Optimizing investments in the scientific enterprise by implementing effective data-driven decision making

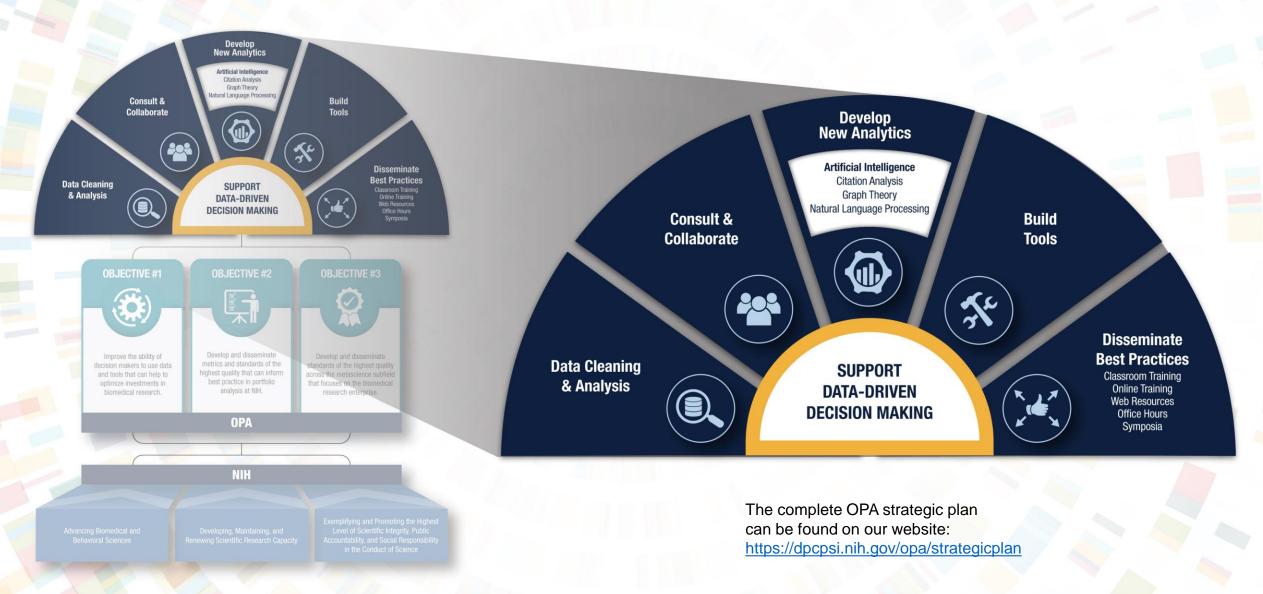
> George Santangelo, Ph.D. Director, Office of Portfolio Analysis DPCPSI/OD National Institutes of Health

- Implement effective data-driven decision making that improves management of existing and planned portfolios
 - o Engage across the enterprise
 - Requirements gathering
 - Build tools (don't buy them)
 - Train, consult, collaborate
- Develop and validate analytics
 - Leverage artificial intelligence/machine learning (AI/ML) tech wherever possible
 - Supervised ML with gold standards (requires high inter-rater reliability!)
 - Language model (LM)-based analysis of scientific content
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- Share analytics, the underlying code, and all input data with the public
 - A public-facing next-gen tool: *iSearch* Analytics



