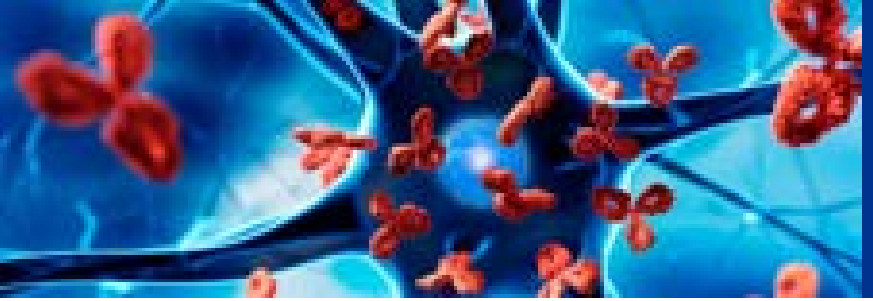


Autoimmune Disease Research

Victoria Shanmugam, MBBS, MRCP, FACR, CCD

Director, Office of Autoimmune Disease Research

National Institutes of Health
Office of Autoimmune Disease Research
Office of Research on Women's Health

Facebook: /NIHORWH
Twitter: @NIH_ORWH

OADRInfo@nih.gov
orwh.od.nih.gov/OADR-ORWH

AUTOIMMUNE DISEASES

- Occur when immune system which normally defends against infection attacks healthy tissues and organs
- May be acute or chronic
- Includes more than 140 diseases
- Affect more than 23.5 million Americans

EPIDEMIOLOGY

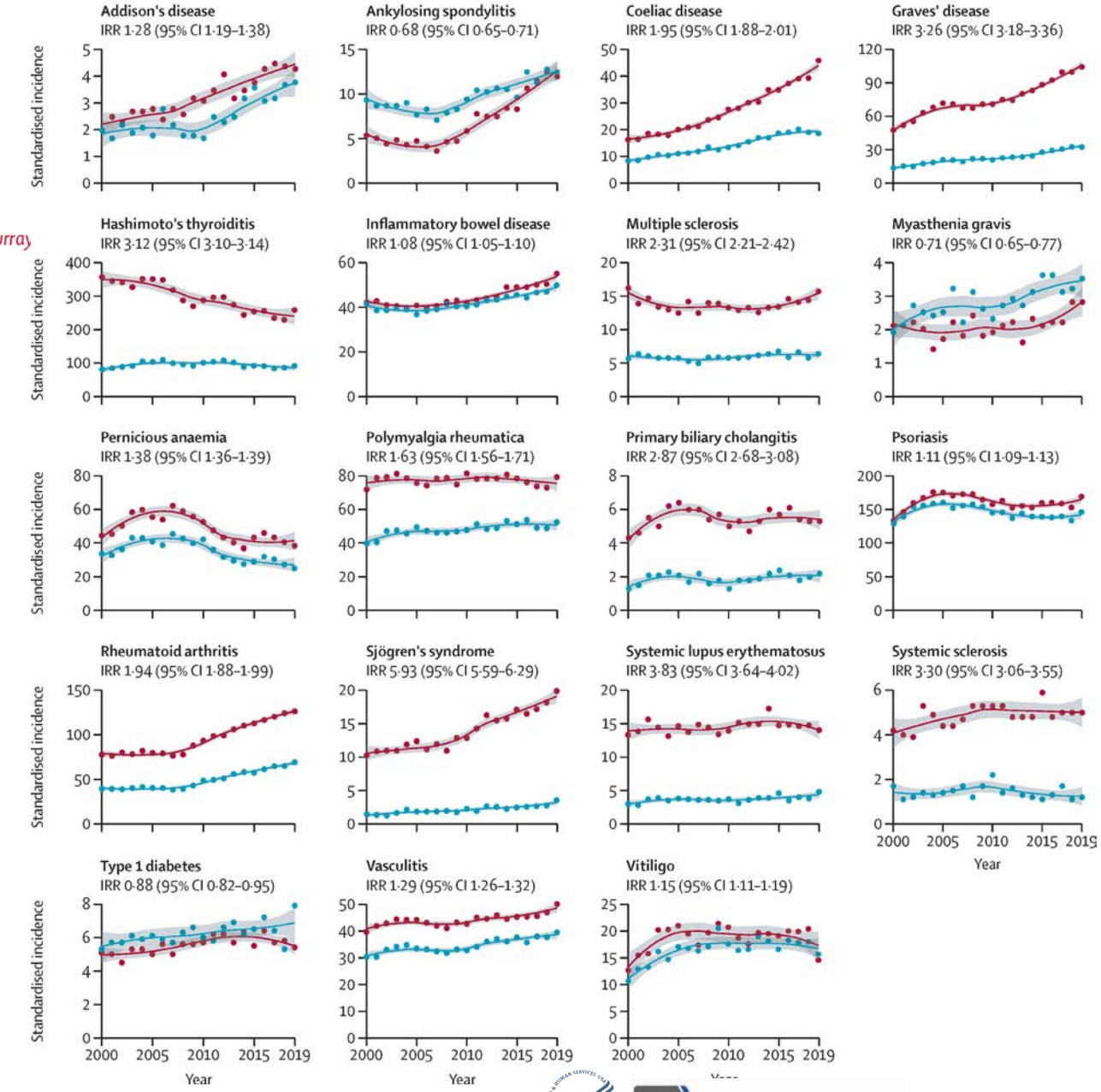
- Autoimmune diseases affect 7-8% of population
- Approximately 23.5 million Americans affected by autoimmune diseases
- Nearly 80% of people with autoimmune diseases are women
- Four times more women than men are affected by autoimmune diseases

Exact prevalence of autoimmune disease in the US is unknown due to lack of longitudinal data repositories

Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK

Nathalie Conrad, Shivani Misra, Jan Y Verbakel, Geert Verbeke, Geert Molenberghs, Peter N Taylor, Justin Mason, Naveed Sattar, John J V McMurray, Iain B McInnes, Kamlesh Khunti, Geraldine Cambridge

- New diagnosis of autoimmune disease occurred in 4.45% of individuals over ~20 yrs
- 19 autoimmune diseases studied
- Affected 10.2% of population
- Prevalence rates increased over time



Lancet 2023; 401 (10391):1878-90

Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK

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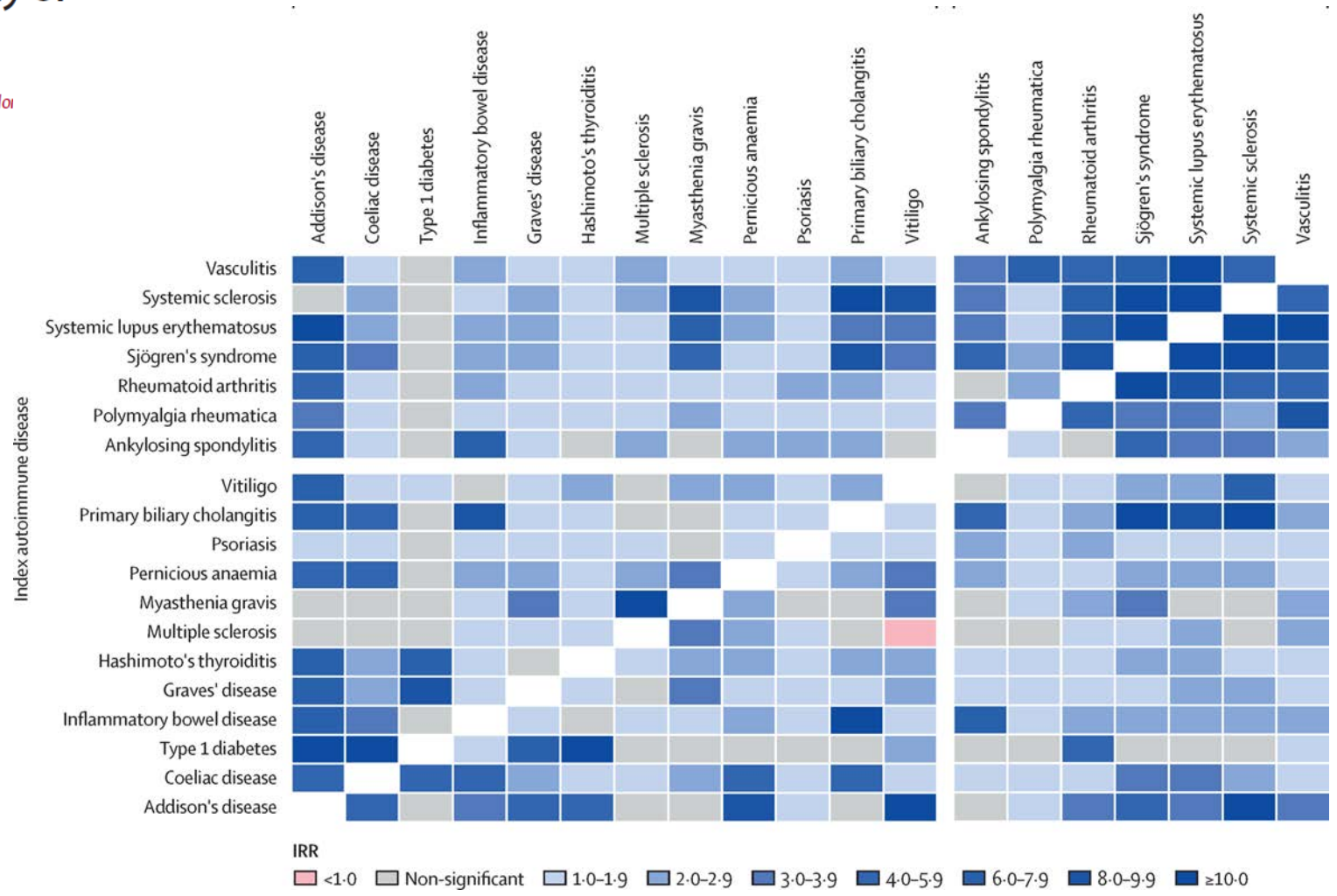
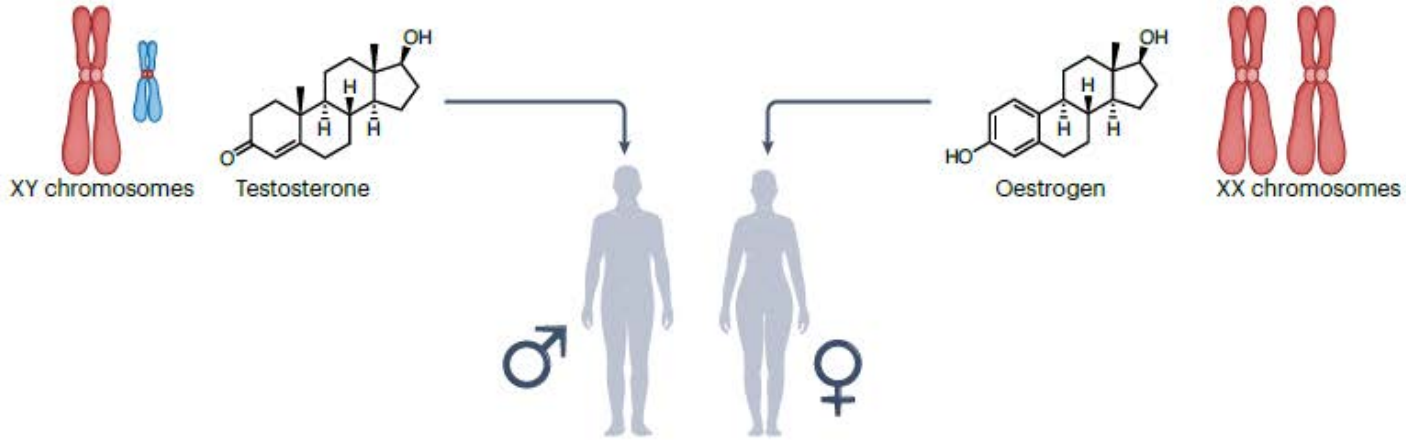


