

# **Neurodegenerative Disorders Division**

Director: Russell Swerdlow, MD

Associate Director: Douglas Wright, PhD

# NDD Sub-Divisions

- Disorders of Cognition
- Disorders of Movement
- Disorders of Strength
- Disorders of Coordination
- Disorders of Peripheral Nerves
- Disorders of Myelin

# Disorders of Cognition

- Heather Anderson
- Andrei Belousov
- Juan Bruses
- Jeff Burns
- In Young Choi
- Rick Dobrowsky
- Robb Krumlauf
- Sang Pil Lee
- Steve Levine
- Eli Michaelis
- Mary Michaelis
- Kathy Newell
- Isaac Onyango
- Russ Swerdlow
- Ron Yu

# Disorders of Movement

- Juan Bruses
- Rick Dobrowsky
- Rich Dubinsky
- Paige Geiger
- Robb Krumlauf
- Kelly Lyons
- Jules Nazzaro
- Isaac Onyango
- Raj Pahwa
- John Stanford
- Russ Swerdlow

# Disorders of Strength

- Rick Barohn
- Mazen Dimachkie
- Rick Dobrowsky
- Mamatha Pasnoor
- John Stanford
- Russ Swerdlow
- Yunxia Wang

# Disorders of Coordination

- Rich Dubinsky
- Doug Wright

# Disorders of Peripheral Nerves

- Rick Barohn
- Merlin Butler
- Mazen Dimachkie
- Rick Dobrowsky
- Paige Geiger
- Patricia Kluding
- Robb Krumlauf
- Wen Liu
- Ken McCarson
- Mamatha Pasnoor
- Peter Smith
- WenFang Wang
- Yunxia Wang
- Doug Wright
- Hao Zhu

# Disorders of Myelin

- Merlin Butler
- Steve Levine
- Sharon Lynch

# Website #1

- Introduction: What is a neurodegenerative disorder?
- Listing of neurodegenerative disorders by category:

| <u>Cognition</u> | <u>Movement</u> | <u>Strength</u> | <u>Coordination</u> | <u>PNS</u> | <u>Myelin</u> |
|------------------|-----------------|-----------------|---------------------|------------|---------------|
| AD               | PD              | ALS             | SCA                 | DM         | MS            |
| FTD              | FTD             | FTD             | FA                  | Amyloid    | CMT           |
| DLB              | DLB             | HSP             | Prion               | FA         |               |
| CBD              | CBD             |                 |                     | MSA        |               |
| PSP              | PSP             |                 |                     | Toxic      |               |
| Prion            | MSA             |                 |                     |            |               |
|                  | HD              |                 |                     |            |               |

# Website #2

- Click Directly on the faculty list
  - Access faculty biographs from the faculty list
- Click on a disease category
  - List of faculty for that category
  - Access faculty biographs for that category

# Mitochondria in Aging & Neurodegeneration

## Principal Investigator

Russell Swerdlow, MD  
Professor, Neurology and  
Molecular & Integrative Physiology

## Co-Investigators

Heather Anderson  
Jeff Burns  
In Young Choi  
Sang Pil Lee  
Eli Michaelis  
Mary Michaelis  
Kathy Newell  
Isaac Onyango  
Paige Geiger  
WenFang Wang  
Hao Zhu

## Training

BA, Psychobiology, NYU  
MD, NYU  
Residency, Neurology, UVA  
Clinical Fellowship, Cognitive Neurology, UVA  
Post-doc, Neurodegenerative Disorders, UVA

## Areas of Interest

Mitochondrial genetics  
Mitochondrial physiology  
Aging  
Neurodegeneration mechanisms  
AD, PD, ALS

# Projects & Approaches

- Mitochondrial function in aging and neurodegenerative diseases
- Cybrid modeling of neurodegenerative diseases
- Mitochondrial biogenesis
- Balance between aerobic-anaerobic metabolism
- Cell culture
  - Lentiviral transfection
- Cybrids
- ETC  $V_{max}$
- Oxygen Consumption
- Oxidative stress
- Immunocytochemistry