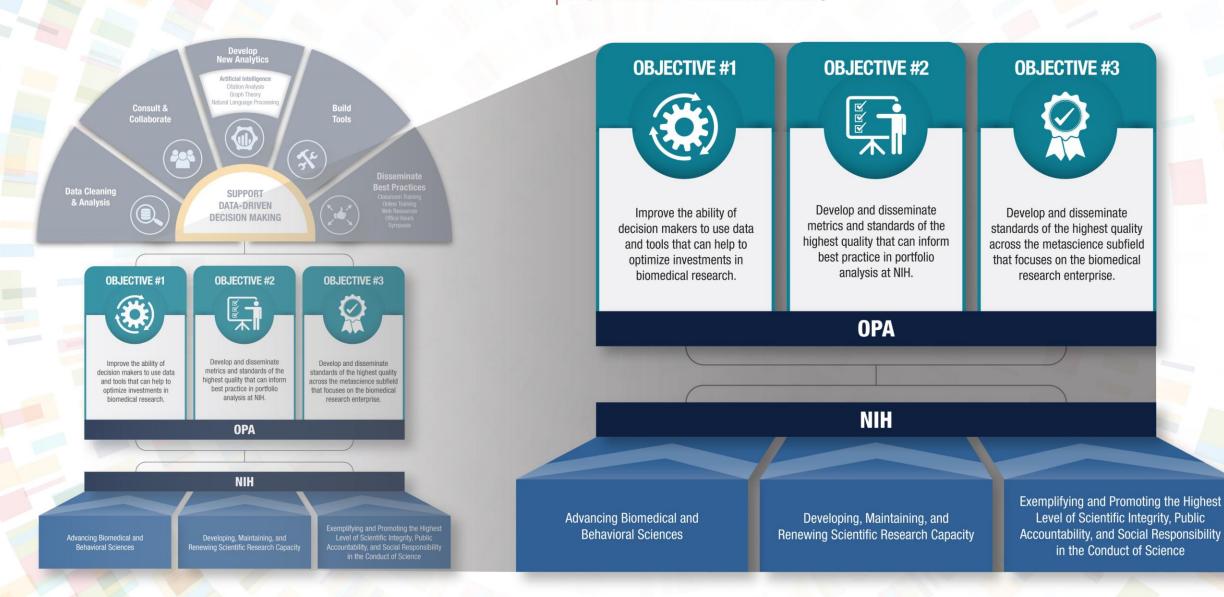
OFFICE OF PORTFOLIO ANALYSIS STRATEGIC PLAN, FISCAL YEARS 2021–2025

OVERARCHING GOAL To accelerate biomedical research by providing access to improved methods of data-driven decision making



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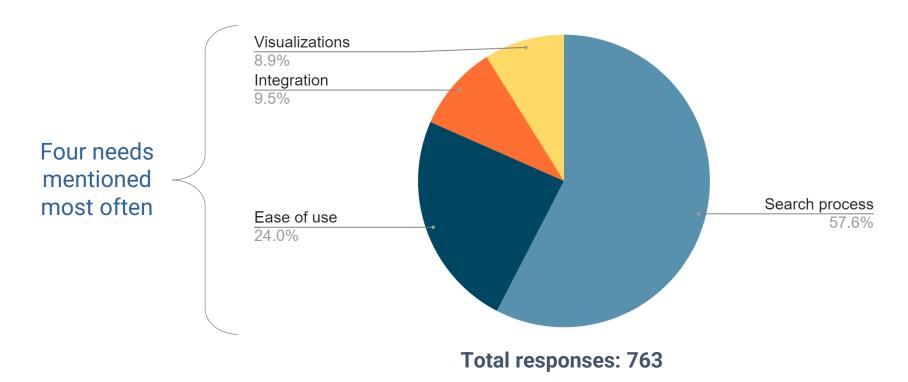


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Research summary

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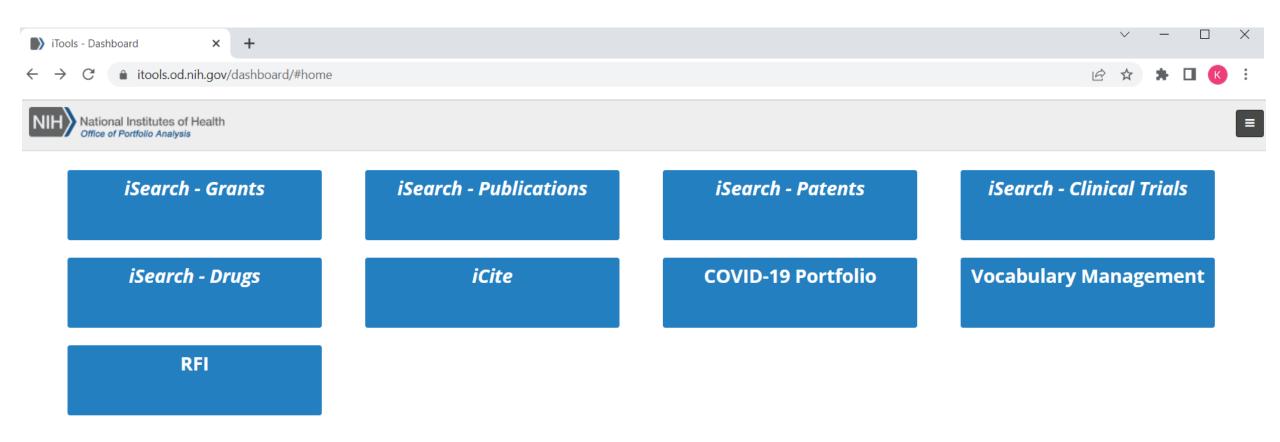


NIH surveys (March 2021 through June 2021)