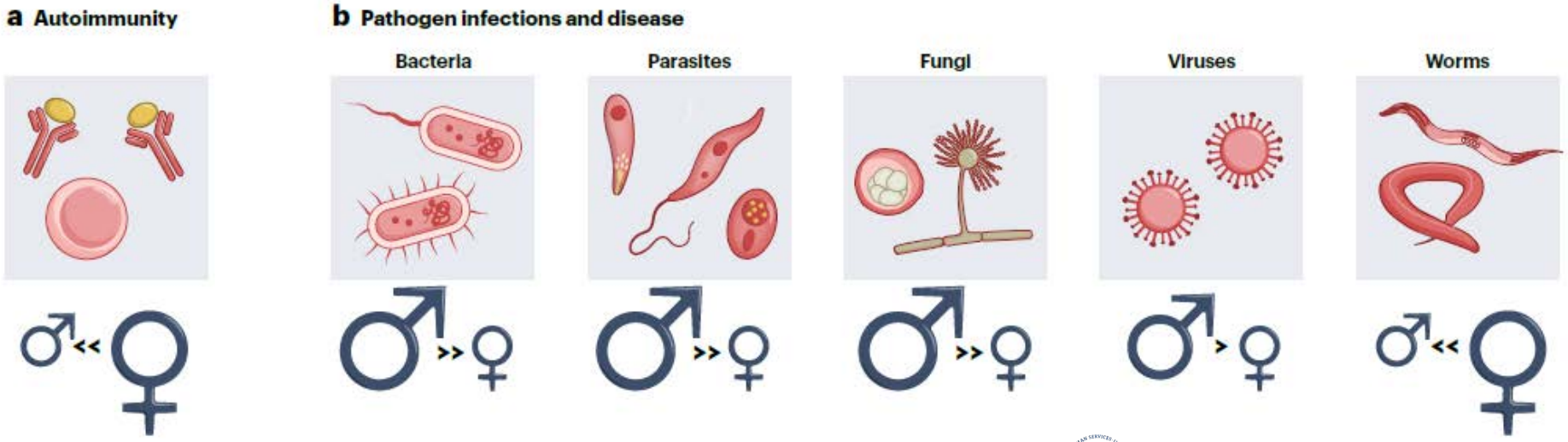
Lancet 2023; 401 (10391):1878-90

Review article

The conneXion between sex and immune responses

Katherine S. Forsyth[1], Nikhil Jiwrajka[1,2], Claudia D. Lovell[1], Natalie E. Toothacre[1] & Montserrat C. Anguera[1]





Nat Rev Immunol 2024, Feb 21

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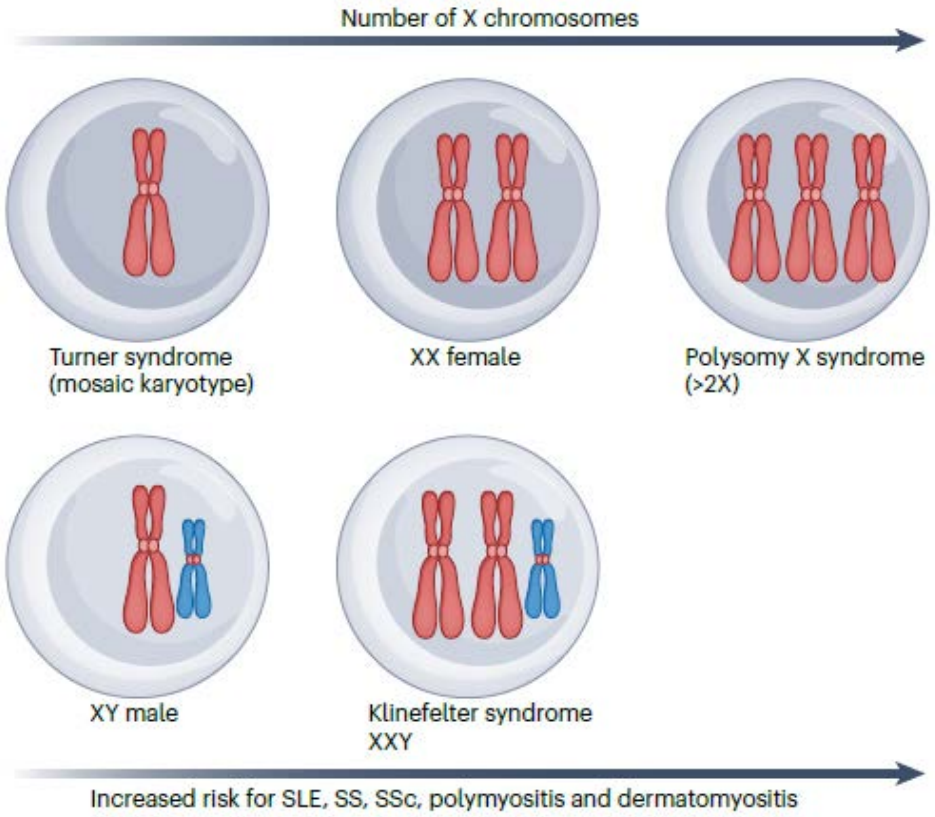
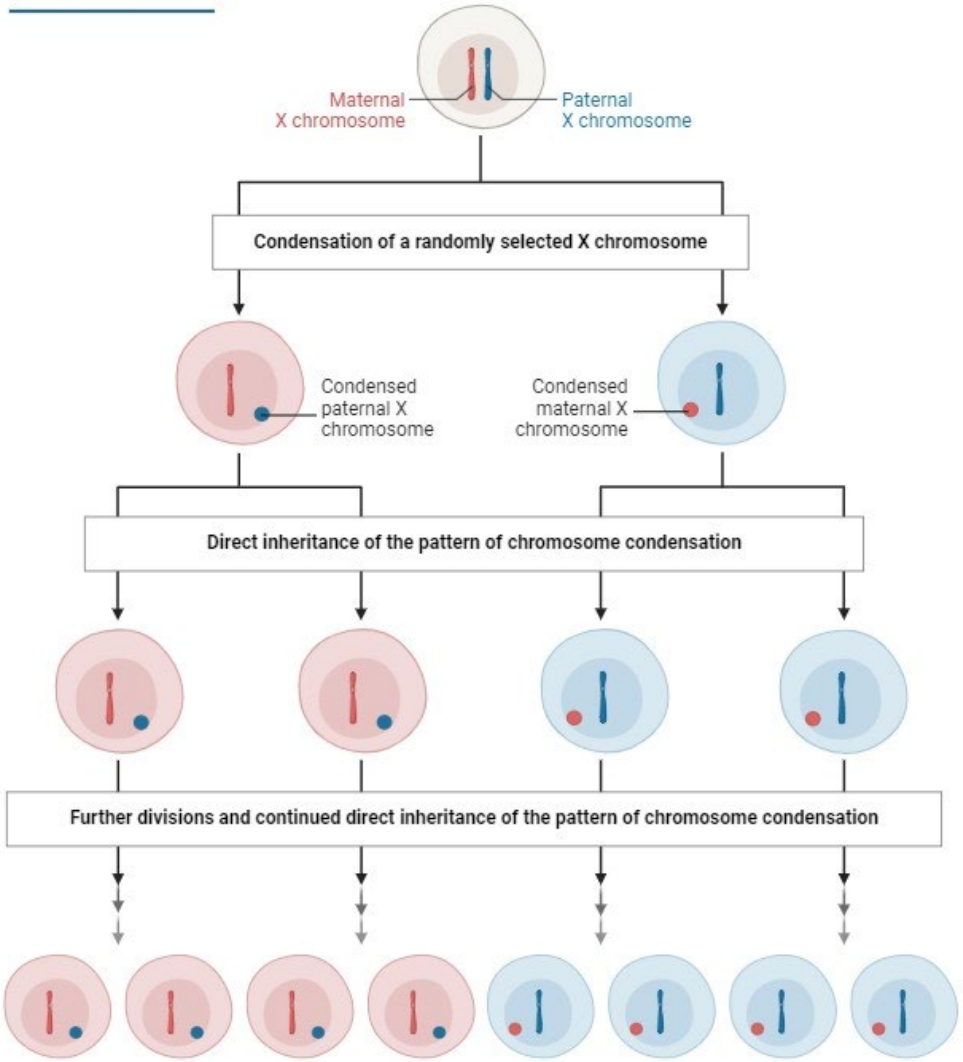


Autoimmune disease	Prevalence in the USA (per 100,000 people)	Incidence in the USA (per 100,000 person-years)	Sex bias (% of affected individuals who are female)
Systemic lupus erythematosus	5–241 (ref. 131)	1.0 – 23.2 (ref. 131)	66–93 (ref. 131) 83.71 (ref. 60)
Sjögren syndrome	22–103 (ref. 132)	3.9 (ref. 133)	90.54 (ref. 60) 96.2 (ref. 133)
Systemic sclerosis (scleroderma)	27.6 (ref. 134)	1.93 (ref. 134)	83.7 (ref. 134) 75–93.5 (ref. 135) 83.80 (ref. 60)
Inflammatory myopathies: polymyositis and dermatomyositis	6.3 (ref. 67)	0.116–0.6 (ref. 67)	65.08 (ref. 60) 60–75 (ref. 67)
Rheumatoid arthritis	1,070 (ref. 136) 1,000 (ref. 67)	75.3 (ref. 136)	73.4 (ref. 136)

Nat Rev Immunol 2024, Feb 21

X-inactivation



Review article

Check for updat

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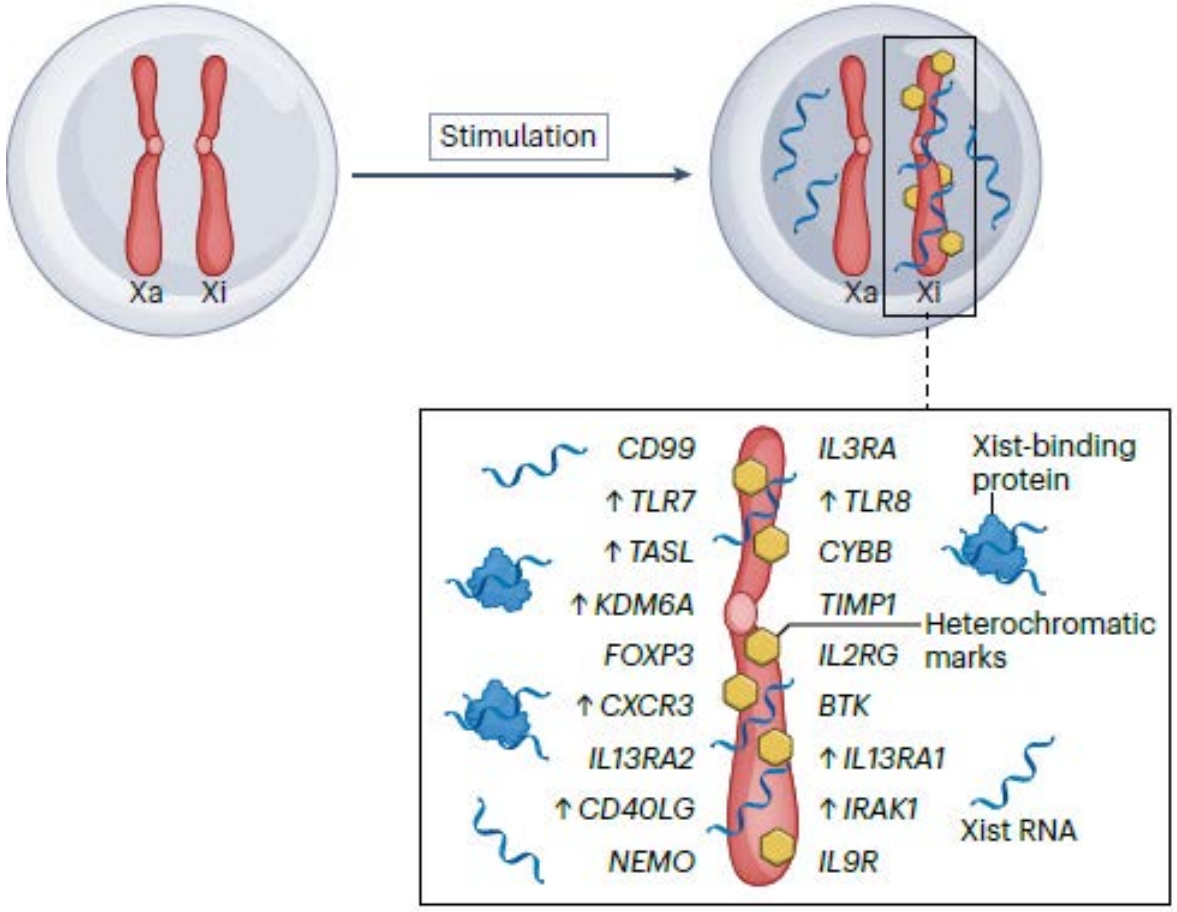