# SYNAPTIC PLASTICITY IN THE CNS DURING DEVELOPMENT AND NEURONAL INJURY

## Principal Investigator

Andrei B. Belousov, Ph.D.  
Associate Professor,  
Molecular & Integrative Physiology

## Co-Investigators

Nancy Berman  
William Brooks  
Joseph Fontes  
Randy Nudo

## Training

*Ph.D.*  
Moscow State University (Moscow, Russia)

*Post-Doctoral Training*  
McGill University (Montreal, Canada)  
Stanford University (CA)

*Assistant and Associate Professor*  
Tulane University (LA)

**Neurophysiology**

## Areas of Interest

Regulation of *gap junctions*  
(electrical synapses) during  
development, traumatic brain  
injury and stroke

# Projects & Approaches

- 1) Developmental regulation of electrical synapses (gap junctions)
- 2) Regulation of electrical synapses during traumatic brain injury and ischemia
- 3) Glutamate-dependent neuronal plasticity: regulation of neurotransmitter phenotype
- 4) Glutamate-dependent neuronal plasticity: homeostatic plasticity

Patch-clamp electrophysiology  
Fura-2 digital calcium imaging  
Transcriptional regulation  
Immunocytochemistry  
Confocal microscopy  
Primary cultures  
Acute slices  
In vivo drug administration  
Herpes simplex virus vectors  
(culture treatments)

# Laboratory of Cellular and Developmental Neuroscience (KLSIC #2052)

## Principal Investigator

Juan L. Brusés MD/PhD  
Associate Professor  
Dept Anatomy and Cell Biology

## Co-Investigators

Christopher Theisen, PhD  
Mitchell McGill, Grad Stud

## Education & Training

- M.D. University of La Plata, Argentina
- Ph.D. University of Buenos Aires
- Psychiatrist University of Buenos Aires

## Postdoctoral Training:

- Dept of Physiology and Neurobiology  
University of Connecticut
- Dept of Genetics and Neuroscience  
Case Western Reserve University

## Positions:

- Senior Research Scientist  
Biochemistry and Biophysics Program  
Sloan-Kettering Institute

## Areas of Interest

- Cellular and molecular mechanism of neural development:
- Synapse formation
  - Axonal growth and regeneration
  - Mental and Neurological disorders

## Collaborators at KUMC

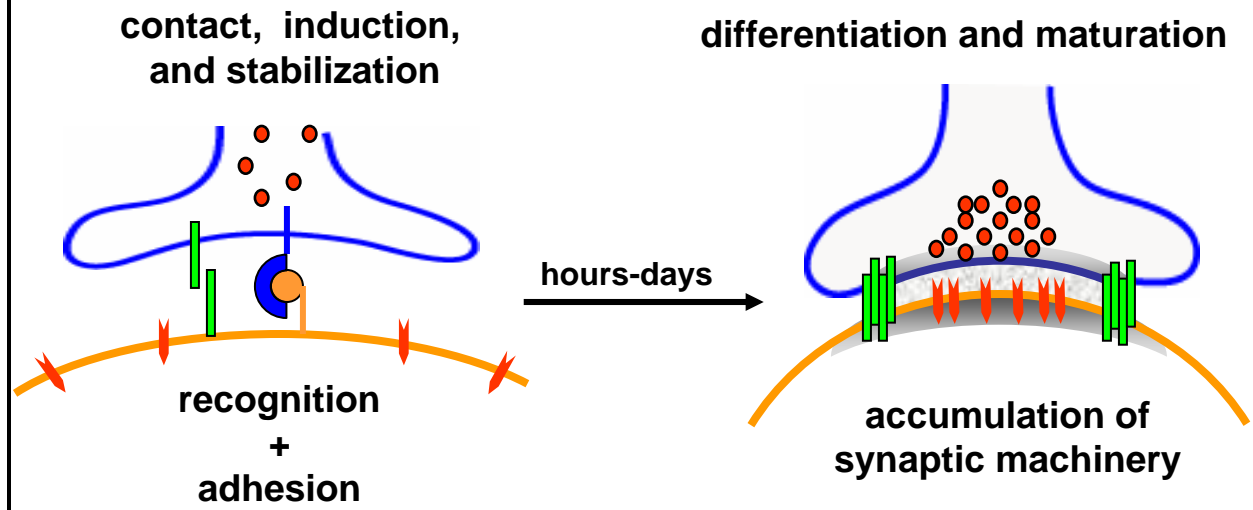
- Drs. J Hellings & M. Butler:  
Molecular mechanisms of Autism and Prader-Willi Syndrome
- Drs. B. Rognish & C. Little:  
Role of N-cadherin in early embryonic development

