NIAMS Research – Focus on Genomics and Genetics

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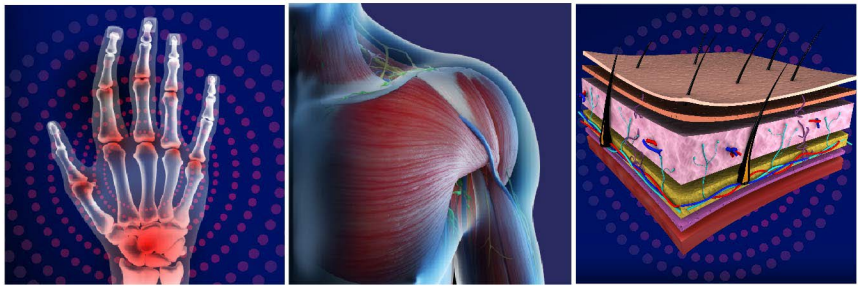


National Human Genome Research Institute
Council Meeting
September 19, 2022

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Outline

- NIAMS Overview
- Selected NIAMS Advances in Genomics and Genetics
- Ongoing Programs and Opportunities for Collaboration

NIAMS Overview—Mission

Research

Training

Dissemination

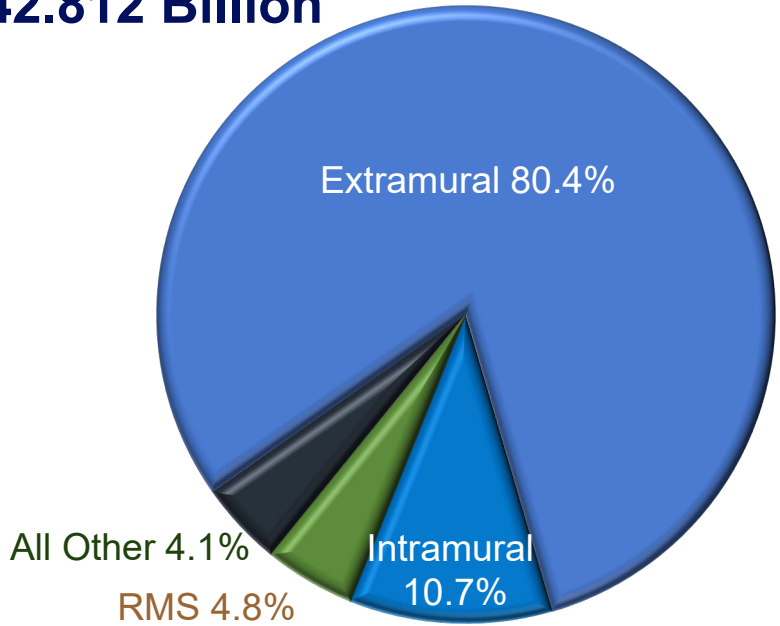
- **Support research** into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases
- **Train basic and clinical scientists** to carry out this research
- **Disseminate information** on research progress in these diseases

NIAMS Overview

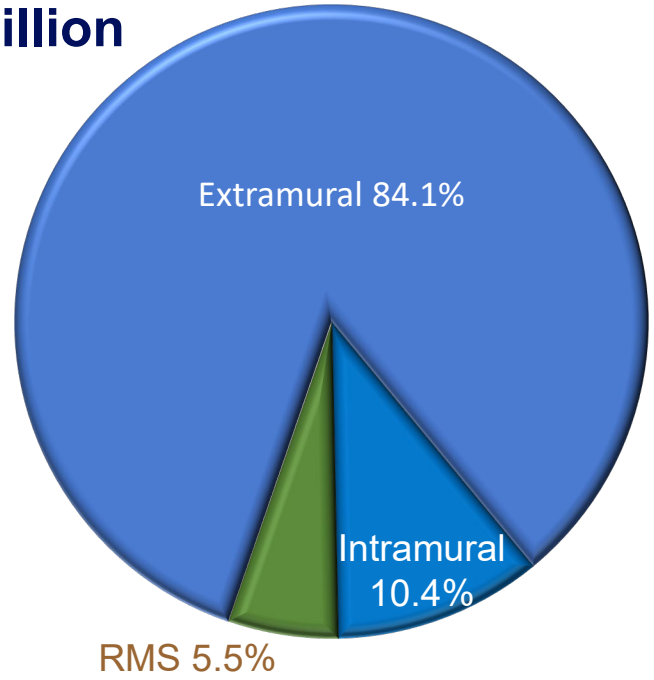
- **Established in 1986**
  - Previously part of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (now the **National Institute of Diabetes and Digestive and Kidney Diseases**)
- **Mission**
  - Research
  - Training
  - Information Dissemination
- **FY 2022 Budget = $656 Million**