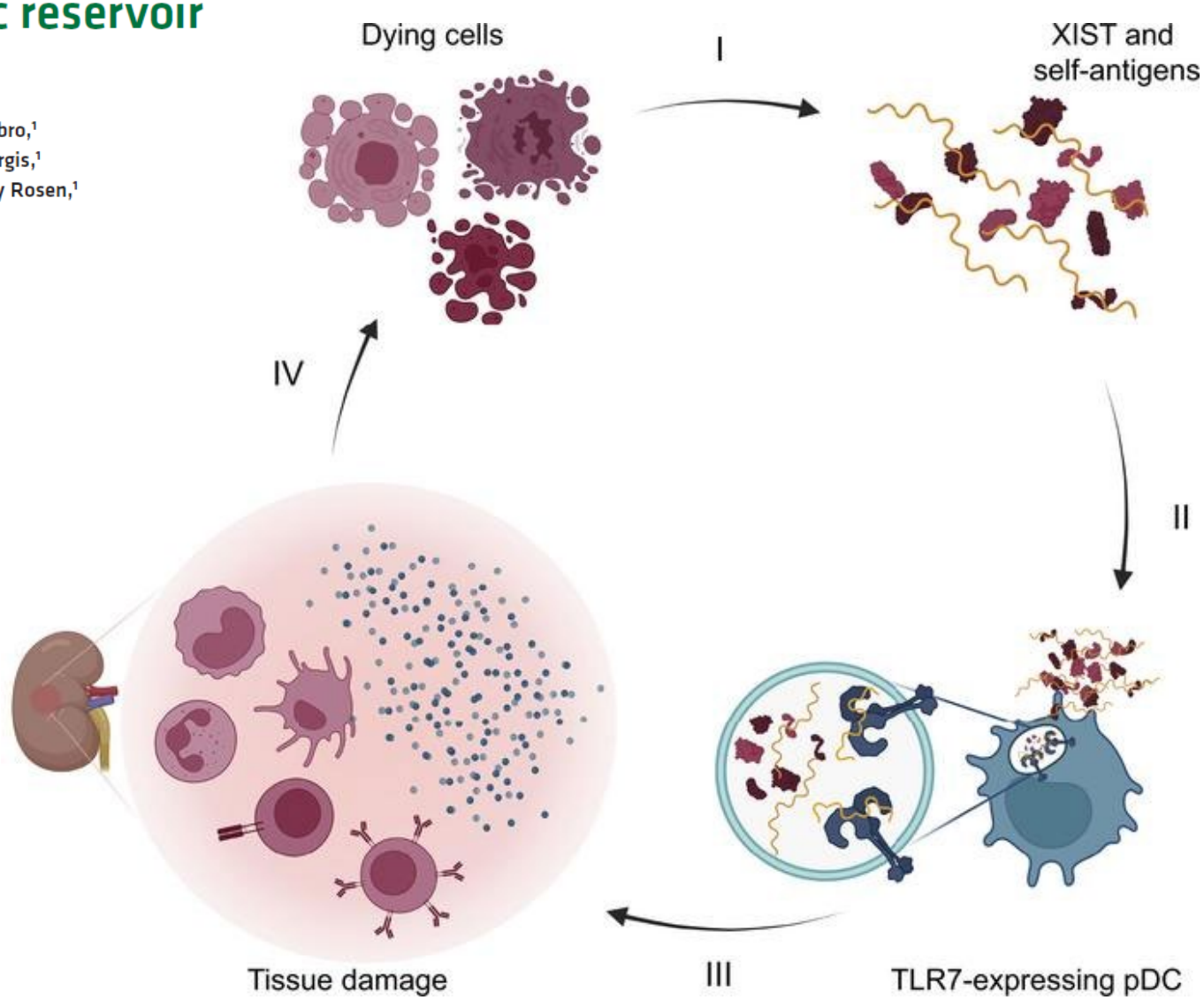
Nat Rev Immunol 2024, Feb 21

JCI insight

RESEARCH ARTICLE

The XIST lncRNA is a sex-specific reservoir of TLR7 ligands in SLE

Jonathan D. Crawford,[1] Hong Wang,[1] Daniela Trejo-Zambrano,[1] Raffaello Cimbro,[1] C. Conover Talbot Jr.,[2] Mekha A. Thomas,[1] Ashley M. Curran,[1] Alexander A. Girgis,[1] John T. Schroeder,[3] Andrea Fava,[1] Daniel W. Goldman,[1] Michelle Petri,[1] Antony Rosen,[1] Brendan Antiochos,[1] and Erika Darrah[1]



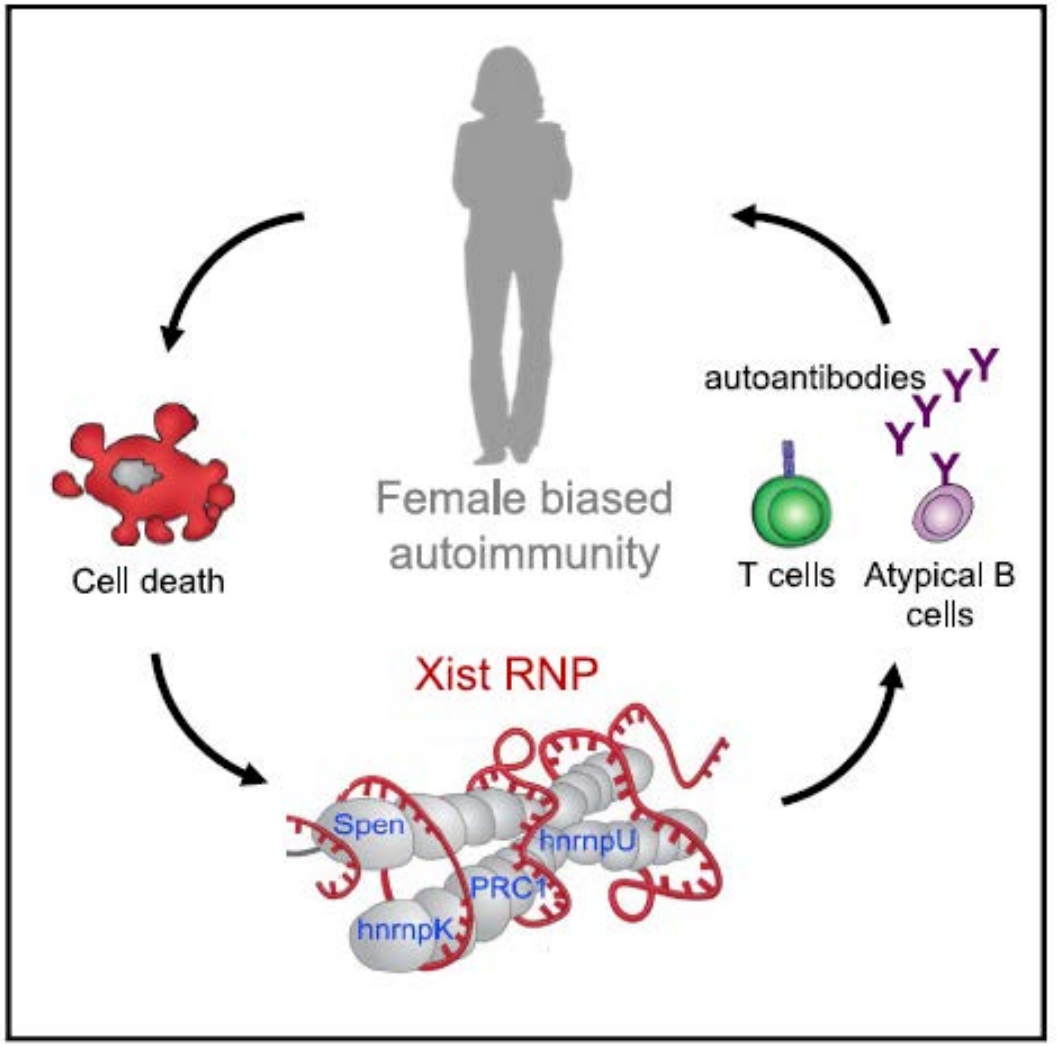
JCI Insight. 2023;8(20):e169344

Cell

Article

Xist ribonucleoproteins promote female sex-biased autoimmunity

Diana R. Dou, Yanding Zhao,
Julia A. Belk, ..., Anton Wutz, Paul J. Utz,
Howard Y. Chang



Cell 187(3):733-749

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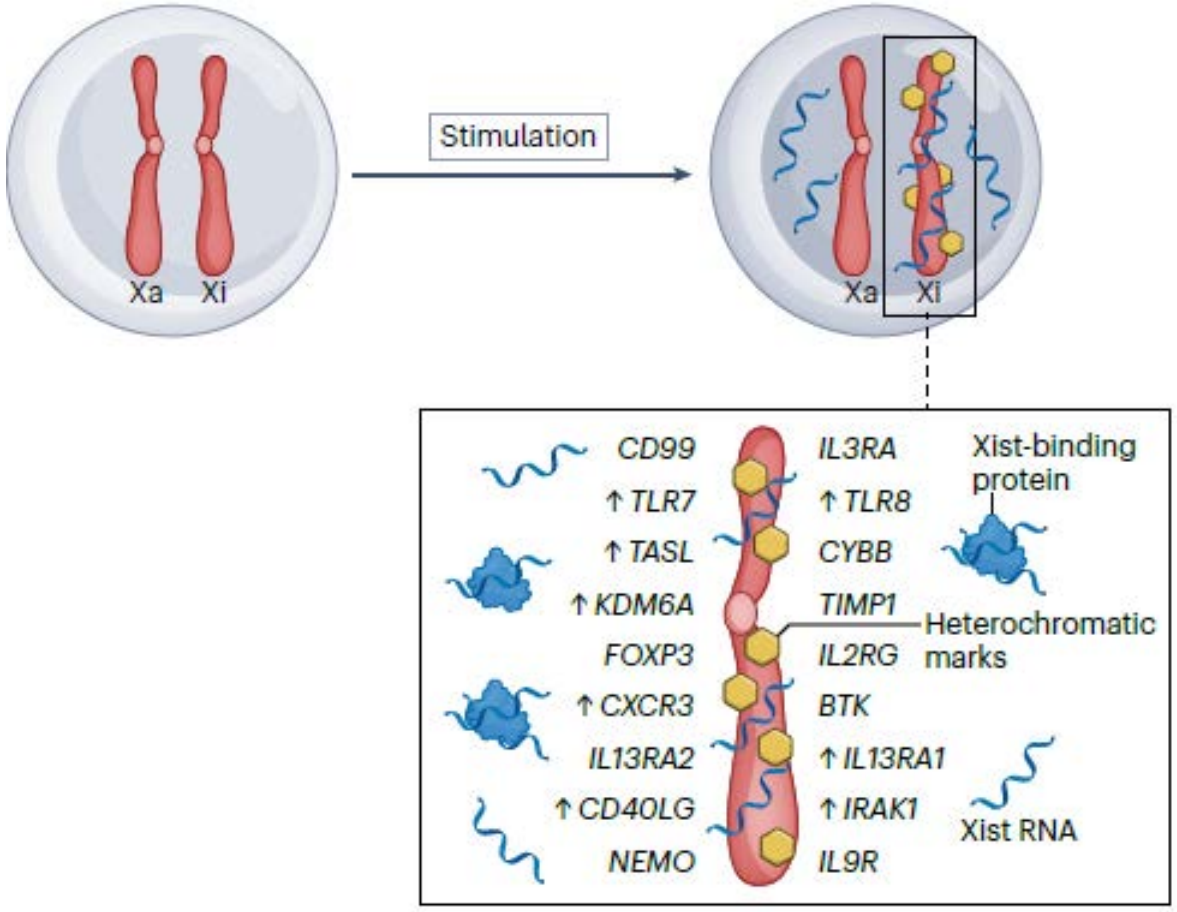