# Projects & Approaches

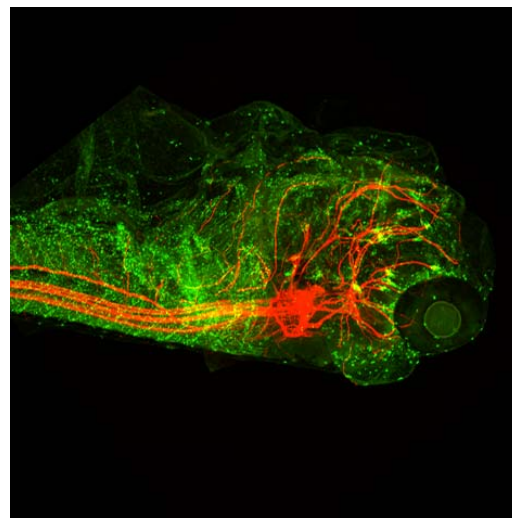
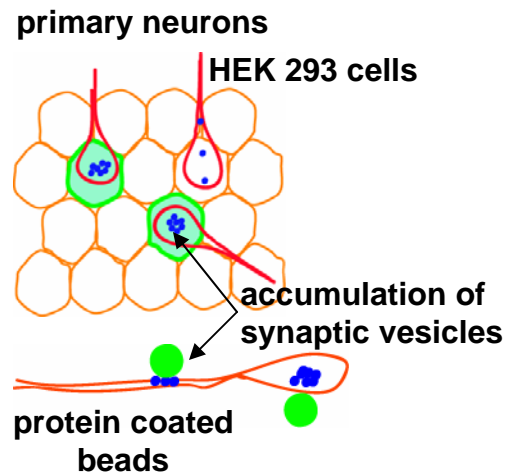
## Synaptic contact



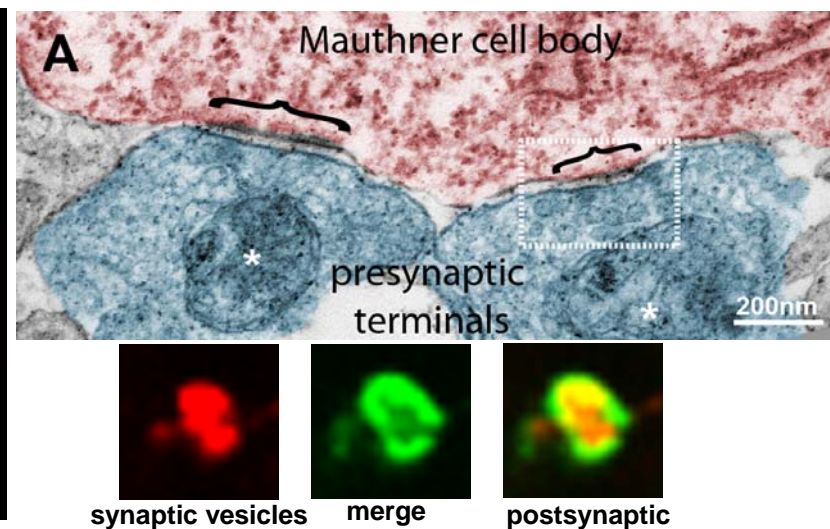
## Synapse Formation



## In vitro assays for synapse formation



## Synapse formation in zebrafish



# Mechanisms in Diabetic Neuropathy

## Principal Investigator

Rick T. Dobrowsky, Ph.D.