NIAMS Overview—FY 2021 Budget

NIH Total Budget: $42.812 Billion



NIAMS Total Budget: $632 Million

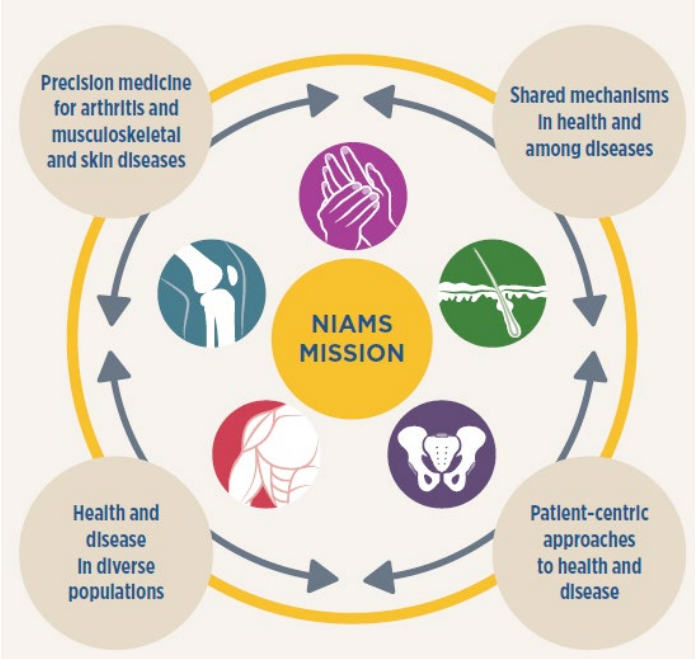


2020-24 Strategic Plan—Five Disease- and Tissue-Specific Sections

- 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

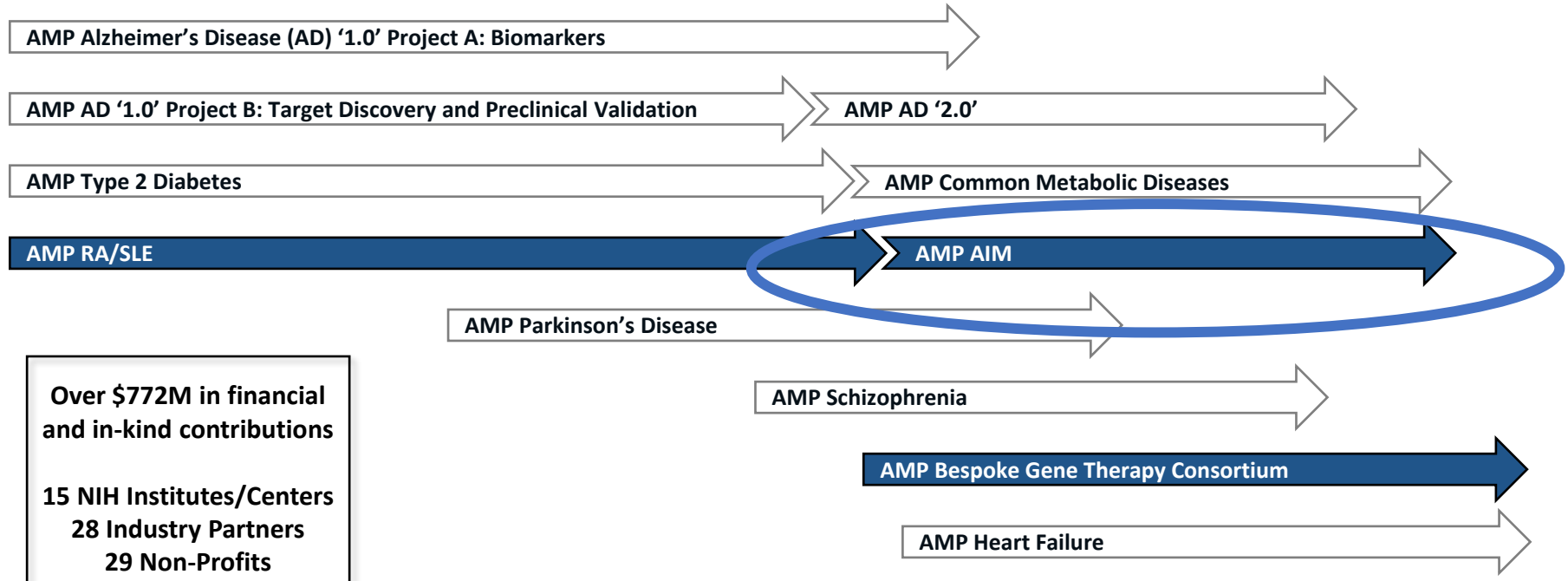
Vacuoles
E1 enzyme,
X-linked
Autoinflammatory
Somatic