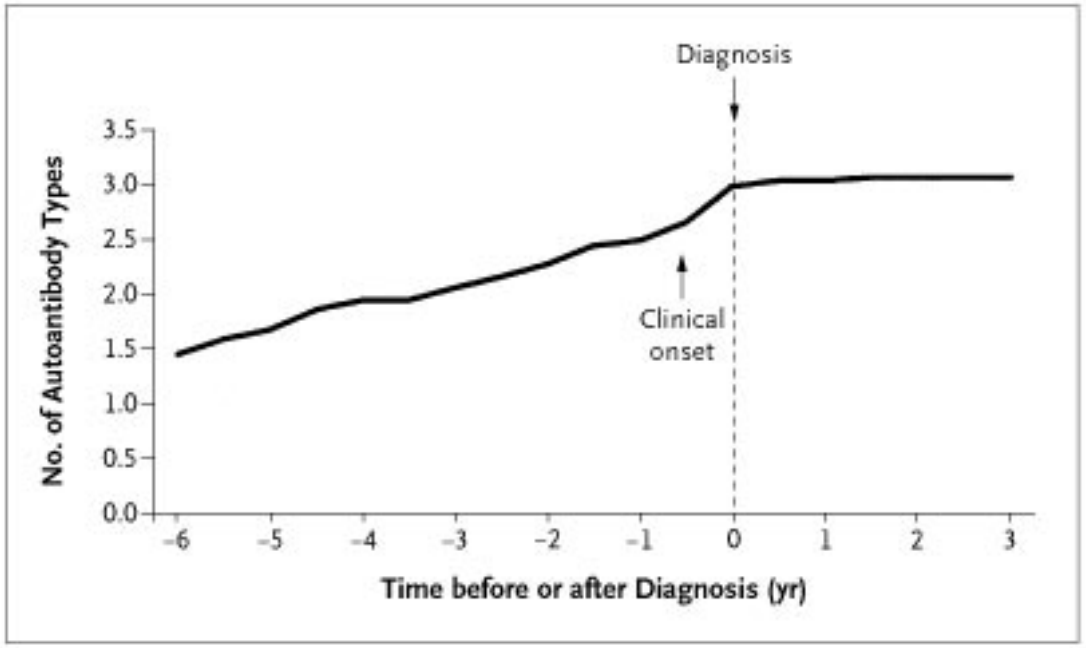
Nat Rev Immunol 2024, Feb 21

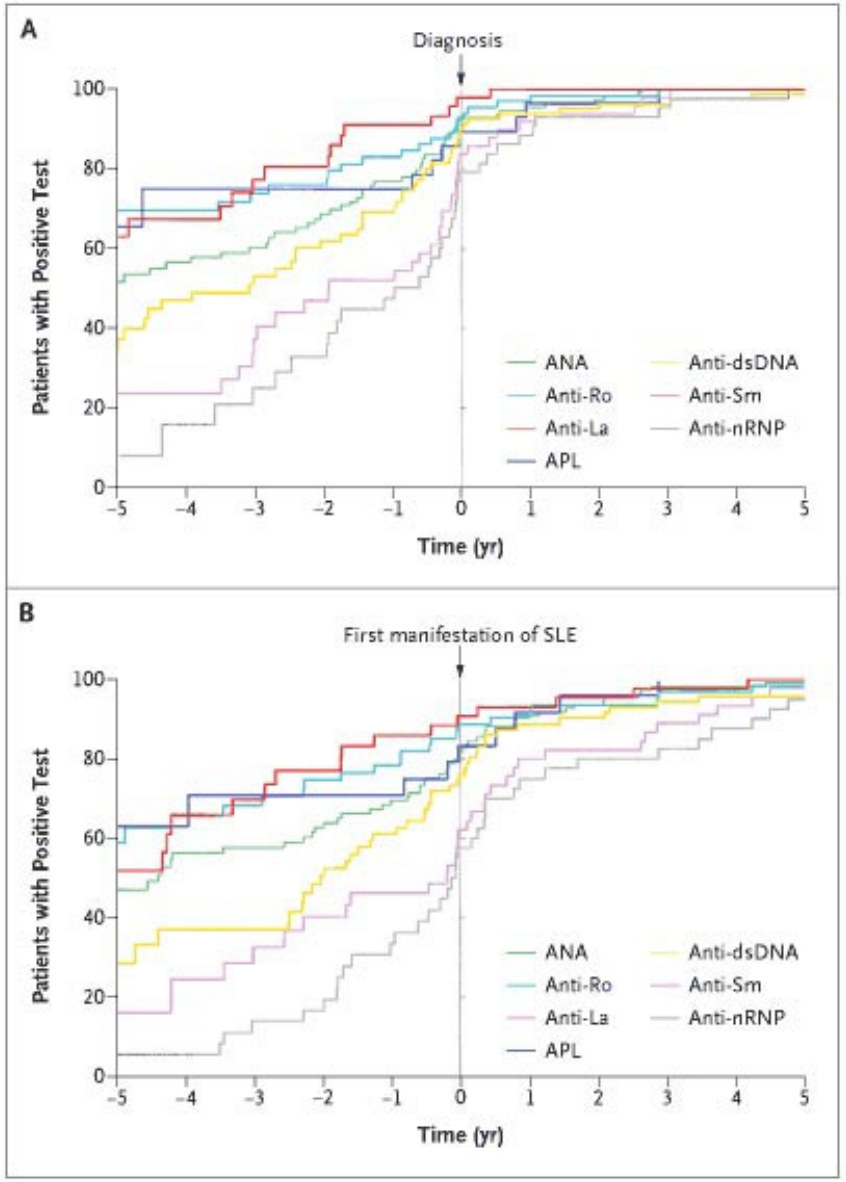
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Development of Autoantibodies before the Clinical Onset of Systemic Lupus Erythematosus

Melissa R. Arbuckle, M.D., Ph.D., Micah T. McClain, Ph.D., Mark V. Rubertone, M.D., R. Hal Scofield, M.D., Gregory J. Dennis, M.D., Judith A. James, M.D., Ph.D., and John B. Harley, M.D., Ph.D.





N Engl J Med 2003;349:1526-1533

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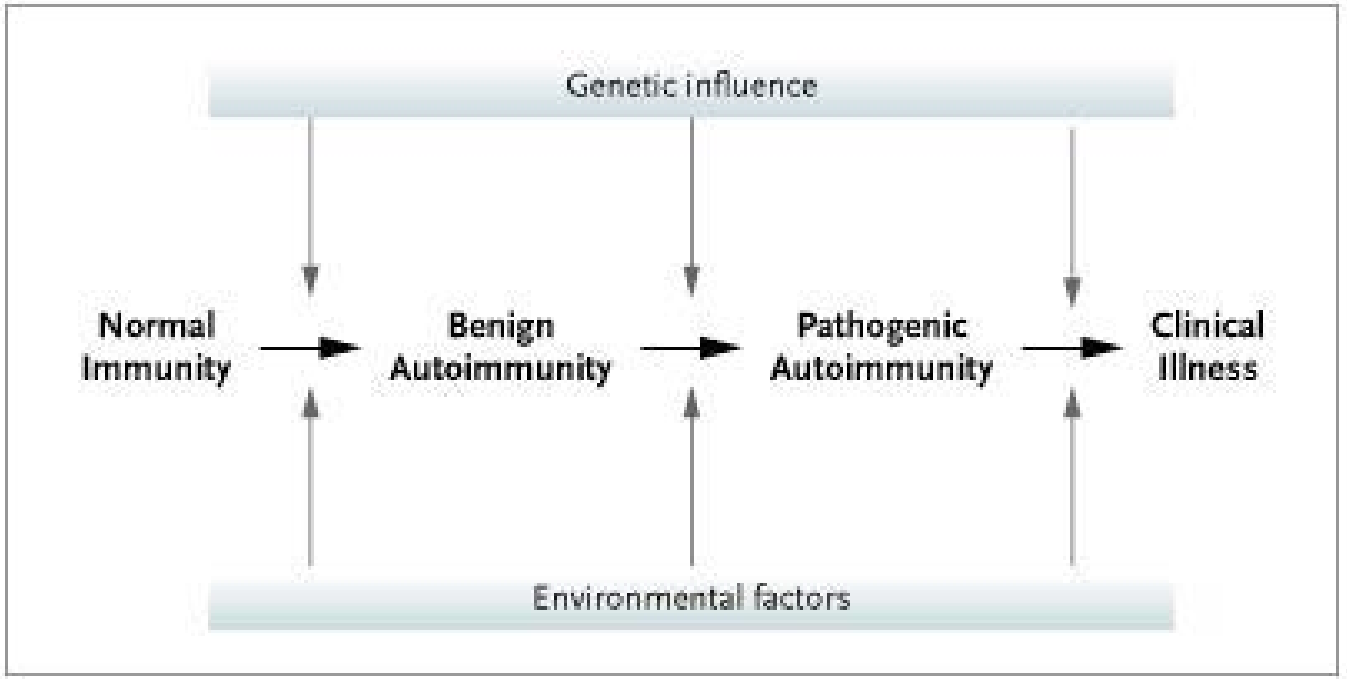
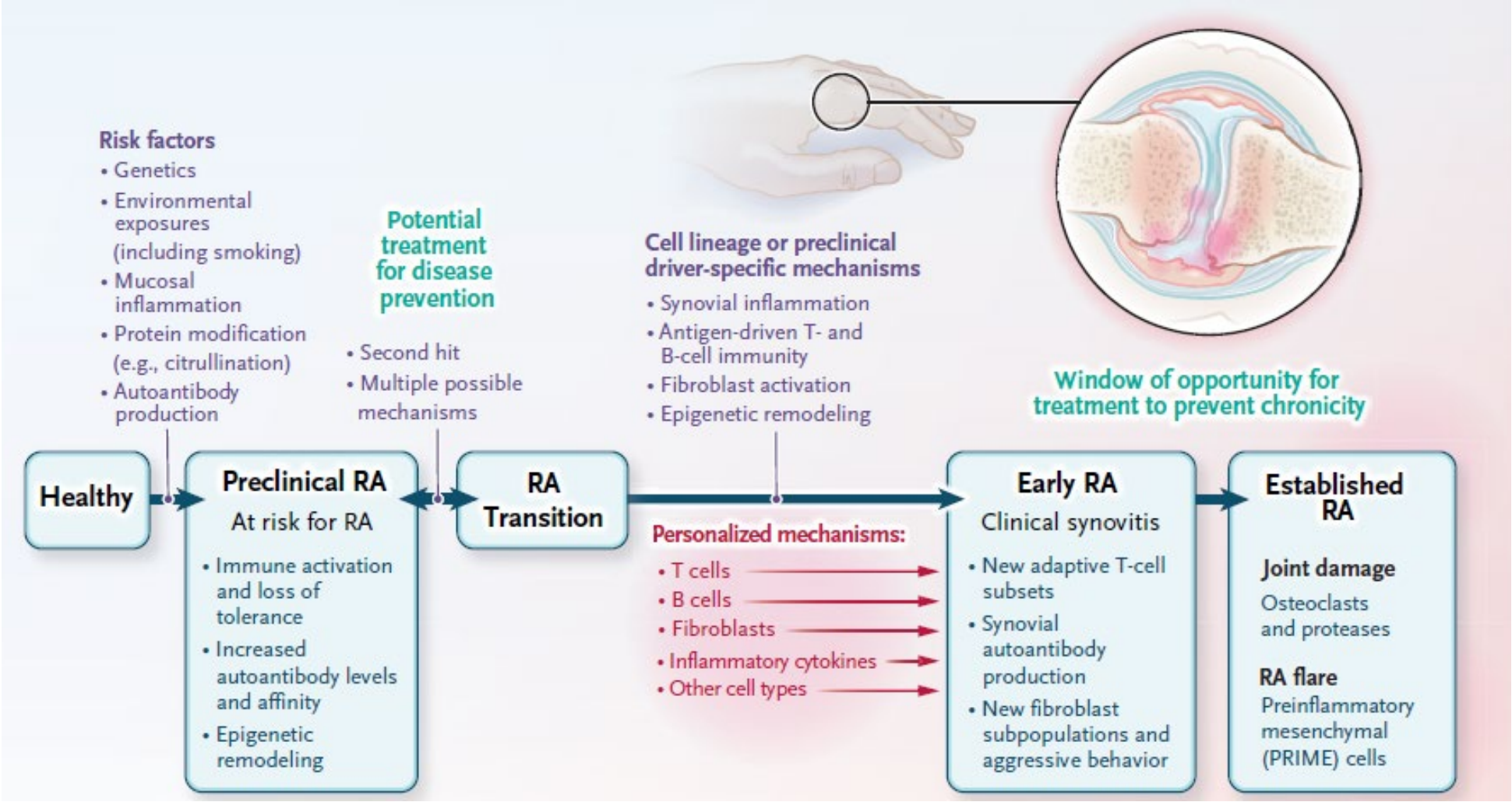


