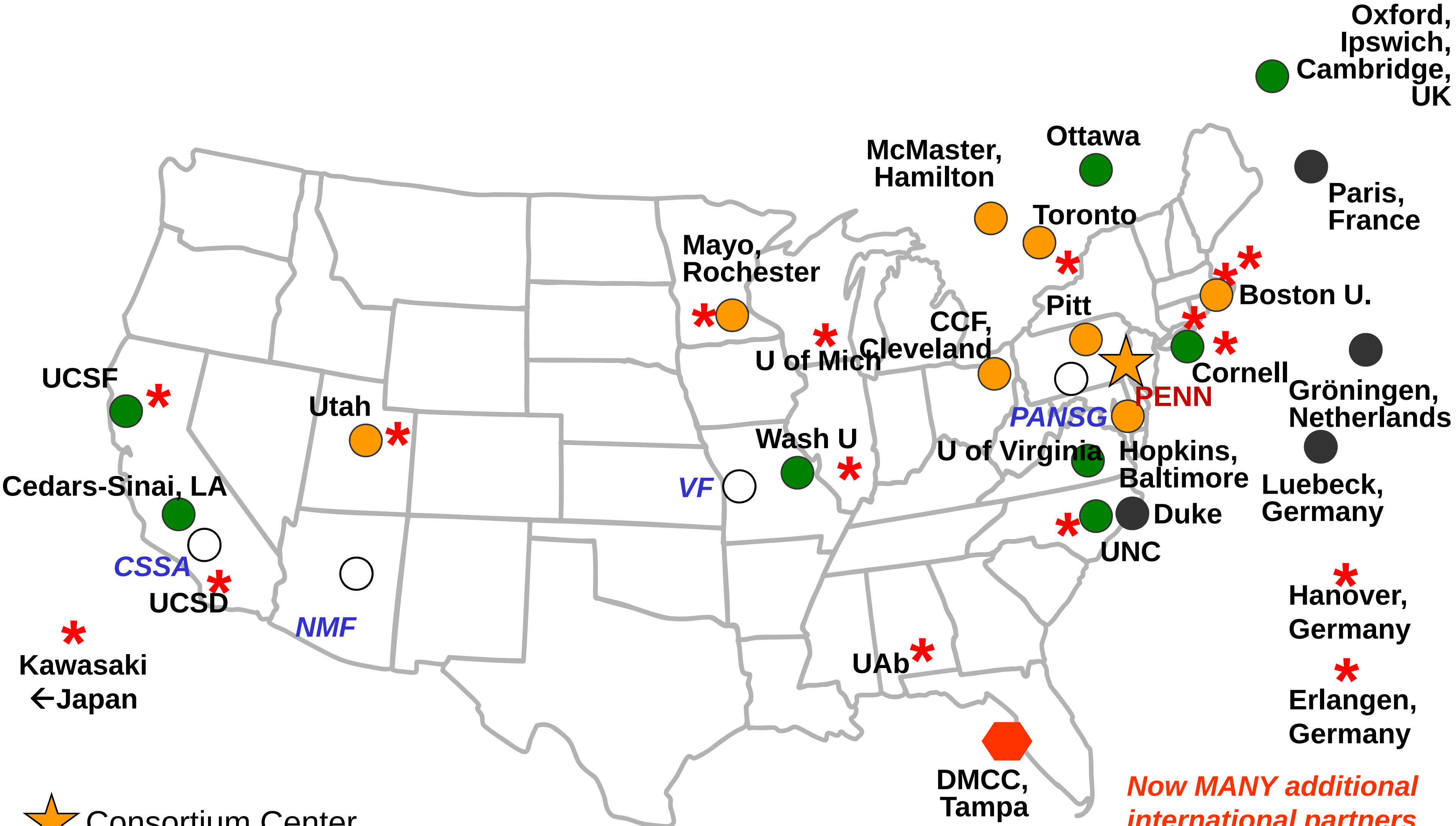
www.RareDiseasesNetwork.org/VCRC

# A Member of the NIH Rare Diseases Clinical Research Network

RARE DISEASES
CLINICAL RESEARCH
NETWORK
Funded by the National Institutes of Health

www.RareDiseasesNetwork.org

# Vasculitis Clinical Research Consortium



*Now MANY additional international partners*

★ Consortium Center

● Primary Clinical Sites; ● Other Sites; ● Affiliated Partners/Sites

○ Affiliated Patient Group; ⬣ DMCC * Biomarker Lab Sites

VASCULITIS
CLINICAL
RESEARCH
CONSORTIUM

VASCULITIS
CLINICAL
RESEARCH
CONSORTIUM

# Current VCRC Protocols

***CLINICAL COHORT / BIOMARKER STUDIES***

| | |
|---|---|
| 02 | Longitudinal Protocol for GCA |
| 03 | Longitudinal Protocol for TAK |
| 04 | Longitudinal Protocol for PAN |
| 05 | Longitudinal Protocol for GPA/MPA |
| 06 | Longitudinal Protocol for CSS |
| 10 | Genetic Repository (One-Time DNA Collection ) |

***OUTCOME MEASURES PROJECTS***

| | |
|---|---|
| 15 | Imaging Protocol for MRI and PET in TAK |
| | OMERACT Vasculitis Working Group Activities |
| | PCORI Projects: PROMIS, Disease-Specific PRO, ICF |

***THERAPEUTIC CLINICAL TRIALS***

| | |
|---|---|
| 22 | Pilot Study of Abatacept in Mild GPA |
| 23 | RCT: Abatacept for GCA/TAK (AGATA) |
| 24 | RCT: Plasma Exchange for AAV (PEXIVAS) |
| 25 | RCT: Rituximab vs. Azathioprine for AAV (RITAZAREM) |
| 26 | RCT of Prednisone in GPA (TAPIR) |

***PATIENT CONTACT REGISTRY STUDIES***

| | |
|---|---|
| 31 | Reproductive Health in Patients with Vasculitis |
| 32 | Vasculitis Pregnancy Registry |
| 33 | Vasculitis Illness Perception Study |
| 34 | Vasculitis Educational Needs Study |

# VCRC GRANT/FUNDING SUPPORT

NIAMS
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Office of Rare Diseases Research
National Center for Advancing Translational Sciences – NIH

NCATS
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES
Catalyzing Innovation

pcori

National Heart Lung and Blood Institute
People Science Health

FDA

RECOVERY.GOV

VASCULITIS FOUNDATION

Genentech
*A Member of the Roche Group*

Bristol-Myers Squibb

ARTHRITIS FOUNDATION®
**Take Control.** We Can Help.™

Perelman School of Medicine
UNIVERSITY of PENNSYLVANIA

CTSA
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VASCULITIS CLINICAL RESEARCH CONSORTIUM

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# IT CAN BE DONE!

# Questions/Comments