NextGen enterprise-wide portfolio analysis at NIH The OPA *iSearch* 2.6 dashboard

https://itools.od.nih.gov/dashboard/#home





The OPA training curriculum

- A free service provided to all NIH administrators
- Online registration



The OPA training team provides analytical resources to support the NIH community in performing analyses to the highest standards

iTools Training Opportunities

iSearch

In this class, you will learn about *iSearch*, NIH's nextgeneration portfolio analysis platform. You will learn how to access extensively-linked global grants, patents, publications, clinical trials and approved drugs.



iSearch - Portfolio Tool

This class will cover how to use the portfolio tool feature available in all of the *iSearch* modules. Existing *iSearch* knowledge is required.



Measuring Research Outputs (*iCite* - RCR and Translation)

This class will introduce you to the *iCite* module within the OPA iTools dashboard. It will provide an overview of bibliometrics and tools used for investigating the impact of research outputs. It combines the previous 'Bibliometrics (*iCite* & RCR)' and 'Translational Science (iTrans)' classes.



RFI Tool

This class will cover how to use the OPA RFI Tool. The RFI Tool streamlines the manual coding of responses to Requests For Information (RFI) or other text data sources e.g. blog comments.





Click Here to Register for a Class

Driving adoption of data-driven decision making at NIH OPA open door consultations

22 NIH Institutes and Centers (ICs) requested OPA consultations between January 2021 and April 2022

Sample projects:

IC	Project description
NCI	Analysis of NIH funding for surgeon scientists. Results of the analysis were published in the February 2021 issue of the Journal of the American College of Surgeons :
	https://www.journalacs.org/article/S1072-7515(20)32577-1/fulltext
NCI	Collaboration to characterize NCI metabolomics research
NCI	Collaboration to characterize and evaluate the NCI training portfolio (Fs, Ks, and Ts)
NCI	Collaboration on portfolio analysis of grants that have supported clinical trials conducted in low- and middle-income countries
NCI	Collaboration on bladder cancer portfolio analysis
NIAID	Collaboration on portfolio analysis to characterize the DAIDS portfolio
NIAID	Compare patient-oriented goals to NIH-funded research on eczema
NIAID	Portfolio analysis of collaborative research of NIAID intramural investigators (with each other and with extramural PIs)
NIDDK	Characterization of program officer portfolios for three program divisions
NIDDK	Collaboration to characterize NIDDK DEM portfolio and assignments to POs
NIDDK	Collaboration on the NIDDK obesity portfolio
NHLBI	Collaborating to automate extraction of NHLBI grants and publications
NHLBI	Analysis of the geographical distribution of the NHLBI obesity portfolio
NHGRI	Collaboration on RNome RNA portfolio analysis
NHGRI	Collaboration on NHGRI AI/ML Genomics portfolio analysis
NICHD	Collaboration to analyze NICHD Rehab Specialties
NICHD	Collaboration on Adolescent HIV portfolio analysis
NIDA	Collaboration to characterize the NIDA health disparities portfolio
NIDA	Characterization of the mobile health portfolio
NIMH	Collaboration to characterize the NIMH health disparities portfolio
NIMH	Collaboration on NIMH/RDoC portfolio analysis
NIDCR	Collaboration on the analysis of Science of Behavior Change policy impact
NEI	Analysis of NEI research portfolio from FY2011-FY2020. Results of the analysis were presented to Mike Chiang
cc	Clinical Center portfolio analysis
NCATS	Collaboration to link NCATS PIs to CMS Open Payments database as an outcome measure
NINR	Collaboration to find duplicate or near duplicate applications submitted by the same investigator teams to multiple ICs so the same project is not unknowingly doubly funded
NINR	Collaboration on portfolio analysis of NIH-funded SDoH research
NIEHS	Collaboration on gene-environment interaction portfolio analysis
NINDS	Collaboration on portfolio analysis of BRAIN PI specialties
NUANAC	