N Engl J Med 2003;349:1526-1533

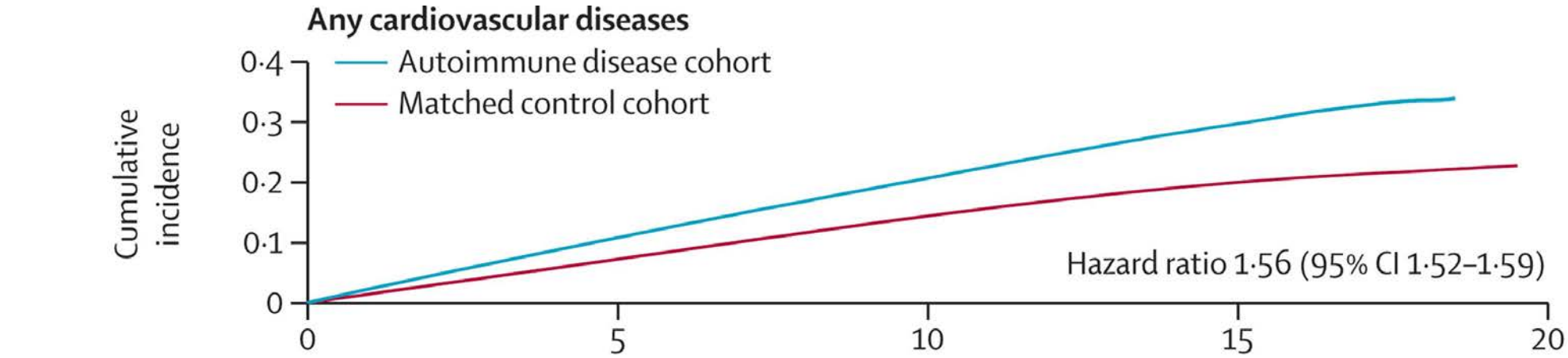
RHEUMATOID ARTHRITIS



N Engl J Med 2023; 388:529-42

Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK

Nathalie Conrad, Geert Verbeke, Geert Molenberghs, Laura Goetschalckx, Thomas Callender, Geraldine Cambridge, Justin C Mason, Kazem Rahimi, John J V McMurray, Jan Y Verbakel



Number at risk

Autoimmune disease cohort	446 449	240 914	111 266	31 533	0
Matched control cohort	2 102 830	1 221 196	628 966	242 364	0

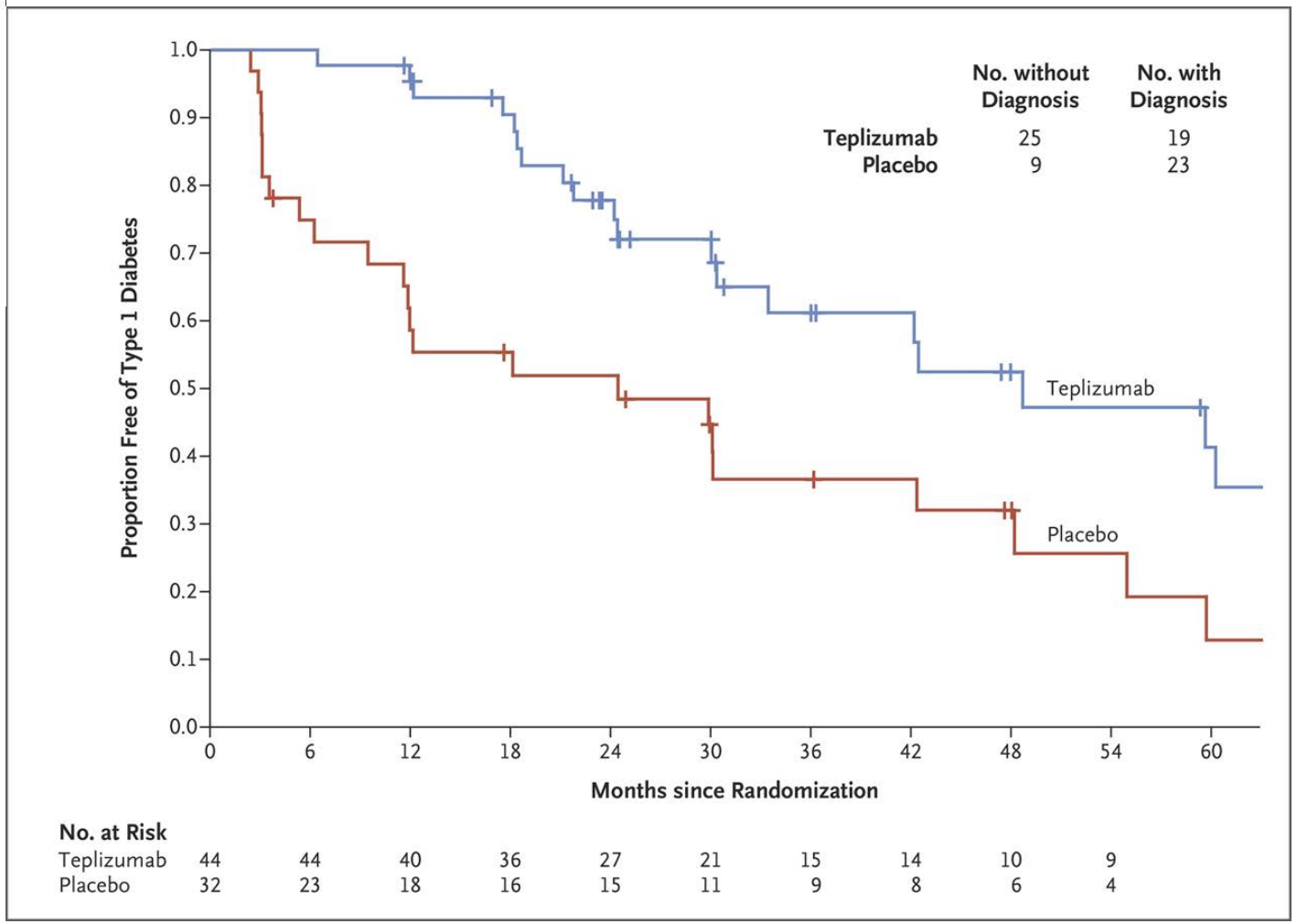
Lancet 2023; 400 (10354):733-743

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 15, 2019 VOL. 381 NO. 7

An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes

Kevan C. Herold, M.D., Brian N. Bundy, Ph.D., S. Alice Long, Ph.D., Jeffrey A. Bluestone, Ph.D., Linda A. DiMeglio, M.D., Matthew J. Dufort, Ph.D., Stephen E. Gitelman, M.D., Peter A. Gottlieb, M.D., Jeffrey P. Krischer, Ph.D., Peter S. Linsley, Ph.D., Jennifer B. Marks, M.D., Wayne Moore, M.D., Ph.D., Antoinette Moran, M.D., Henry Rodriguez, M.D., William E. Russell, M.D., Desmond Schatz, M.D., Jay S. Skyler, M.D., Eva Tsalikian, M.D., Diane K. Wherrett, M.D., Anette-Gabriele Ziegler, M.D., and Carla J. Greenbaum, M.D., for the Type 1 Diabetes TrialNet Study Group*

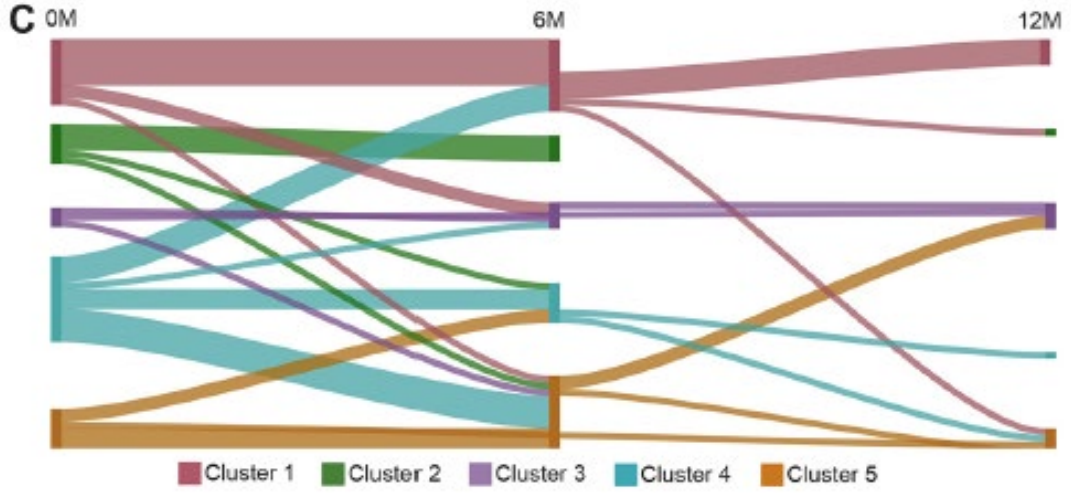


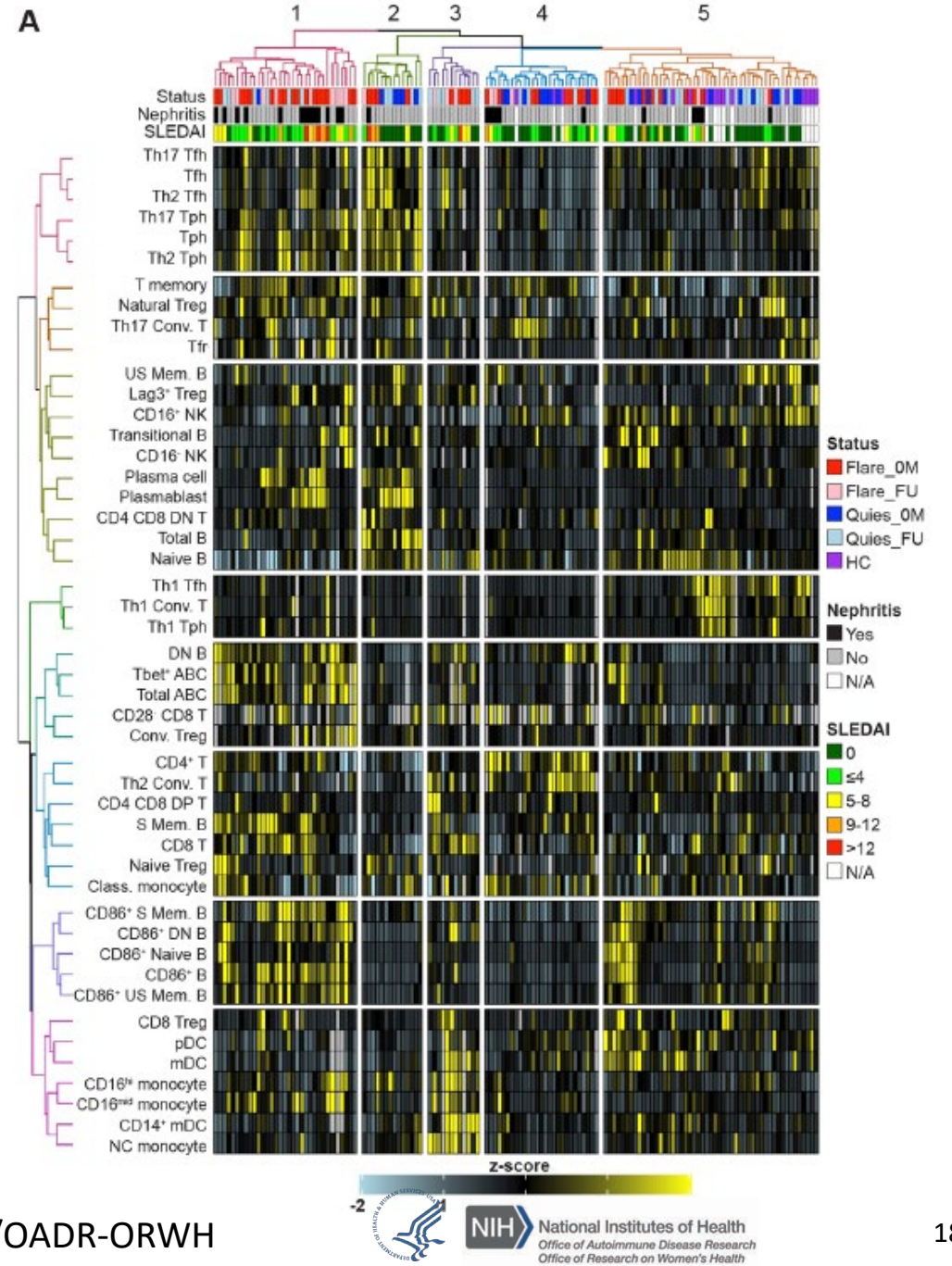
Arthritis & Rheumatology
Vol. 0, No. 0, Month 2024, pp 1–13
DOI 10.1002/art.42776

American College of Rheumatology
Empowering Rheumatology Professionals

Different Immunologic Profiles Are Associated With Distinct Clinical Phenotypes in Longitudinally Observed Patients With Systemic Lupus Erythematosus