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®

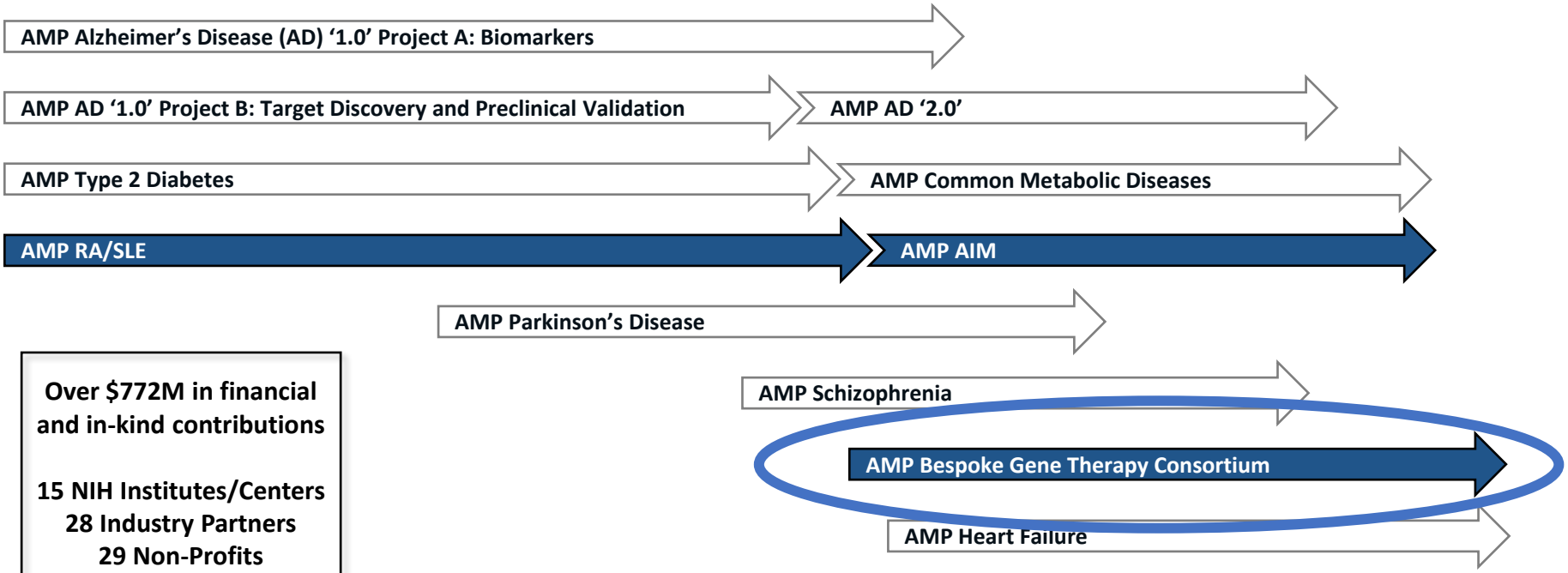


AMP® Autoimmune and Immune-Mediated Diseases (AMP® AIM) Goals

- **Index and map cells and pathways in**
  - Psoriasis and psoriatic arthritis
  - Sjögren's disease
