Correspondence
Jean Bousquet, Institute of Allergology, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany.
Email: jean.bousquet@orange.fr

ORCID

Bernardo Sousa-Pinto https://orcid.org/0000-0002-1277-3401
Jean Bousquet https://orcid.org/0000-0002-4061-4766

REFERENCES

1. Basch E, Barbera L, Kerrigan CL, Velikova G. Implementation of patient-reported outcomes in routine medical care. *Am Soc Clin Oncol Educ Book*. 2018;38:122-134.
2. Weldring T, Smith SM. Patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs). *Health Serv Insights*. 2013;6:61-68.
3. Bousquet J, Arnavielhe S, Bedbrook A, et al. MASK 2017: ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma multimorbidity using real-world-evidence. *Clin Transl Allergy*. 2018;8:45.
4. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43(2):343-373.
5. GINA report 2021. https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf. Accessed January 30, 2022
6. Bakdash JZ, Marusich LR. Repeated measures correlation. *Front Psychol*. 2017;8:456.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

DOI: 10.1111/all.15249

Research impact analysis of international funding agencies in the realm of allergy and immunology

To the Editor,

A longitudinal approach should be employed for research and development (R&D) on allergic and immunological diseases across all life stages. To strategically use limited public funds in promoting such R&D, their characteristics of long-term research support and societal implementation should be considered.[1] However, outcomes of the funding research evaluation have focused on conventional, shortsighted indicators. To determine the kind of indicators needed for the funding strategy, we compared the research impact of funding agencies (FAs) in the UK, US, and Japan, utilizing indices related to research substantiality[2] and analyzing index words/abstracts connected with the national strategy for allergy and immunology.[3]

We used AMEDfind—an open database of top-down R&D projects funded by AMED—and selected 53 awards for a Practical Research Project for Allergic Diseases and Immunology (AMED-PPAI) (Figure S1). 1053 papers with verified PubMed IDs were included. As the controls, we selected the Hypersensitivity, Autoimmune, and Immune-mediated Diseases Study Section (NIH-HAI), an immunology-focused project in the Americas, and Human Immunology Unit (MRC-HIU), that in Europe, extracting 373 US papers and 118 UK papers, published in 2015–2019, respectively (see Appendix S1 for all methods).

The Field-Weighted Citation Impact (FWCI)—evaluating research paper quality—was highest for MRC-HIU following NIH-HAI and AMED-PPAI (Table 1, Figure 1A). Although the international co-authorship rate was lowest in the AMED-PPAI, the annual trend showed a gradual increase (Figure 1B, Table 1). The number of top 10% most cited papers[2]/value, evaluating funding efficiency, was highest for MRC-HIU (Table 1).

To characterize these outputs, we performed natural language analyses of the top 50 FWCI papers from three FAs and top 100 papers on this topic during 2015–2019 (Figure 1C–E).[4] Although all FAs produced mainly basic allergy/immunology study papers (e.g., clusters 0, 1, 2, and 9 in Figure 1D), AMED-PPAI produced relatively

Abbreviations: AMED-PPAI, Practical Research Project for Allergic Diseases and Immunology of the Japan Agency for Medical Research and Development; EU, European Union; FA, Funding agency; FWCI, Field-Weighted Citation Impact; MeSH, Medical Subject Headings; METI, Ministry of Economy, Trade and Industry of Japan; MEXT, Ministry of Education, Culture, Sports, Science and Technology of Japan; MHLW, Ministry of Health, Labour and Welfare of Japan; MRC-HIU, Human Immunology Unit of the Medical Research Council; NIH-HAI, Hypersensitivity, Autoimmune, and Immune-mediated Diseases Study Section of the National Institutes of Health; R&D, Research and development; UK, United Kingdom; UMAP, Uniform Manifold Approximation and Projection; US, United States of America.

TABLE 1 Comparison of publications and societal impact of research funded by international funding agencies

	AMED-PPAI	MRC-HIU	NIH-HAI	UK comparator	Mann–Whitney–Wilcoxon distribution *p* values
FWCI	1.92	3.45	2.48		
No. of publications (2015–2019)	1053	118	373		
Value of awards (million USD, 2015–2019)	23.6	8.86	35.3		
No. of publications/value	37.3	9.35	7.09		
International co-authorship percentage	1.36	4.17	1.60		
No. of top 10% most cited papers	10.2	5.3	3.9		
No. of top 10% most cited papers/value	0.432	0.598	0.110		
No. of awards	53			1376	N/A
Value of awards (million USD, 2013–2018)	20.9			521	N/A
Mean value/award	0.393			0.379	.71
Mean funding peirod (years)	2.90			3.00	.071
No. of intellectual properties/value	0.00473			0.00155	.039(*)
No. of publications/value	0.509			0.118	2.43E−13(***)
Ratio of CC–BY papers	0.350			0.486	N/A
Value of further funding/value	1.58			2.97	.0019(**)
No. of engagement activities/value	0.0909			0.100	.71

Abbreviations: AMED-PPAI, Practical Research Project for Allergic Diseases and Immunology of the AMED; FWCI, Field-Weighted Citation Impact; MRC-HIU, Human Immunology Unit of the MRC; N/A, not applicable; NIH-HAI, Hypersensitivity, Autoimmune, and Immune-mediated Diseases Study Section of the NIH; No, number; USD, United States Dollar.