Kieran Manion,[1] Carolina Muñoz-Grajales,[2] Michael Kim,[2] Eshetu Atenafu,[3] Zoha Faheem,[2] Dafna D. Gladman,[4] Murray Urowitz,[4] Zahi Touma,[4] and Joan E. Wither[4]



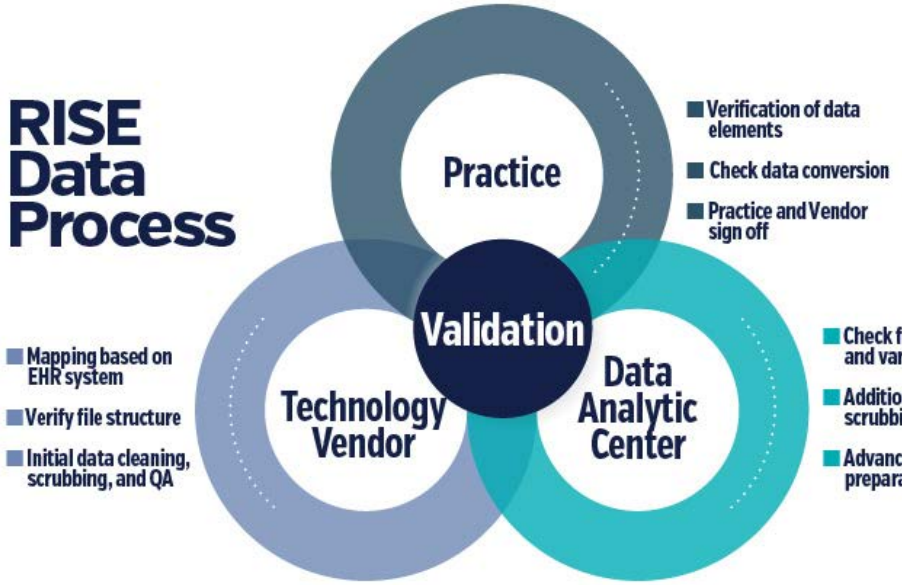


MANY EXISTING REGISTRIES FOR AUTOIMMUNE RESEARCH

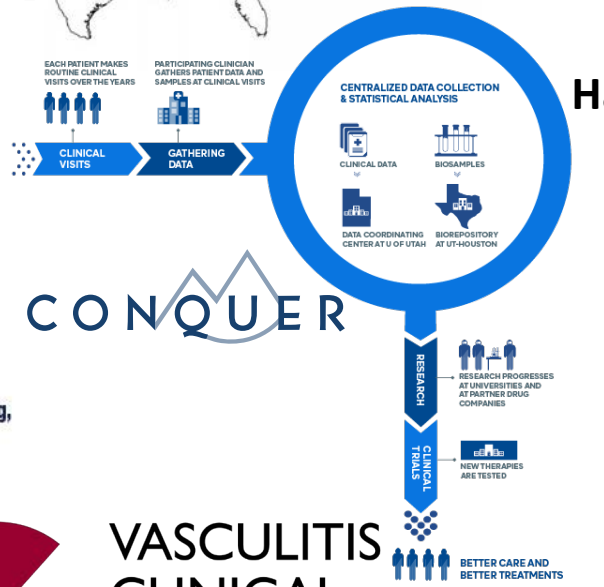
FORWARD
The National Databank for Rheumatic Diseases

Autoimmune Registry

CARRA



HEALTH Study
Harnessing Epidemiology to Advance Lupus Treatment and Health



CONQUER

LUMEN Study
Lupus Midwest Network

CLUES
California Lupus Epidemiology Study
Searching for answers

VASCULITIS CLINICAL RESEARCH CONSORTIUM

GOAL
Georgians Organized Against Lupus

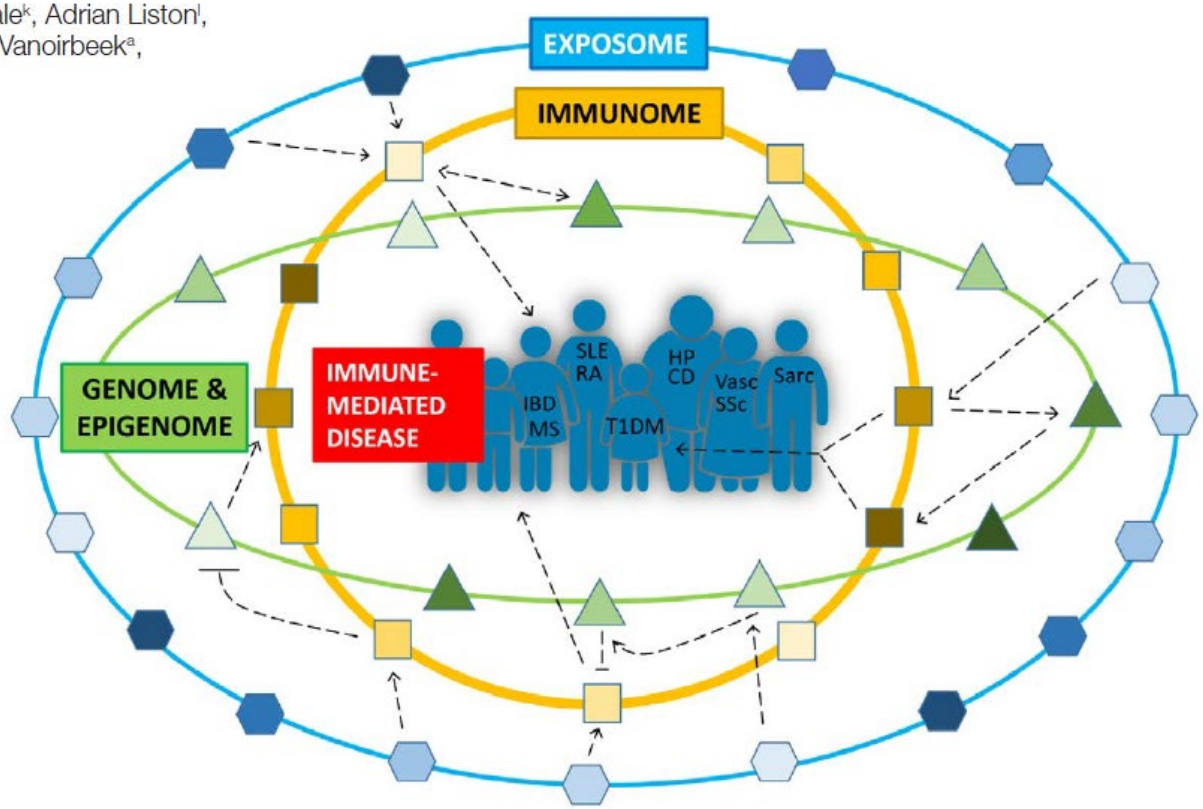
Original Research Article

ENVIRONMENTAL EPIDEMIOLOGY

OPEN

The EXIMIOUS project—Mapping exposure-induced immune effects: connecting the exposome and the immunome

Steven Ronsmans[a], Karin Sørig Hougaard[b], Tim S. Nawrot[a,c], Michelle Plusquin[c], François Huaux[d], María Jesús Cruz[e], Horatiu Moldovan[f], Steven Verpaele[g], Murali Jayapala[h], Michael Tunney[i], Stéphanie Humblet-Baron[j], Hubert Dirven[k], Unni Cecilie Nygaard[k], Birgitte Lindeman[k], Nur Duale[k], Adrian Liston[l], Esben Meulengracht Flachs[m], Kenneth Kastaniegaard[n], Matthias Ketzel[o], Julia Goetz[p], Jeroen Vanoirbeek[a], Manosij Ghosh[a,*], Peter H. M. Hoet[a,*], The EXIMIOUS Consortium§



Environ Epi 6:e193

Original Research Article

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Table 1.

Overview of study populations included in the EXIMIOUS project

		Time course			
	Study Population	**Prenatal**	**0–18 years**	**18–65 years**	**> 65 years**
General population and birth cohorts	The LifeLines Cohort				
	ENVIRonAGE				
	DOC*X				
	DOC*X Generation				
Occupational	Waste workers				
	Park workers				
	Workers exposed to mineral dust and organic solvents				
Disease	Sarcoidosis				
	Hypersensitivity pneumonitis				
	Systemic Sclerosis				
	Systemic Lupus Erythematosus				
	Rheumatoid Arthritis				

Environ Epi 6:e193

Original Research Article

ENVIRONMENTAL EPIDEMIOLOGY

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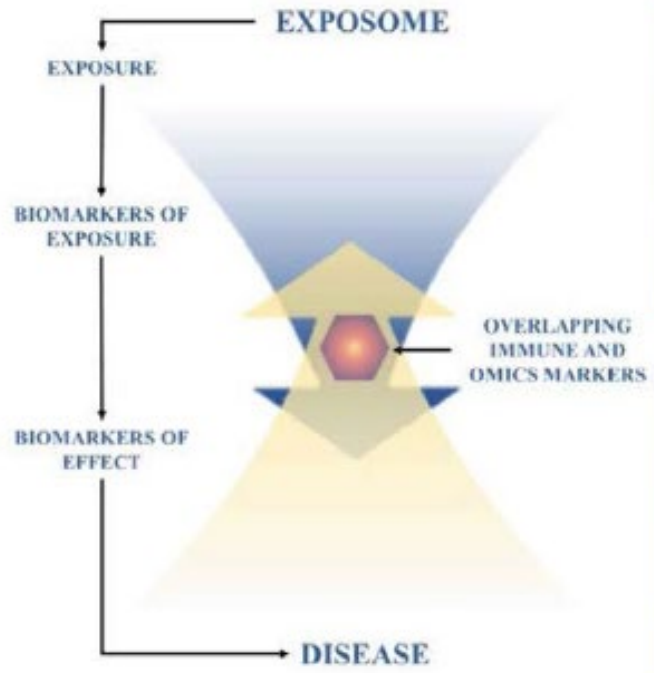


FIRST APPROACH: STARTING FROM THE EXPOSOME

We will begin with cohorts that cover the entire lifespan: general and birth cohorts (LifeLines, DOC*X and DOC*X Generation, ENVIRONAGE) and occupational cohorts (park workers, paint factory workers, miners, metallurgy workers, waste handlers and administrative workers).

SECOND APPROACH: STARTING FROM THE DISEASE

In this approach, we start from cohorts of people that have potentially exposure-related, immune-mediated diseases, like systemic sclerosis (SSc), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), sarcoidosis and hypersensitivity pneumonitis (HP).