## Co-Investigators

Doug Wright, Ph.D.  
Brian Blagg, Ph.D.

## Training

Ph.D- NC State University

Postdoc- Duke University  
Medical Center

## Areas of Interest

Neuregulin signaling in diabetic neuropathy

Proteomic approaches in diabetic neuropathy

# Projects & Approaches

- Effect of Glucose-induced Oxidative Stress on the Schwann Cell Mitochondrial Proteome
    - Sponsor- NIH-NIDDK
- 

- Altered Neuregulin Signaling in Diabetic Neuropathy
    - Sponsor- NIH-NINDS
- 

- Inhibition of Heat Shock Proteins in the Treatment of Diabetic Neuropathy
  - Sponsor- JDRF

- In vitro analysis of the effect of hyperglycemia on the mitochondrial proteome of Schwann cell (SC) and DRG neurons,
- Quantitative proteomics using SILAC

- Myelinated SC/DRG co-cultures to investigate mechanisms by which hyperglycemia increases neuregulin-induced demyelination
- Mouse models to examine role of Erb B2 activation in contributing to diabetic neuropathy

- Effect of novel C-terminal Hsp90 inhibitors as a therapeutic approach in treating neuropathy

# Muscle Physiology

## Principal Investigator

Paige C. Geiger, Ph.D.

## Co-Investigators

John Stanford, Ph.D.

Russell Swerdlow, M.D.

Hao Zhu, Ph.D.

## Training

University of Kansas, B.A. Chemistry, English

Mayo Graduate School, Ph.D. Physiology

University of Florence, Italy, Muscle biophysics

Washington University in St. Louis, Muscle metabolism

## Areas of Interest

Mechanisms of insulin resistance

Heat shock protein function in skeletal muscle

Brain insulin signaling

Estrogen and insulin action

# Projects & Approaches

- Targeting heat shock proteins to prevent insulin resistance
  - Aging and high fat diet models of insulin resistance
  - Stress kinase inactivation, mitochondrial function
- The role of estrogen receptors in glucose regulation
  - OVX model in rats, NCB5OR mice
  - ER $\alpha$ / $\beta$  expression, GLUT4, NF $\kappa$ B
- Oxidative stress/metabolic dysfunction as common pathologies to Type 2 diabetes and Parkinson's Disease
  - 6-OHDA PD model; high fat diet model of insulin resistance
  - CNS and peripheral metabolism, oxidative stress

## Techniques

Western blot

PCR

Immunoprecipitation

Enzyme/kinase assays

Immunohistochemistry

Confocal microscopy

*In vitro* muscle glucose uptake

*In vitro/situ* muscle contraction

Single fiber force & velocity

Exercise training: swim & treadmill

*In vivo* muscle plasmid transfection & electroporation

# Persistent Pain and CNS Plasticity

## Principal Investigator

**Kenneth E. McCarson, Ph.D.**  
Associate Professor  
Pharmacology, Toxicology  
and Therapeutics  
Director, KIDDRC/KUMC  
Rodent Behavior Facility

## Co-Investigators

**Peter Smith, Ph.D.**  
**Nancy Berman, Ph.D.**  
**Beth Levant, Ph.D.**  
**Doug Wright, Ph.D.**  
**Brad Taylor, Ph.D. (U. Ky)**

**Michelle Winter**  
**Andrew Ralya**

## Training

**BChE Georgia Tech, 1984**  
Chemical Engineering/Biopsychology

**PhD in Pharmacology,**  
**Medical College of Georgia, 1991**

Spinal Substance P release and content  
**Postdoctoral Fellow**, Anatomy/Neurobiology,  
**Washington University** (James E. Krause, PhD)  
Neurokinin receptor gene expression

