NIAMS Research – Focus on Genomics and Genetics

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National Human Genome Research Institute
Council Meeting
September 19, 2022
Outline

• NIAMS Overview

• Selected NIAMS Advances in Genomics and Genetics

• Ongoing Programs and Opportunities for Collaboration
NIAMS Overview—Mission

- **Support research** into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases
- **Train basic and clinical scientists** to carry out this research
- **Disseminate information** on research progress in these diseases
NIAMS Overview

- Established in 1986
  - Previously part of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (now the National Institute of Diabetes and Digestive and Kidney Diseases)

- Mission
  - Research
  - Training
  - Information Dissemination

- FY 2022 Budget = $656 Million
NIAMS Overview—FY 2021 Budget

NIH Total Budget: $42.812 Billion

NIAMS Total Budget: $632 Million

Extramural 80.4%
Intramural 10.7%
RMS 4.8%
All Other 4.1%
2020-24 Strategic Plan—Five Disease- and Tissue-Specific Sections

- Rheumatic and Autoimmune Diseases
- Skin Biology and Diseases
- Bone Biology and Diseases
- Muscle Biology and Diseases
- Joint Biology and Diseases and Orthopaedics
2020-24 Strategic Plan—Cross-cutting Themes

- **Shared mechanisms** in health and among diseases
- **Patient-centric approaches** to health and disease
- **Precision medicine** for arthritis and musculoskeletal and skin diseases
- **Health and disease** in diverse populations

Help Create the NIAMS 2025-2029 Strategic Plan

• Request for Information (NOT-AR-22-023, until Nov. 30)
  • Cross-cutting thematic research opportunities
  • Bold aspirations

• Broad community input essential to
  • Improve research
  • Ensure representation of all
  • Address health disparities and health equity

https://rfi.grants.nih.gov/?s=62acc588887e00004c006a82
NIAMS Advances in Genetics—Dux4 in Facioscapulohumeral Dystrophy

• In 2010, discovered the genetic and molecular mechanism of FSHD—abnormal expression of transcription factor Dux4 in adult muscles

• Improved understanding of disease mechanisms and variability
  • Additional mutations on other chromosomes
  • Epigenetic repression of Dux4 in 95% of muscle fibers

• Developing gene therapy approaches, together with new imaging techniques to identify and target affected muscles
NIAMS Advances in Genetics—VEXAS Syndrome

- Adult-onset inflammatory disease
- Identified in 2020 by NIAMS and NHGRI scientists with international team
- Genome-first approach – caused by mutation in UBA1 gene

Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic
NIAMS Advances in Genetics—
Genome Research in African American Scleroderma Patients (GRASP) Consortium

• Large cohort of African-American scleroderma patients

• Identification of ancestry-specific variants that contribute to increased disease risk and severity in African-Americans

• Collaboration between NIAMS, NHGRI, intramural and extramural researchers – 25 centers across US
Opportunities: Team Science
Accelerating Medicines Partnership®

AMP Alzheimer’s Disease (AD) ‘1.0’ Project A: Biomarkers
AMP AD ‘1.0’ Project B: Target Discovery and Preclinical Validation
AMP Type 2 Diabetes
AMP RA/SLE
AMP Parkinson’s Disease
AMP Common Metabolic Diseases
AMP AIM
AMP Alzheimer’s Disease (AD) ‘2.0’
AMP Schizophrenia
AMP Bespoke Gene Therapy Consortium
AMP Heart Failure

Over $772M in financial and in-kind contributions
15 NIH Institutes/Centers
28 Industry Partners
29 Non-Profits

AMP® Autoimmune and Immune-Mediated Diseases (AMP® AIM) Goals

• Index and map cells and pathways in
  • Psoriasis and psoriatic arthritis
  • Sjögren’s disease
  • Rheumatoid arthritis
  • Systemic lupus erythematosus

• Discover how these pathways and cells interact through new analytics in different diseases to identify specific and shared disease mechanisms
Accelerating Medicines Partnership®

AMP Alzheimer’s Disease (AD) ‘1.0’ Project A: Biomarkers

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AMP Type 2 Diabetes

AMP RA/SLE

AMP AIM

AMP Parkinson’s Disease

AMP Common Metabolic Diseases

AMP Schizophrenia

AMP Bespoke Gene Therapy Consortium

AMP Heart Failure

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AMP Bespoke Gene Therapy Consortium