NIAMS Analysis of the back pain portfolio



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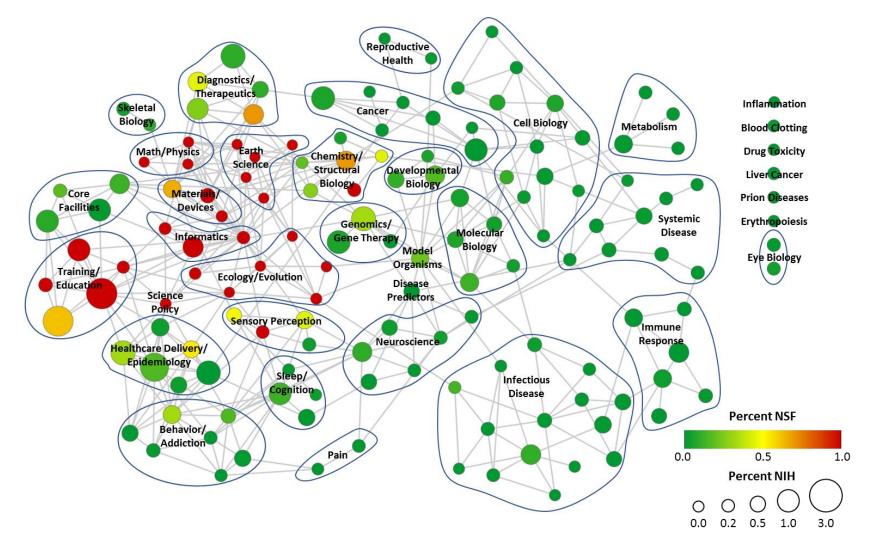
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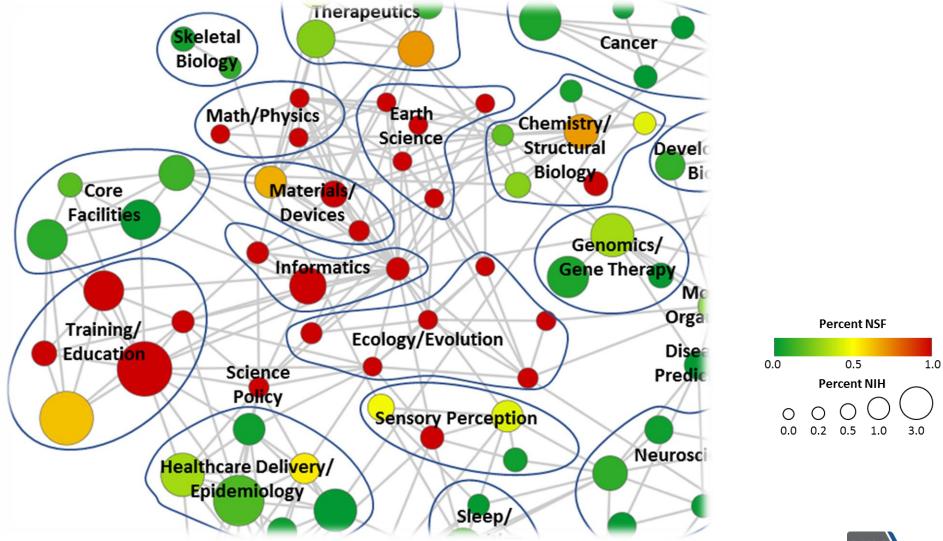


Using AI/ML to identify overlap between the NIH and NSF portfolios





Using AI/ML to identify overlap between the NIH and NSF portfolios



National Institutes of Health Office of Portfolio Analysis

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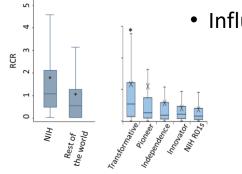
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OPA AI to track and predict the impact of NIH decision-making

Track and parameterize:

The publicly available OPA tool



- Influence using bibliometric data
 - The Relative Citation Ratio (RCR)
 - Hutchins BI et al. PLoS Biology 2016 14:e1002541
 - Hutchins BI et al. PLoS Biology 2017 15:e2003552

The triangle of biomedicine, APT scores

iCite 2.0

Influence module Translation module Open Citation Collection Hutchins et al. *PLOS Biology* 2019 17:e3000385

- 2015 Opdivo (83.8B) FDA Approval Clinical Translational
 - Development of drugs and devices

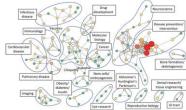
Disambiguated drug and lead compound name, FDA data