## Areas of Interest

Pain Neurobiology  
Neurokinin Receptor Function  
Sex Differences in Pain  
Pain and Depression

# Projects & Approaches

- CNS targets for Estrogen in modifying inflammatory pain
- Common mechanisms (BDNF, hippocampal neurogenesis) linking pain, stress, and clinical depression
- Role of neurokinin receptors in central sensitization and cutaneous wound healing
- Regulation of spinal NPY and NK-1 receptor coupling during persistent pain
- Spinal adrenergic pain control mechanisms
- Analyses of Rodent Behavior
- GPCR coupling assays (GTP $\gamma$ S)
- Nuclease Protection Assays
- PCR, nucleic acid techniques
- Western Blots, EMSA
- Lipid Raft Analysis
- Immunofluorescence
- Wound Closure assays
- Rodent models of acute thermal or mechanical pain
- Rodent models of persistent inflammatory or neuropathic pain
- Rodent models of stress, anxiety and depression
- Manipulation of sex hormone status

# Peripheral Autonomic Axon Degeneration

## Principal Investigator

Peter Smith

## Training

Duke

## Areas of Interest

NIH NINDS, R01, Mechanisms of sympathetic axon pruning  
NIH NHLB, RO1, NGF and post-infarct sympathetic neuroplasticity,

## Co-Investigators



Wohaib Hasan, PhD  
Research Assistant  
Professor in Physiology  
PhD University College London



Dora Agbas, PhD  
Research Assistant  
Professor in Physiology  
PhD Josef Attila University

Tim Donohue, Eva Selfridge  
Rick Dobrowsky

# Projects & Approaches

- How do targets control their innervation?
- What are the cellular/molecular mechanisms regulating target attractive and repulsive signals?
- What are the cellular mechanisms underlying axon dying back?
- What regulates axo-axonal associations?
- How do peripheral neurons regulate each other's phenotype?
- Mechanisms regulating axon loss in diabetes

- Expression and SNP Microarrays
- Laser Capture Microdissection
- PCR, nucleic acid techniques
- Blots, IPs
- siRNA
- Immunofluorescence
- Confocal microscopy
- Electron microscopy
- In Vivo physiology
- Pharmacology
- Explant Cultures
- Dissociated Primary Neuron Cultures
- Compartmented Chamber Cultures
- Behavioral analyses

# Motor Function in Aging and Age-Related Neurodegenerative Disease

## Principal Investigator

John A. Stanford, PhD

## Co-Investigators

Hongyu Zhang, PhD

Susan Smittkamp, PhD

Jill Morris

Heather Spalding

## Areas of Interest

Normal Aging

Parkinson's disease

Amyotrophic Lateral Sclerosis

Motor Effects of Drugs in the Elderly

## Training

BA – University of Mississippi (Psychology)

MA – University of Kansas (Psychology)

PhD – University of Kansas (Psychology)

Postdoc – University of Kentucky (Neurobiology of Aging)

# Projects

- Orolingual Motor Function in Normal Aging
- Bulbar and Spinal Motor Function in Rodent Models of ALS (Geiger & Nishimune)
- Isometric Force Control in Rat Model of PD
- Relationships between PD and Type II Diabetes (Geiger)
- Behavioral and Cross Tolerance to the Motor Effects of Benzodiazepines and Ethanol
- Electrophysiological Recording of Basal Ganglia Nuclei During Behavior in Rats (Imig)
- Force Training and Orofacial Motor Cortical Plasticity (Nudo)

# Approaches

Mostly Behavioral, but also:

Stereotaxic Procedures

HPLC-EC

Multi-Unit Electrophysiology

Some standard Molecular

Biology Techniques (e.g.,  
Western Blots, PCR)