  - Rheumatoid arthritis
  - Systemic lupus erythematosus

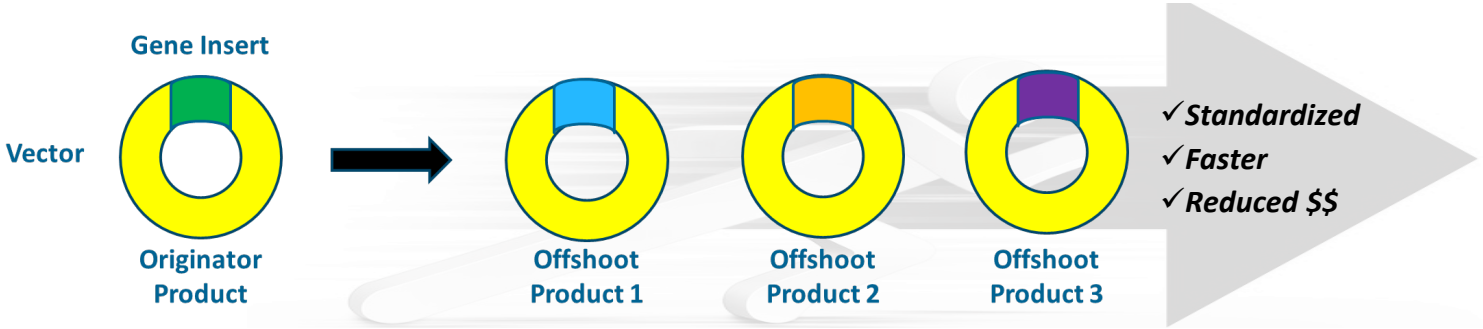
- **Discover how these pathways and cells interact through new analytics in different diseases to identify *specific and shared disease mechanisms***