• Language model (LM) analysis of NIH investments and publications

• Translational progress / clinical trials (CTs) and tech transfer / patents

- Hutchins BI et al. PLoS Biology 2019 17(10):e3000416

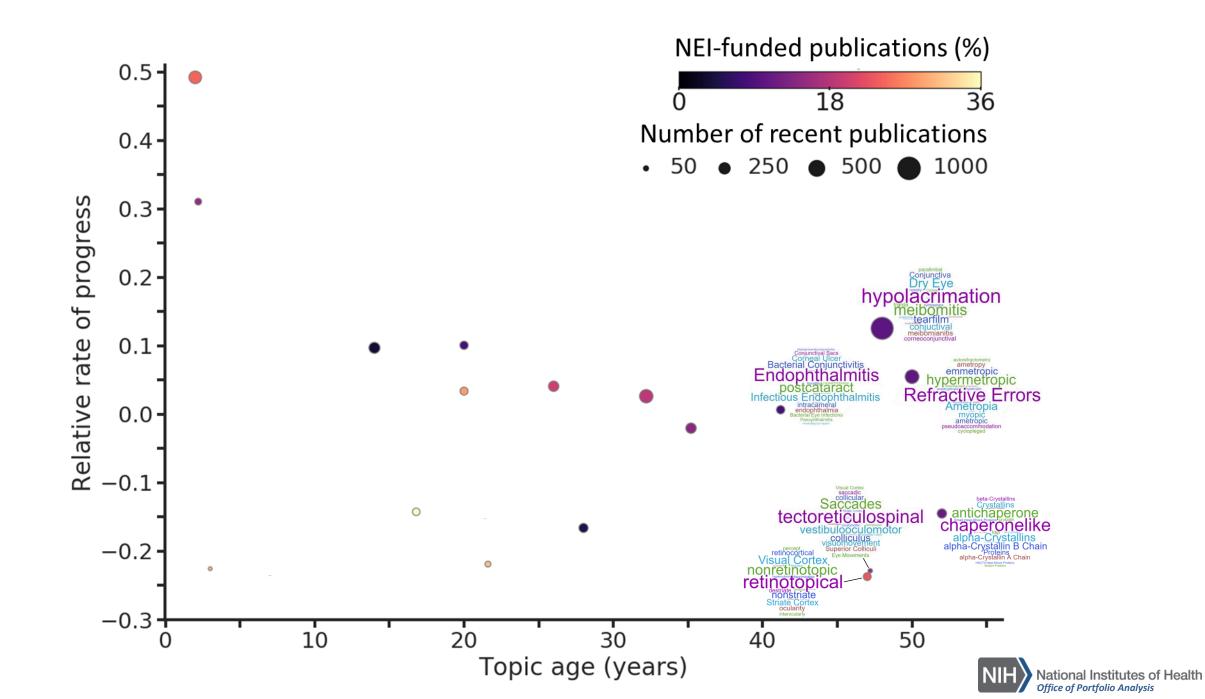
- Hoppe et al. Science Advances 2019 5:eaaw7238