# Doug Wright

# Peripheral Neuropathy



## Principal Investigator

Doug Wright, PhD  
Associate Professor  
Anatomy and Cell Biology

## Co-Investigators

Mamatha Pasnoor, MD  
Mazen Dimachkie, MD  
Richard Barohn, MD  
Paige Geiger, PhD  
Patty Kluding, PhD  
Wen Liu, PhD  
Ken McCarson, PhD  
Peter Smith, PhD

## Training

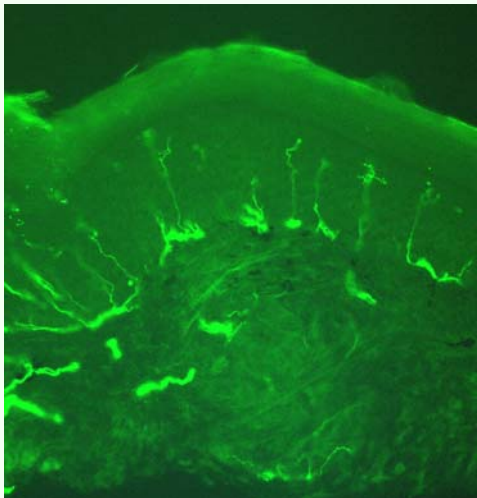
BS, Biology, Illinois State University  
PhD, Biology, University of Kentucky  
Post-doc, Neurology, Washington Univ.

## Areas of Interest

Peripheral Neuropathy  
Diabetes  
Neurotrophins  
Fibromyalgia  
Chronic Pain

# Projects & Approaches

- Modeling neuropathy in rodents
  - Diabetes-induced damage to epidermal axons
  - Diabetes-induced damage to muscle spindle axons
  - The role of neurotrophins in diabetic neuropathy



- Rodent surgery
- Neuronal tract-tracing
- Microarrays
- Laser capture microdissection
- PCR, nucleic acid techniques
- In situ hybridization
- Western Blots
- Peripheral nerve physiology
- Immunofluorescence
- Confocal microscopy
- Electron microscopy
- Pharmacology
- Behavioral analyses
- Drug delivery

# Fatty Acid Metabolism, Diabetes and Aging in Mice

## Principal Investigator

Hao Zhu, PhD

## Co-Investigators

WenFang Wang, PhD  
Susan Carlson, PhD  
Daniel J. Aires, MD  
Russell Swerdlow, MD  
In-young Choi, PhD  
David Alvertini, PhD  
Paige Geiger, PhD

## Training

Fudan University (China), BS  
University of Texas – Austin, PhD  
Harvard Medical School, postdoc

## Areas of Interest

Fatty Acid Metabolism  
Aging and Oxidative Stress  
Hormonal Influence on Diabetes

# Projects & Approaches

**Role of fatty acid metabolism in diabetes and lipoatrophy in the Ncb5or knock-out mice**

**Anti-aging in mice through antioxidant and intermittent fasting**

**Gender difference in fatty acid metabolism and diabetes**

- enzymatic assay
- cultured hepatocytes, islets, etc
- cellular ultrastructure (EM)
- molecular markers (microarray, qPCR, Western)
- lipid profiling (TLC and GC)
- ROS and GSH/GSSH (HPLC-EC)
- animal studies through dietary modulation, imaging, metabolic and behavior monitoring

# Neuromuscular Research Center

## Physician Scientists

- **Richard Barohn, MD – Professor & Chairman, Dept. of Neurology**
  - BA/MD – University of Missouri – Kansas City School of Medicine
  - Residency – Wilford Hall USAF Medical Center
  - Neuromuscular Fellowship – Ohio State University
  - Areas of interest – Neuromuscular (MND, MD, Neuropathies, NMJ)
- **Arthur Dick, MD – Professor & Director, MDA Clinic**
  - MD – University of Maryland School of Medicine
  - Residency – University of Kansas Medical Center
  - Neurology Research Fellow – University of Miami School of Medicine
  - Areas of interest - ALS
- **Mazen Dimachkie, MD – Professor & Director, Neuromuscular Section**
  - MD – American University of Beirut
  - Residency – UT –Health Science Center
  - EMG & Neuromuscular Disease Fellowship – UT-Health Science Center
  - Areas of interest – Neuromuscular (MND, MD, Neuropathies, NMJ)