Accelerating Medicines Partnership®



AMP Bespoke Gene Therapy Consortium

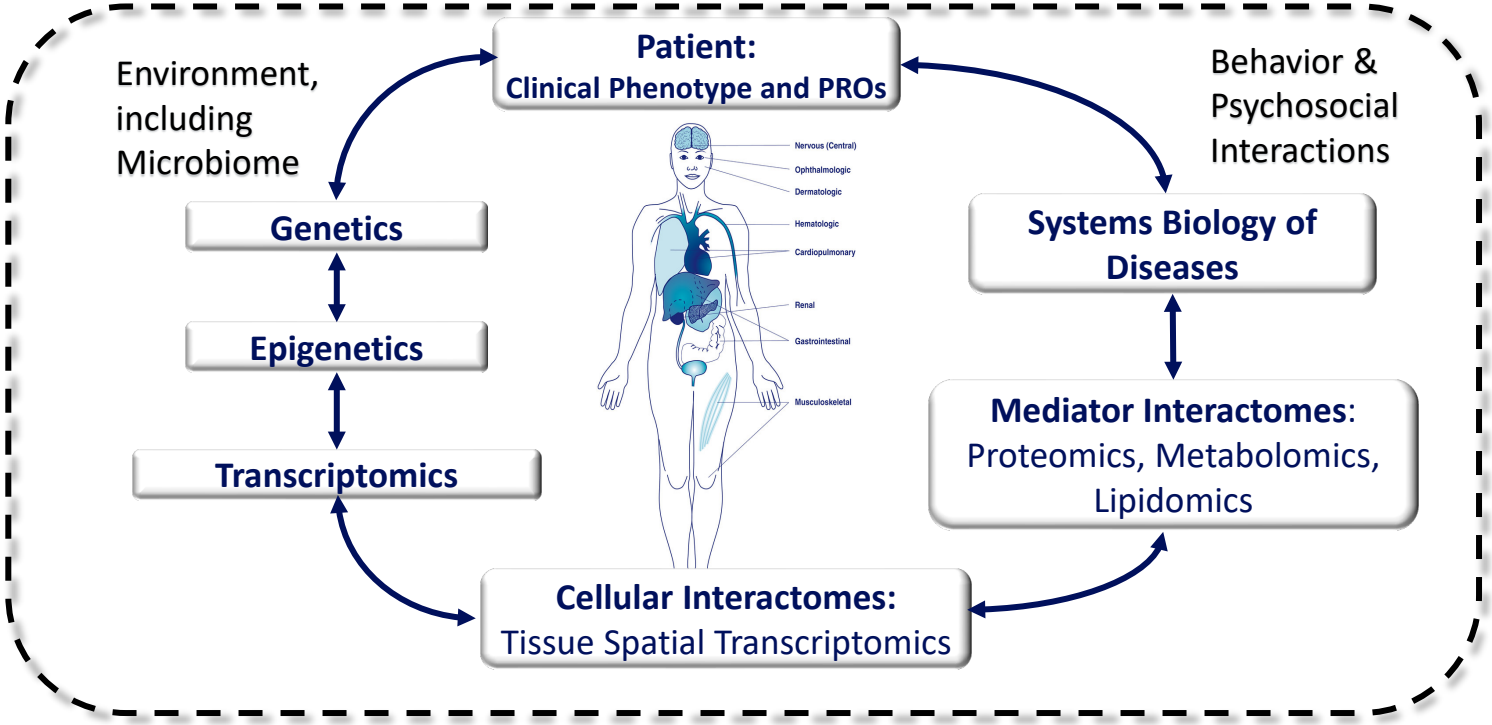
- Generate a streamlined clinical and regulatory framework for gene therapy
- Four areas related to developing gene therapies:
  - basic research
  - clinical research
  - manufacturing and production
  - regulatory requirements