Environ Epi 6:e193

EXPOSOME

OVER TIME/LIFE STAGES

GENOME

EPIGENOME

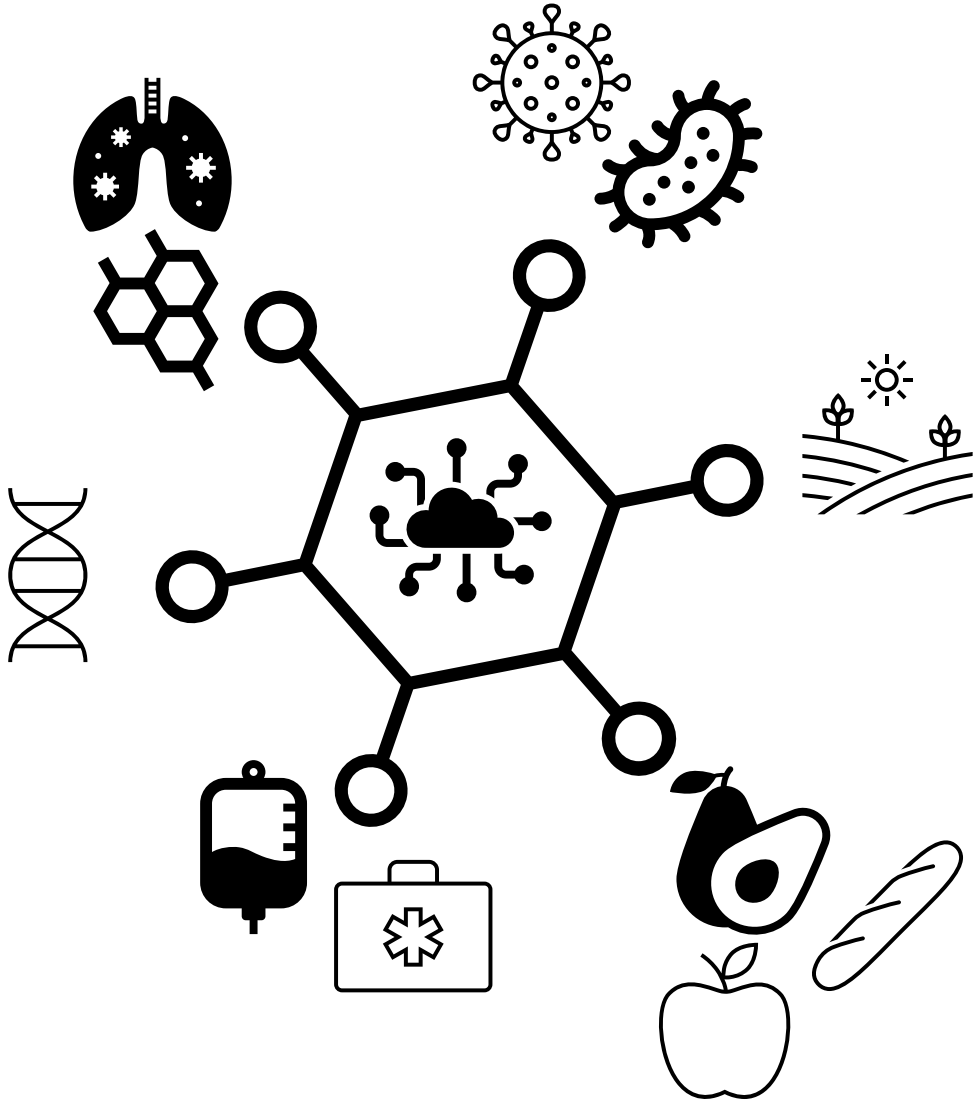
TRANSCRIPTOME

PROTEOME

METABOLOME

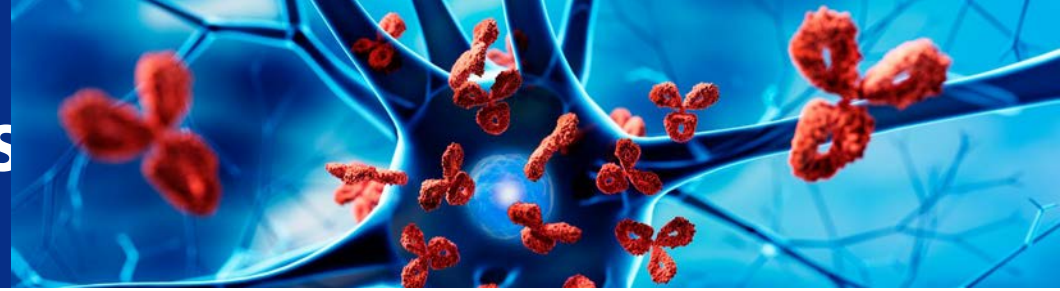
MICROBIOME

IMMUNOME



https://nap.nationalacademies.org/catalog/26554/enhancing-nih-research-on-autoimmune-disease

Office of Autoimmune Disease Res



Women bear a disproportionate burden of autoimmune disease compared to men. Aligned with content from the 2022 NASEM Report, Congress directed NIH to establish the OADR within ORWH.

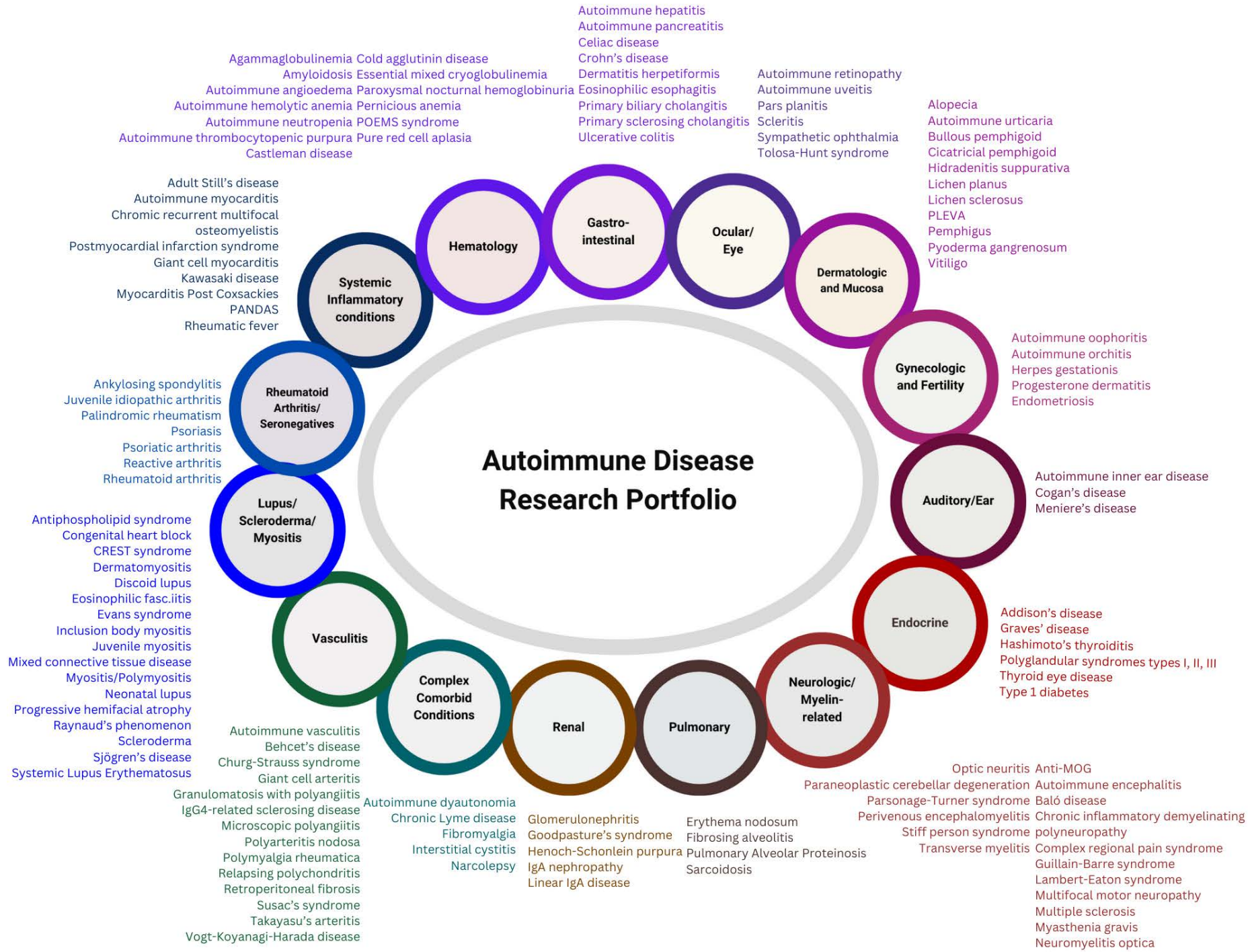
P.L. 117-328 Consolidated Appropriations Act of 2023 directed OADR-ORWH to:

1. Coordinate development of multi-Institute and Center (IC) strategic research plan
2. Identify emerging areas of innovation and research opportunity
3. Coordinate and foster collaborative research across ICs
4. Annually evaluate NIH Autoimmune Disease Research (ADR) portfolio
5. Provide resources to support planning, collaboration, and innovation
6. Develop publicly accessible central repository for ADR

P.L. 117-328 Consolidated Appropriations Act of 2023

Division H--Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 2023

https://nap.nationalacademies.org/catalog/26554/enhancing-nih-research-on-autoimmune-disease


Autoimmune Disease Research Portfolio
Hematology
Agammaglobulinemia
Amyloidosis
Autoimmune angioedema
Autoimmune hemolytic anemia
Autoimmune neutropenia
Autoimmune thrombocytopenic purpura
Castleman disease
Cold agglutinin disease
Essential mixed cryoglobulinemia
Paroxysmal nocturnal hemoglobinuria
Pernicious anemia
POEMS syndrome
Pure red cell aplasia
Gastro-intestinal
Autoimmune hepatitis
Autoimmune pancreatitis
Celiac disease
Crohn's disease
Dermatitis herpetiformis
Eosinophilic esophagitis
Primary biliary cholangitis
Primary sclerosing cholangitis
Ulcerative colitis
Ocular/ Eye
Autoimmune retinopathy
Autoimmune uveitis
Pars planitis
Scleritis
Sympathetic ophthalmia
Tolosa-Hunt syndrome
Dermatologic and Mucosa
Alopecia
Autoimmune urticaria
Bullous pemphigoid
Cicatricial pemphigoid
Hidradenitis suppurativa
Lichen planus
Lichen sclerosus
PLEVA
Pemphigus
Pyoderma gangrenosum
Vitiligo
Gynecologic and Fertility
Autoimmune oophoritis
Autoimmune orchitis
Herpes gestationis
Progesterone dermatitis
Endometriosis
Auditory/Ear
Autoimmune inner ear disease
Cogan's disease
Meniere's disease
Endocrine
Addison's disease
Graves' disease
Hashimoto's thyroiditis
Polyglandular syndromes types I, II, III
Thyroid eye disease
Type 1 diabetes
Neurologic/ Myelin-related
Optic neuritis
Paraneoplastic cerebellar degeneration
Parsonage-Turner syndrome
Perivenous encephalomyelitis
Stiff person syndrome
Transverse myelitis
Anti-MOG
Autoimmune encephalitis
Baló disease
Chronic inflammatory demyelinating polyneuropathy
Complex regional pain syndrome
Guillain-Barre syndrome
Lambert-Eaton syndrome
Multifocal motor neuropathy
Multiple sclerosis
Myasthenia gravis
Neuromyelitis optica
Pulmonary
Erythema nodosum
Fibrosing alveolitis
Pulmonary Alveolar Proteinosis
Sarcoidosis
Renal
Glomerulonephritis
Goodpasture's syndrome
Henoch-Schonlein purpura
IgA nephropathy
Linear IgA disease
Complex Comorbid Conditions
Autoimmune dyautonomia
Chronic Lyme disease
Fibromyalgia
Interstitial cystitis
Narcolepsy
Vasculitis
Autoimmune vasculitis
Behcet's disease
Churg-Strauss syndrome
Giant cell arteritis
Granulomatosis with polyangiitis
IgG4-related sclerosing disease
Microscopic polyangiitis
Polyarteritis nodosa
Polymyalgia rheumatica
Relapsing polychondritis
Retroperitoneal fibrosis
Susac's syndrome
Takayasu's arteritis
Vogt-Koyanagi-Harada disease
Lupus/ Scleroderma/ Myositis
Antiphospholipid syndrome
Congenital heart block
CREST syndrome
Dermatomyositis
Discoid lupus
Eosinophilic fasc.iitis
Evans syndrome
Inclusion body myositis
Juvenile myositis
Mixed connective tissue disease
Myositis/Polymyositis
Neonatal lupus
Progressive hemifacial atrophy
Raynaud's phenomenon
Scleroderma
Sjögren's disease
Systemic Lupus Erythematosus
Rheumatoid Arthritis/ Seronegatives
Ankylosing spondylitis
Juvenile idiopathic arthritis
Palindromic rheumatism
Psoriasis
Psoriatic arthritis
Reactive arthritis
Rheumatoid arthritis
Systemic Inflammatory conditions
Adult Still's disease
Autoimmune myocarditis
Chromic recurrent multifocal osteomyelistis
Postmyocardial infarction syndrome
Giant cell myocarditis
Kawasaki disease
Myocarditis Post Coxsackies
PANDAS
Rheumatic fever