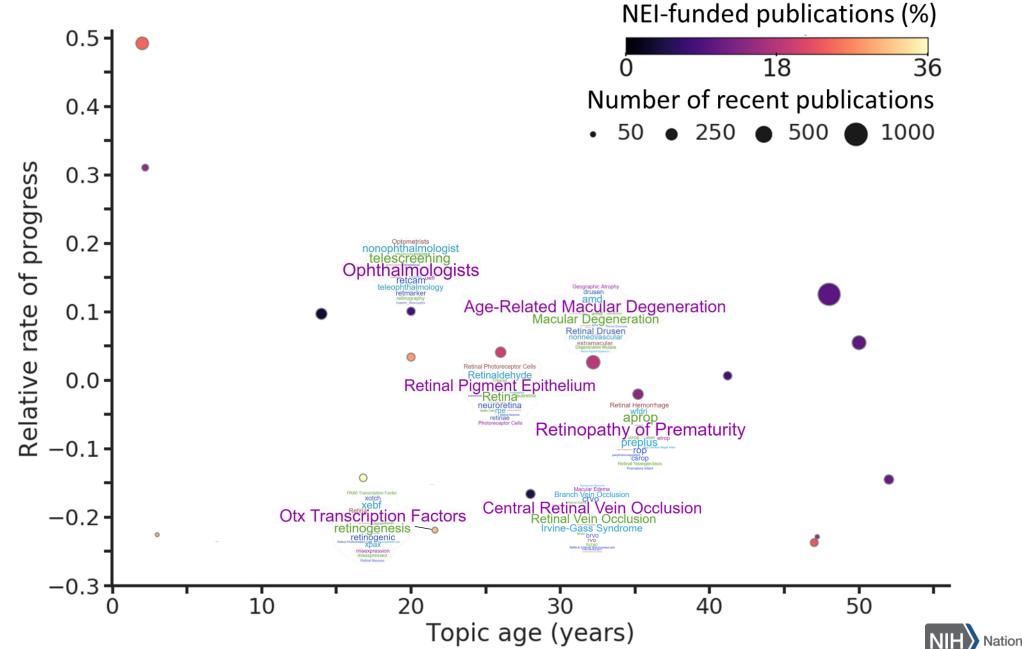




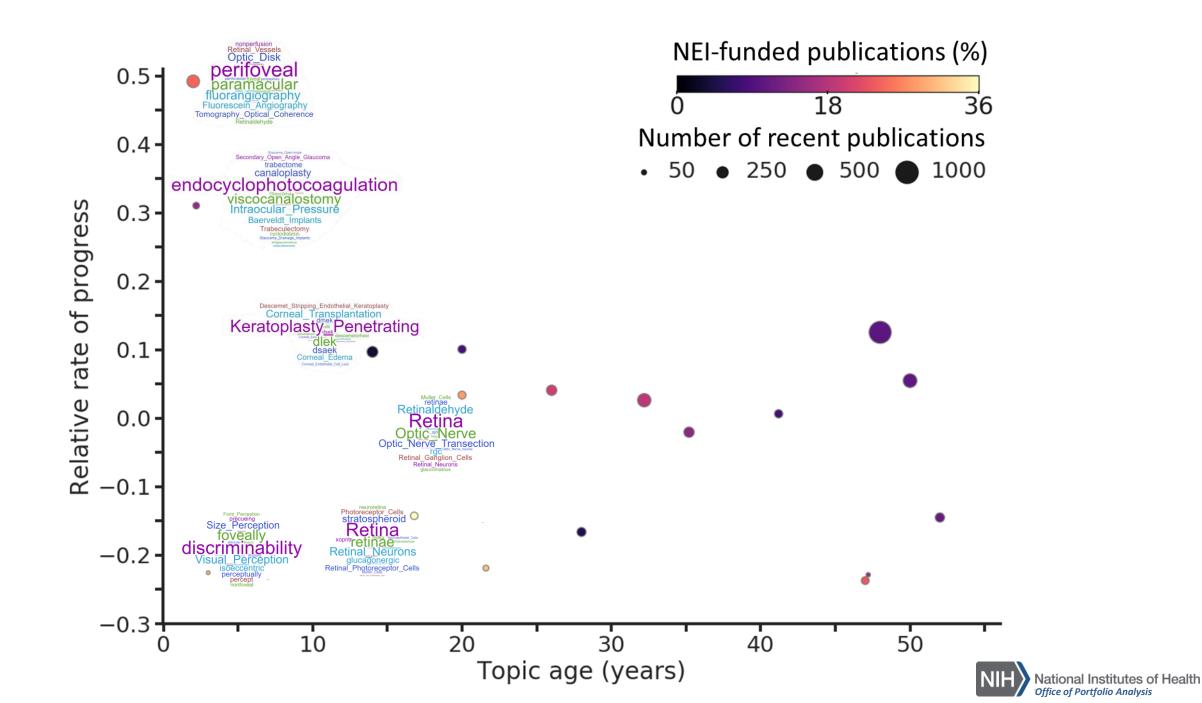
- Rate of scientific progress and emergence
 Prediction of transformative breakthroughs in biomedical research
 - Santangelo et al. U.S. Patent Application No. 63/257,818







National Institutes of Health Office of Portfolio Analysis



	NEI-funded public	ations (%)
0.5 -	0 18	36
1		
0.4 -	Number of recent pu	blications
-	• 50 • 250 • 500	0 🛑 1000
0.3 - OCTA = Optical Coherence Tomography	Angiography	
PubYear Title		RCR NEI PI/
2015 Retinal vascular layers imaged by fluorescein angiography	and OCTA	69.7 none
2012 Split-spectrum amplitude-decorrelation angiography with	optical coherence tomography	59.6 Huang,
2015 Image artifacts in OCTA		49.8 Fujimo
2017 Detailed vascular anatomy of the human retina by projecti	on-resolved OCTA	32.9 Huang,
2014 Quantitative OCTA of choroidal neovascularization in age-r	elated macular degeneration	32.9 Huang,
2014 OCTA of optic disc perfusion in glaucoma		31.9 Huang,
2015 Quantitative OCTA of vascular abnormalities in the living h	uman eye	30.9 Huang,
2015 OCTA of the Peripapillary Retina in Glaucoma		30.4 Huang,
2015 OCTA in Diabetic Retinopathy: A Prospective Pilot Study		27.6 none
2016 OCTA Vessel Density in Healthy, Glaucoma Suspect, and Gl	aucoma Eyes	25.2 Weinre
2016 Quantifying Microvascular Density and Morphology in Dial	betic Retinopathy Using Spectral-Domain OCTA	22.8 Wang,
		22.2 Duker,