Bespoke Gene Therapy Consortium

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

Approved Concept: Systems Biology of Inflammation



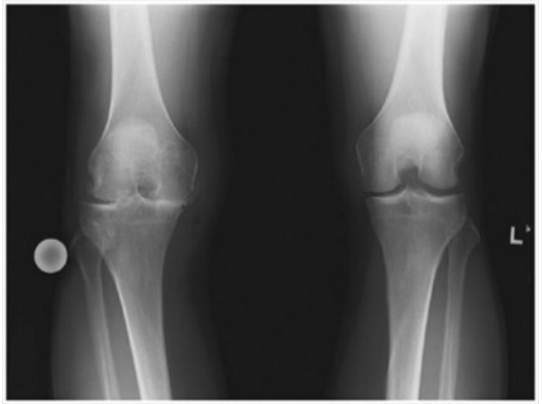
Integration and Collaboration

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

Regenerative Medicine

- Regenerative Medicine Innovation Project

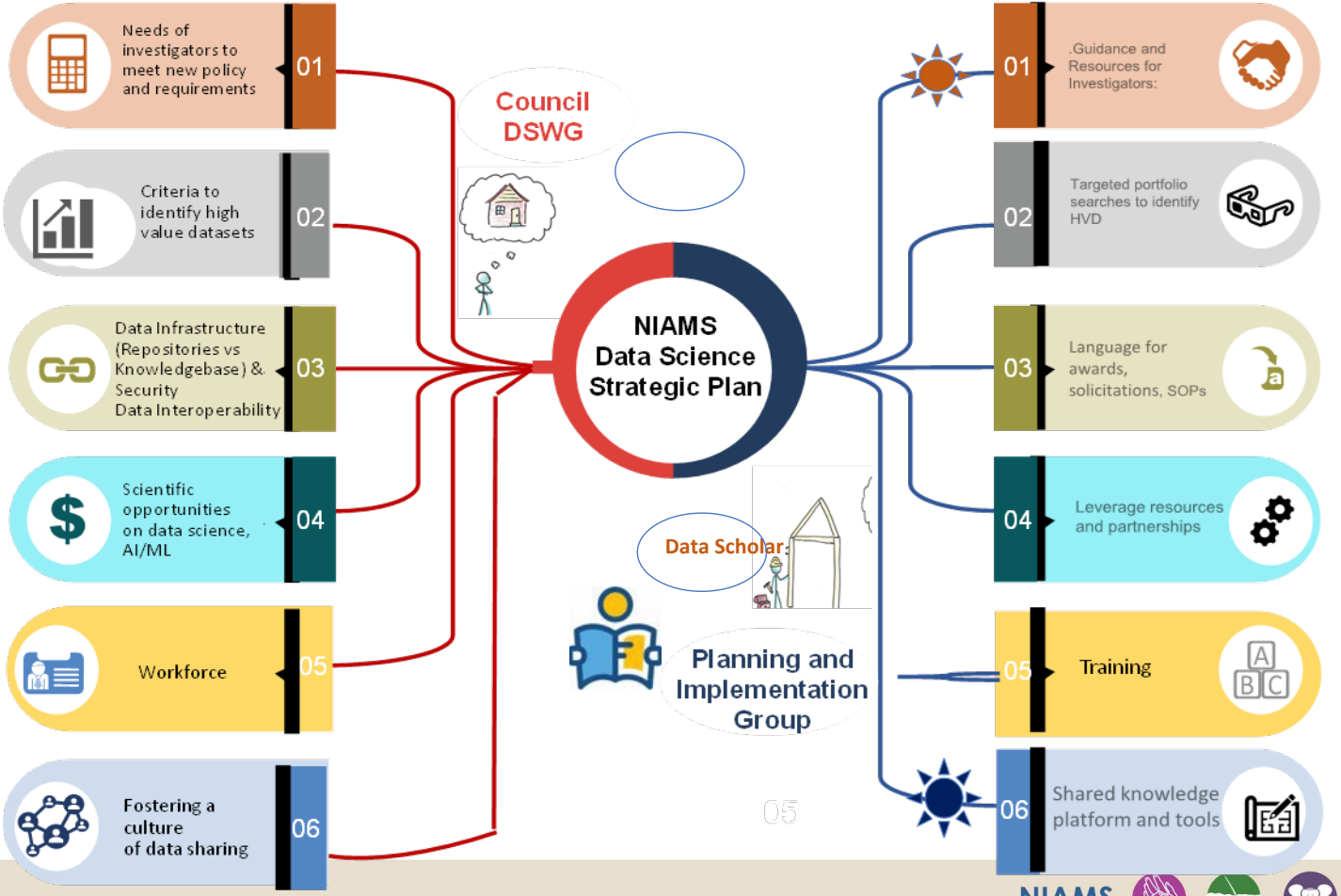
- Cartilage Preservation and Restoration in Knee OA Roundtable
  (September 22, on videocast)



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

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

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QUESTIONS