OADR Fiscal Year 2023 Funding
Hematology
Agammaglobulinemia
Amyloidosis
Autoimmune angioedema
Autoimmune hemolytic anemia
Autoimmune neutropenia
Autoimmune thrombocytopenic purpura
Castleman disease
Cold agglutinin disease
Essential mixed cryoglobulinemia
Paroxysmal nocturnal hemoglobinuria
Pernicious anemia
POEMS syndrome
Pure red cell aplasia
Gastro-intestinal
Autoimmune hepatitis
Autoimmune pancreatitis
Celiac disease
Crohn's disease
Dermatitis herpetiformis
Eosinophilic esophagitis
Primary biliary cholangitis
Primary sclerosing cholangitis
Ulcerative colitis
Ocular/ Eye
Autoimmune retinopathy
Autoimmune uveitis
Pars planitis
Scleritis
Sympathetic ophthalmia
Tolosa-Hunt syndrome
Dermatologic and Mucosa
Alopecia
Autoimmune urticaria
Bullous pemphigoid
Cicatricial pemphigoid
Hidradenitis suppurativa
Lichen planus
Lichen sclerosus
PLEVA
Pemphigus
Pyoderma gangrenosum
Vitiligo
Gynecologic and Fertility
Autoimmune oophoritis
Autoimmune orchitis
Herpes gestationis
Progesterone dermatitis
Endometriosis
Auditory/Ear
Autoimmune inner ear disease
Cogan's disease
Meniere's disease
Endocrine
Addison's disease
Graves' disease
Hashimoto's thyroiditis
Polyglandular syndromes types I, II, III
Thyroid eye disease
Type 1 diabetes
Neurologic/ Myelin-related
Optic neuritis
Paraneoplastic cerebellar degeneration
Parsonage-Turner syndrome
Perivenous encephalomyelitis
Stiff person syndrome
Transverse myelitis
Anti-MOG
Autoimmune encephalitis
Baló disease
Chronic inflammatory demyelinating polyneuropathy
Complex regional pain syndrome
Guillain-Barre syndrome
Lambert-Eaton syndrome
Multifocal motor neuropathy
Multiple sclerosis
Myasthenia gravis
Neuromyelitis optica
Pulmonary
Erythema nodosum
Fibrosing alveolitis
Pulmonary Alveolar Proteinosis
Sarcoidosis
Renal
Glomerulonephritis
Goodpasture's syndrome
Henoch-Schonlein purpura
IgA nephropathy
Linear IgA disease
Complex Comorbid Conditions
Autoimmune dyautonomia
Chronic Lyme disease
Fibromyalgia
Interstitial cystitis
Narcolepsy
Vasculitis
Autoimmune vasculitis
Behcet's disease
Churg-Strauss syndrome
Giant cell arteritis
Granulomatosis with polyangiitis
IgG4-related sclerosing disease
Microscopic polyangiitis
Polyarteritis nodosa
Polymyalgia rheumatica
Relapsing polychondritis
Retroperitoneal fibrosis
Susac's syndrome
Takayasu's arteritis
Vogt-Koyanagi-Harada disease
Lupus/ Scleroderma/ Myositis
Antiphospholipid syndrome
Congenital heart block
CREST syndrome
Dermatomyositis
Discoid lupus
Eosinophilic fasciitis
Evans syndrome
Inclusion body myositis
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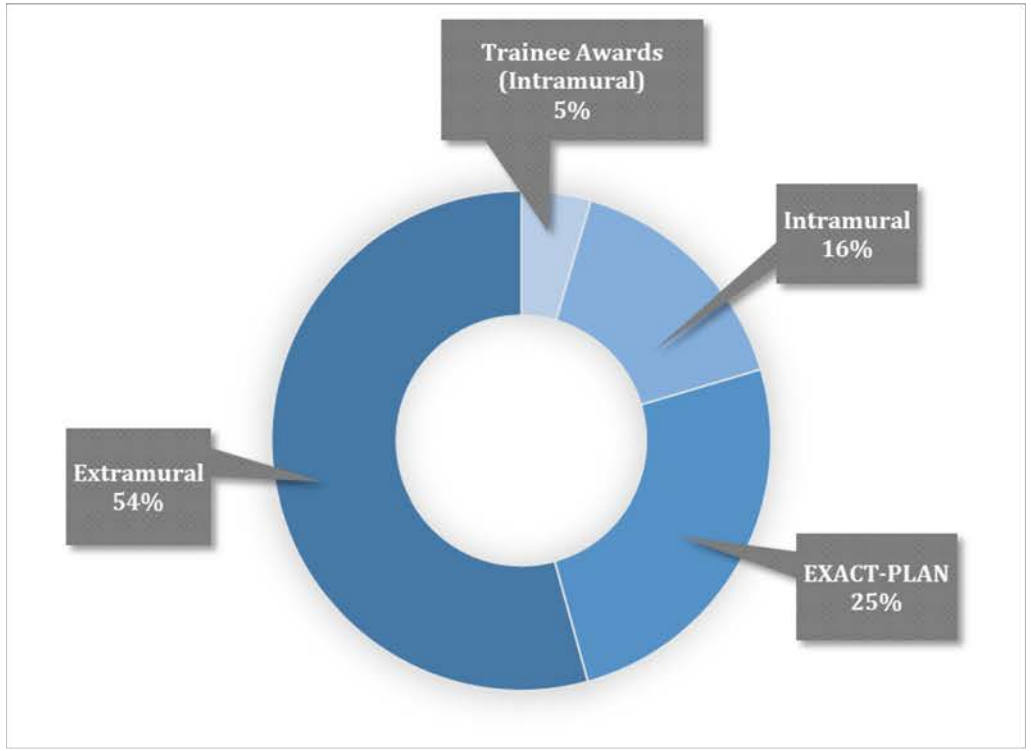
PANDAS
Rheumatic fever

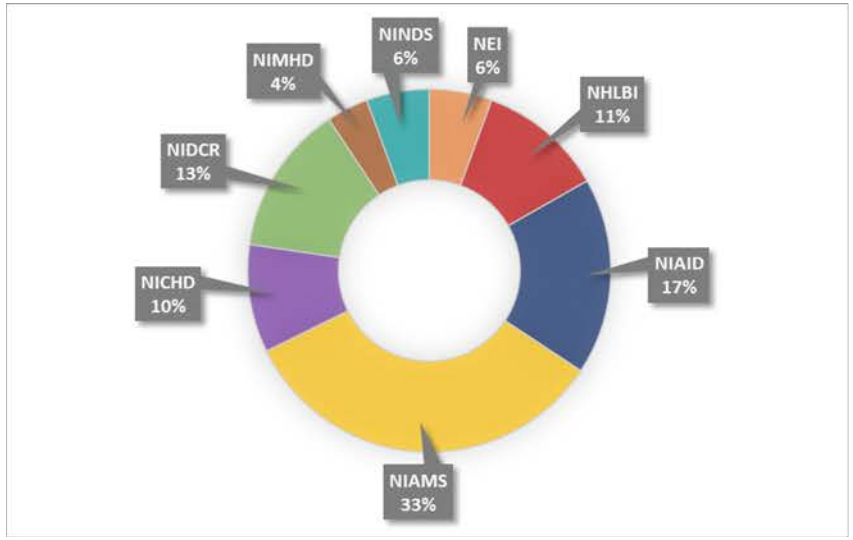
OADR FY23 Funding Summary

[a] OADR Total Funding by Activity

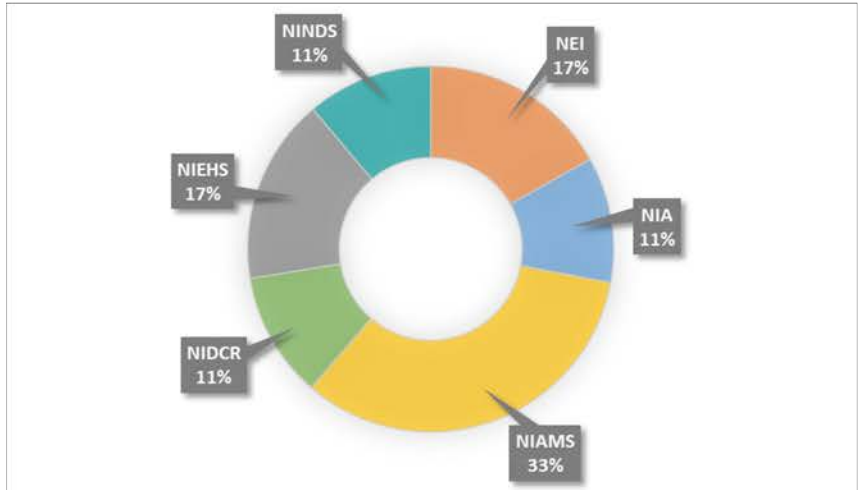


**Abbreviations: NEI = National Eye Institute; NHLBI = National Heart, Lung, and Blood Institute; NIAID = National Institute of Allergy and Infectious Diseases; NIAMS = National Institute of Arthritis and Musculoskeletal and Skin Diseases; NICHD = National Institute of Child Health and Human Development; NIDCR = National Institute on Dental and Craniofacial Research; NIMHD = National Institute on Minority Health and Health Disparities; NINDS = National Institute on Neurological Disorders and Stroke; NIEHS = National Institute of Environmental Health Science.*

[b] OADR Extramural Funding by Institute/Center



[c] OADR Intramural Funding by Institute/Center



EXACT PLAN

- NOT-OD-23-112
- Developed in collaboration with NIAMS and NIEHS, and multiple other ICOs
- Support the design, development, and implementation of future national, interdisciplinary, collaborative, team science research network to study to the interplay of genome, microbiome, exposome and immunome in the development of autoimmune disease

Meet the 2023 EXACT-PLAN Award Recipients

John Pearce
Ph.D.

Jill Norris
Ph.D., M.P.H.

Marc Natter
M.D.

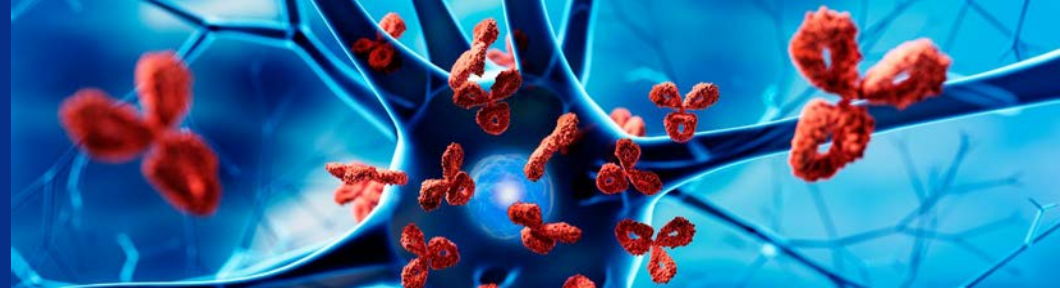
Jane Buckner
M.D.

Wilson Laio
M.D.

Brigitte Frohnert
M.D., Ph.D.

OADR-ORWH Science Talks

Xist-ing Data: Why Might Autoimmune Diseases Be More Common in Women?



Tuesday, April 23, 202412 p.m. to 2 p.m. EDT

Virtual Meeting

Time	Session
12:00 – 12:05 p.m.	Welcome & Opening Remarks Victoria Shanmugam, MBBS, MRCP, FACR, CCD, Director, NIH Office of Autoimmune Disease Research in the Office of Research on Women's Health
12:05 pm – 12:35 p.m.	**X Chromosome Inactivation and Immune Responses** **Montserrat Anguera, Ph.D.**, Associate Professor, Department of Biomedical Sciences, University of Pennsylvania School of Veterinary Medicine
12:35 pm – 1:05 p.m.	**Xist Ribonucleoproteins Promoting Autoimmunity in Women** **Diana Dou, Ph.D.**, Postdoctoral Scholar, Stanford University
1:05 pm – 1:35 p.m.	**Xist lncRNA as a Sex Specific Reservoir of TLR7 Ligands in Lupus** **Brendan Antiochos, M.D.**, Assistant Professor of Medicine and Director Johns Hopkins Vasculitis Center, Division of Rheumatology at Johns Hopkins Medicine
1:35 pm – 1:55 p.m.	**Moderated Discussion: Dr. Marie Mancini, NIAMS; Dr. Stacey Ferguson, NIAID** Drs. Anguera, Dou, and Antiochos
1:55 pm – 2:00 p.m.	Closing Remarks

Save the Date: 8th Annual Vivian W. Pinn Symposium

- Wednesday, May 15, 1:00 pm to 5:00 pm ET held virtually

Time	Session	Speaker
1:00–1:15 p.m.	Opening Remarks	Dr. Janine Clayton
1:15–2:00 p.m.	Keynote Address	Dr. Jane Buckner
2:00–2:45 p.m.	Inside Innovation: Intramural Impact at NIH	Dr. Laura Lewandowski Dr. Steven Holland Dr. Alison Motsinger-Reif and Ms. Jasmine Mack
2:45–3:00 p.m.	Break	
3:00–3:45 p.m.	Fireside Chat	Dr. David Fajgenbaum Dr. Vicki Shanmugam
3:45–4:30 p.m.	Capstone Speaker	Dr. Gail Kerr
4:30–4:45 p.m.	Remarks by Dr. Vivian Pinn	Dr. Vivian Pinn
4:45–5:00 p.m.	Closing Remarks	TBD

THANK YOU

Questions?

Connect with us:

- OADRInfo@nih.gov
- www.orwh.od.nih.gov/OADR-ORWH

National Institutes of Health
Office of Autoimmune Disease Research
Office of Research on Women's Health