Topic age (years)

NEI PI/author

Huang, David

Huang, David

Huang, David

Huang, David

Huang, David

Huang, David

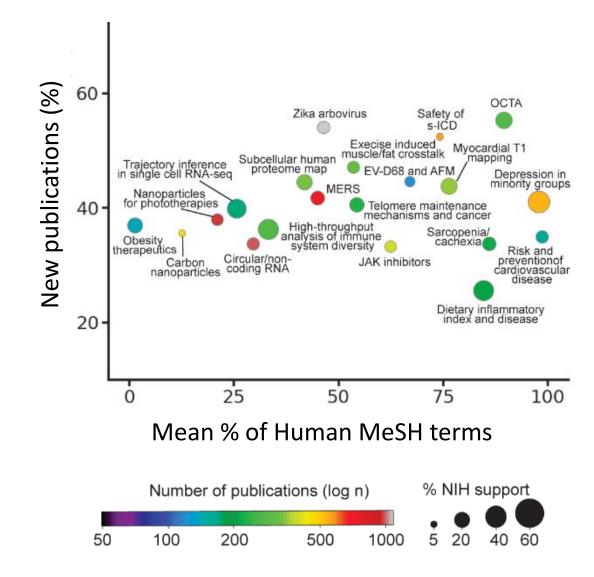
Weinreb, Robert

Wang, Ruikang

Duker, Jay

Fujimoto, James

Topics that signaled transformative breakthroughs between 2014 and 2017





Emergence of mRNA vaccines: Flow of information

1 Cationic liposome-mediated RNA transfection RCR 8.19 Proc Natl Acad Sci 1989

2 Characterization of a messenger RNA RCR 2.26 polynucleotide vaccine vector Cancer Res 1995

3 In vivo application of RNA leads to induction of RCR 3.12 specific cytotoxic T lymphocytes and antibodies Eur J Immunol 2000

4 Polarization of immunity induced by direct RCR 1.46 injection of naked sequence-stabilized mRNA vaccines Cell Mol Life Sci 2004

5 Suppression of RNA recognition by Toll-like RCR 12.70 receptors: the impact of nucleoside modification and the evolutionary origin of RNA Immunity 2005

6 Results of the first phase I/II clinical RCR 2.75 vaccination trial with direct injection of mRNA J Immunother 2008

7 Incorporation of pseudouridine into mRNA yields RCR 7.86 superior nonimmunogenic vector with increased translational capacity and biological stability *Mol Ther 2008*

8 Incorporation of pseudouridine into mRNA enhances RCR 3.45 translation by diminishing PKR activation Nucleic Acids Res 2010

1

9 Nucleoside modifications in RNA limit activation of RCR 2.43 2'-5'-oligoadenylate synthetase and increase resistance to cleavage by RNase L Nucleic Acids Res 2011

10 Generating the optimal mRNA for therapy: HPLC RCR 5.75 purification eliminates immune activation and improves translation of nucleoside-modified, protein-encoding mRNA Nucleic Acids Res 2011

11 Protective efficacy of in vitro synthesized, specific RCR 6.60 mRNA vaccines against influenza A virus infection Nat Biotechnol 2012

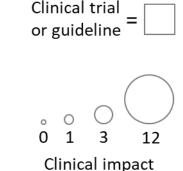
12 Validation of the wild-type influenza A human challenge RCR 4.05 model H1N1pdMIST: an A(H1N1)pdm09 dose-finding investigational new drug study Clin Infect Dis 2015

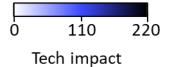
13 Optimization of Lipid Nanoparticle Formulations for RCR 7.44 mRNA Delivery in Vivo with Fractional Factorial and Definitive Screening Designs Nano Lett 2015

14 Expression kinetics of nucleoside-modified mRNA RCR 8.56 delivered in lipid nanoparticles to mice by various routes J Control Release 2015 15 Preclinical and Clinical Demonstration of

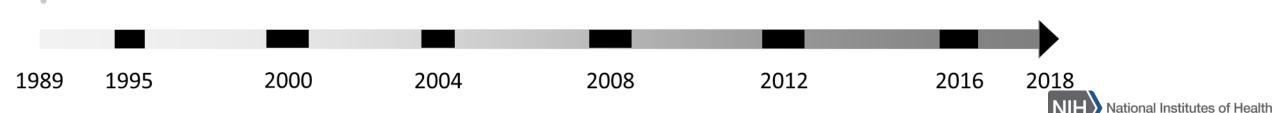
RCR 12.92 Immunogenicity by mRNA Vaccines against H10N8 and H7N9 Influenza Viruses Mol Ther 2017