# Neuromuscular Research Center

## Physician Scientists

- **April McVey, MD – Associate Professor & Director, ALSA Clinic**
  - MD – Baylor College of Medicine
  - Residency - Wilford Hall USAF Medical Center
  - Fellowship – California Pacific Medical Center
  - Areas of interest - ALS
- **Mamatha Pasnoor, MD – Assistant Professor & CoDirector, KUMC NP Center**
  - MD – Osmania Medical College, India
  - Residency – University of Kansas Medical Center
  - Neurophysiology Fellowship – University of Kansas Medical Center
  - Areas of interest - Neuropathy
- **Yunxia Wang, MD – Assistant Professor & Director, Neurology Clinic**
  - MD – Taishan Medical College in China
  - Residency – University of Kansas Medical Center
  - Neurophysiology Fellowship – University of Kansas Medical Center
  - Areas of interest – ALS, Myopathy

# Neuromuscular Research Projects

- **ALS**
  - Neuroimaging in ALS \*
  - Talampanel
  - Ceftriaxone
  - Lithium \*
  - Mirapex
  - DNA Banking in ALS
  - Dextromethorphan/Quinidine in Pseudobulbar Affect
- **Neuropathy**
  - CSPN
  - Exercise
  - VEGF
  - CIDP Database
  - IVIG in MMN
  - MMN Substudy – NCV \*
  - CIDP database
  - Autonomic neuropathy- orthostatic hypotension
- **MG**
  - Eculizimab in MG
  - Methotrexate in MG \*
- **IBM**
  - Arimoclomol \*
  - Microarray Gene Substudy\*
- **Myositis/Myopathy**
  - Etanercept in DM \*
  - Rituximab in DM/PM
  - Medi 545 in DM
  - International Myositis Classification Criteria
  - SNP analysis in myositis
- **Muscular Dystrophy**
  - Gentamicin in DMD
  - PTC 124 in DMD & Beckers
  - Myozyme in Pompe
- **Channelopathies**
  - CINCH \* U54RR019482
  - Mexiletine in NDM \* R01FDR03454
  - HYP/HOP

# Essential Team Members / Collaborators

- **Neuromuscular/ CN Fellows**

- Faisal Raja, MD
- Farhan Ahmed, MD
- Srinivas Bandi, MD

- **Research Coordinators**

- Laura Herbelin, BS – Research Instructor, CCRP
- Victoria Watts, RN – CCRP
- Sheri Copeland, RN

- **Research Assistants**

- Maureen Walsh
- Mimi Michaels

- **Clinical Evaluators**

- Alham Al-Sharmen, PT

- **Current Collaborators:**

- Doug Wright, PhD  
Neuropathy
- Patty Kluding, Ph.D  
Neuropathy
- Richard McCallum, MD  
Neuropathy
- Peter Smith, Ph.D.  
IBM
- Phil Gallagher, Ph.D.  
IBM
- Stan Svojanovsky, Ph.D.  
IBM

- **Future Collaborators:**

- Paige Geiger, Ph.D  
ALS
- John Stanford, Ph.D.  
ALS
- Wen Liu, Ph.D.  
ALS

# Others...

- Heather Anderson
- Andrei Belousov
- Jeff Burns
- Merlin Butler
- In Young Choi
- Rick Dobrowsky
- Rich Dubinsky
- Patricia Kluding
- Robb Krumlauf
- Sang Pil Lee
- Steve Levine
- Wen Liu
- Sharon Lynch
- Kelly Lyons
- Eli Michaelis
- Mary Michaelis
- Jules Nazzaro
- Kathy Newell
- Isaac Onyango
- Raj Pahwa
- WenFang Wang
- Ron Yu

Thank You!