• Generate a streamlined clinical and regulatory framework for gene therapy
• Four areas related to developing gene therapies:
  • basic research
  • clinical research
  • manufacturing and production
  • regulatory requirements

fnih.org/BGTC
# Bespoke Gene Therapy Consortium

<table>
<thead>
<tr>
<th>Disease Name (pseudonym)</th>
<th>Affected Gene</th>
<th>BGTC Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital hereditary endothelial dystrophy (CHED)</td>
<td>SLC4A11</td>
<td>Eye / Cornea</td>
</tr>
<tr>
<td>MPS VI corneal disease</td>
<td>ARSB</td>
<td>Eye / Cornea</td>
</tr>
<tr>
<td>Leber congenital amaurosis 16 (LCA16)</td>
<td>KCNJ13</td>
<td>Eye / Retina</td>
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<tr>
<td>Retinitis pigmentosa (RP) - CNGB1</td>
<td>CNGB1</td>
<td>Eye / Retina</td>
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<tr>
<td>NPHP5-RD</td>
<td>NPHP5</td>
<td>Eye / Retina</td>
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<tr>
<td>Charcot Marie tooth disease type 4J (CMT4J)</td>
<td>FIG4</td>
<td>Neurological</td>
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<tr>
<td>Multiple sulfatase deficiency</td>
<td>SUMF1</td>
<td>Neurological</td>
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<tr>
<td>Spastic paraplegia, type 47 (SPG47)</td>
<td>AP4B1</td>
<td>Neurological</td>
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<tr>
<td>Spastic paraplegia 50 (SPG50)</td>
<td>AP4M1</td>
<td>Neurological</td>
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<td>Barth syndrome</td>
<td>TAZ</td>
<td>Cardiac</td>
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<tr>
<td>PGM1-congentital disorder of glycosylation (CDG) (PGM1 deficiency)</td>
<td>PGM1</td>
<td>Inborn error of metabolism</td>
</tr>
<tr>
<td>Propionic acidemia</td>
<td>PCCB</td>
<td>Inborn error of metabolism</td>
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<tr>
<td>Fibrodysplasia ossificans progressiva (FOP)</td>
<td>ACVR1</td>
<td>Orthopaedic</td>
</tr>
<tr>
<td>Mucopolysaccharidosis IVA (MPS IVA, Morquio A syndrome)</td>
<td>GALNS</td>
<td>Orthopaedic</td>
</tr>
</tbody>
</table>
Approved Concept: Systems Biology of Inflammation

- Integration and Collaboration
  - Across Research Teams
  - Across Platforms
  - Across Diseases
  - Across NIH Institutes, Centers, and Offices

Patient: Clinical Phenotype and PROs

Systems Biology of Diseases

Mediator Interactomes: Proteomics, Metabolomics, Lipidomics

Cellular Interactomes: Tissue Spatial Transcriptomics

- Genetics
- Epigenetics
- Transcriptomics

Environment, including Microbiome

Behavior & Psychosocial Interactions
Regenerative Medicine

• Regenerative Medicine Innovation Project

• Cartilage Preservation and Restoration in Knee OA Roundtable
  (September 22, on videocast)
Opportunity: Data Science

• New NIH data sharing policy, effective January 2023

• Training data scholars

• NIAMS Data Science Strategy Working Group
NIAMS Data Science WG Infographic

NIAMS Data Science Strategic Plan

01- Needs of investigators to meet new policy and requirements
02- Criteria to identify high value datasets
03- Data Infrastructure (Repositories vs Knowledgebase) & Security Data Interoperability
04- Scientific opportunities on data science, AI/ML
05- Workforce
06- Fostering a culture of data sharing

Council DSWG

01- Guidance and Resources for Investigators
02- Targeted portfolio searches to identify HVD
03- Language for awards, solicitations, SOPs
04- Leverage resources and partnerships
05- Training
06- Shared knowledge platform and tools

Data Scholar
Planning and Implementation Group
NIAMS
NIAMS Data Science Strategy Working Group

• **Charge:** Provide general guidance to the NIAMS on opportunities in data science, big data, and bioinformatics to further arthritis and musculoskeletal and skin disease insights

• **Potential areas for targeted recommendations**
  ✓ Investigators’ needs to meet new data sharing and management policies
  ✓ NIAMS role in fostering a culture of data sharing
  ✓ Data infrastructure, data interoperability and security
  ✓ Criteria to identify high value datasets
  ✓ Training and workforce
  ✓ AI/ML scientific opportunities
  ✓ Leveraging lessons learned and NIH and community resources
QUESTIONS