16 Safety and immunogenicity of a mRNA rabies vaccine RCR 7.50 in healthy adults: an open-label, non-randomised, prospective, first-in-human phase 1 clinical trial Lancet 2017





Office of Portfolio Analysis



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iSearch Analytics

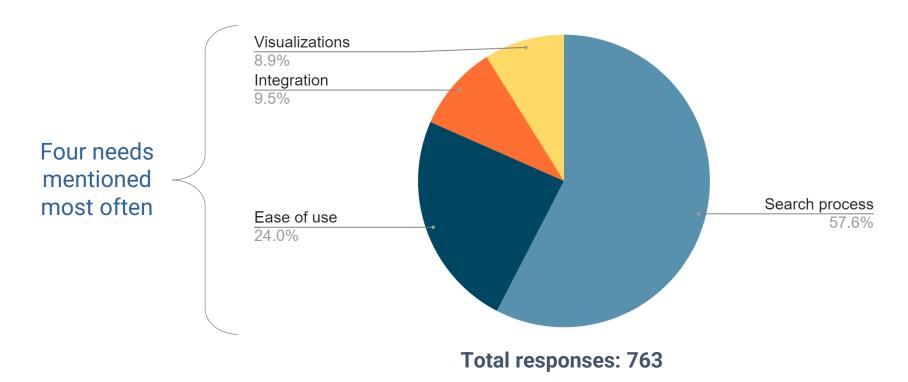
look for our public beta launch in September!





Research summary

What do NIH users care about most?



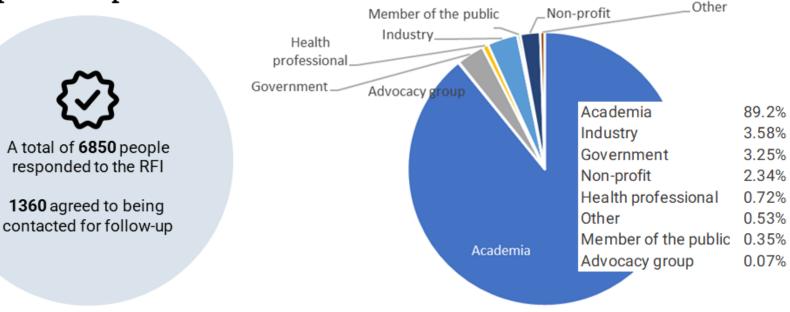
NIH surveys (March 2021 through June 2021)



Research summary

Who are the prospective public users? How can we best meet their analytical needs?

September 2021 Request for Information (RFI) public responses



Respondent categories

Interviews & User testing

- NIH Staff
- Staff of other government agencies
- Public RFI respondents who agreed to be contacted





Transformative functionality

Three major new features



Goes beyond PubMed: Adds preprints and continues progress towards comprehensive coverage of publications



Person Disambiguation*

Provides highly cleaned person-level data and metrics

3 Visualizations Reimagined

Language Model (LM) organizes the information for users

Automated, multi-layered, interactive displays with Al-generated labels to guide searches and exploration



National Institutes of Health Office of Portfolio Analysis

*Yu et al. (2021) The effect of mentee and mentor gender on scientific productivity of applicants for NIH training fellowships. bioRxiv 10.1101/2021.02.02.429450

Transformative functionality

Examples of the analytical power of this new tool



Map research topics, drill down on sub-topics (Grants, pubs, CTs)

- Just "click around"
- Use keywords
- Optimize searches by using both strategies
- Find overlapping investments
- Find research gaps



Transformative functionality

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- Find experts in any area of biomedical research
- Identify the subset funded by NIH, VA, FDA, CDC etc.
- Find all of their co-authors
- For the awardees above, find all of their co-PIs

- Review the careers of individuals or groups
 - Publications
 - Preprints
 - Clinical trials
 - Patents
 - NIH support

Find research gaps

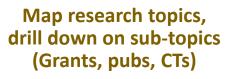


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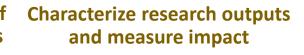




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- Highly influential pubs and/or those with
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- Verified clinical impact
- Verified tech impact

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Characterize research outputs and measure impact

- Highly influential pubs and/or those with
- High translational potential
- Verified clinical impact
- Verified tech impact



Explore topics predicted to produce future scientific breakthroughs

- Find the very recent seminal papers on each topic
- Characterize the investments that funded or are funding each topic



• Find research gaps

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