*$p < .05$, **$p < .01$, ***$p < .001$.

more clinically relevant outputs (clusters 3 and 8). Further, we analyzed MeSH headings for relevance to national unique Strategic Outlook toward 2030 formulated by the Ministry of Health, Labour and Welfare of Japan (Figure 1F, Table S1).[3] While most projects were pathogenic studies, AMED-PPAI funded research published more papers on precision medicine and host-extrinsic factor relations (Action I-2, I-3). The Action II and III groups were not strongly represented.

To assess societal impact, we utilized ResearchFish—a widely used database of the FAs in Europe[5]—to randomly select 1376 UK-funding awards and their reports, trend-matched for the AMED-PPAI (UK comparator) (Table S2). The number of intellectual properties and publications per value was higher for AMED-PPAI, while the open access rate and new funding amount obtained were higher in the UK comparator (Table 1). Despite the similar number of engagement activities, their outreach targets differed (AMED toward public and media; the UK towards students, patients, and industry; Figure 1G).

The purpose of this study is not to compete for superiority among countries or FAs but to expand the possibilities for multidimensional interpretation of trends and characteristics of funded outcomes using multiple indicators rather than uniform one. Due to the limitation of open databases, we focused on three countries for the funding impact analysis, whereas scholarly output in this realm is also increasing in other countries and jurisdictions, including the EU (Figure S2). China's growth is particularly remarkable, and additional analysis is desirable with public funding status.[6] Furthermore, the indices used have different trends among countries, and their balance should be carefully considered to reflect each country's science and technology policies.

In conclusion, we conducted impact analyses from multiple perspectives, including indicators related to substantiality[2] and index words profiling/clustering based on the national strategy.[3] These findings may inform international collaborative long-term research that strategically leverages each research funding institution's strengths.

KEYWORDS

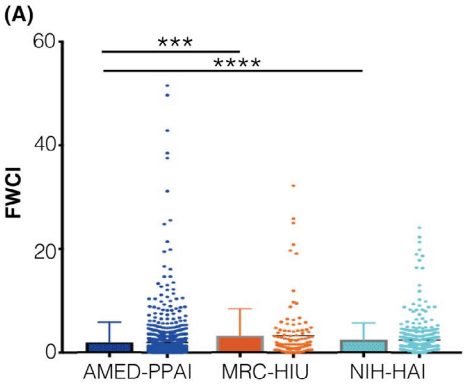
allergy, immunology, research impact analysis, research strategy, substantiality index

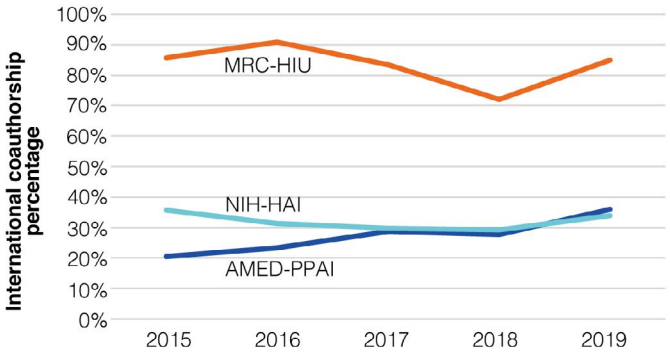
FUNDING INFORMATION

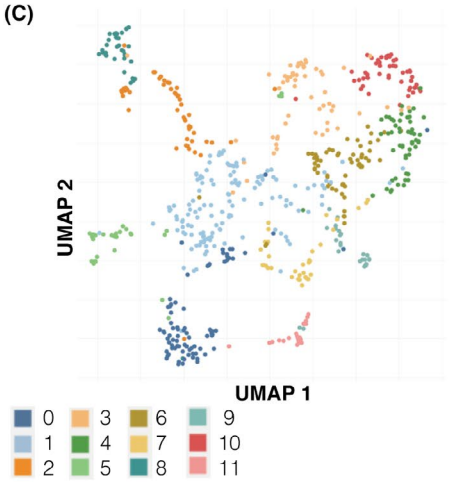
This research was supported by the Scientific Research Fund of the Ministry of Health, Labour and Welfare, Japan (201913009A, 21FE2001), JSPS KAKENHI (Grant Numbers: 16H06580 and 17K01173), and JST/RISTEX research funding program "Science of Science, Technology and Innovation Policy" (JPMJRX19B3).

ACKNOWLEDGEMENTS

We extend our special gratitude to Prof. Warwick Anderson (Former Secretary-General, International Human Frontier Science Program Organization) for his valuable suggestions regarding the manuscript. We also acknowledge Dr. Gavin Reddick at Interfolio UK for his support in the societal impact analysis.

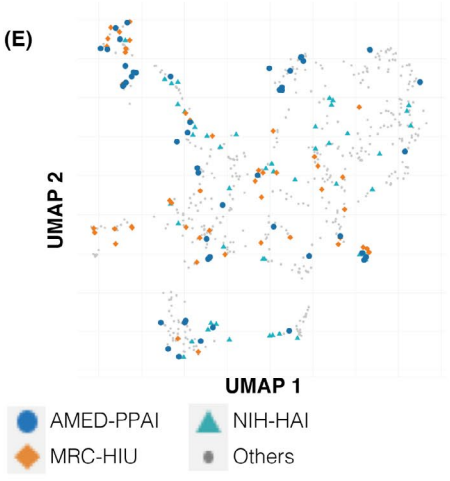


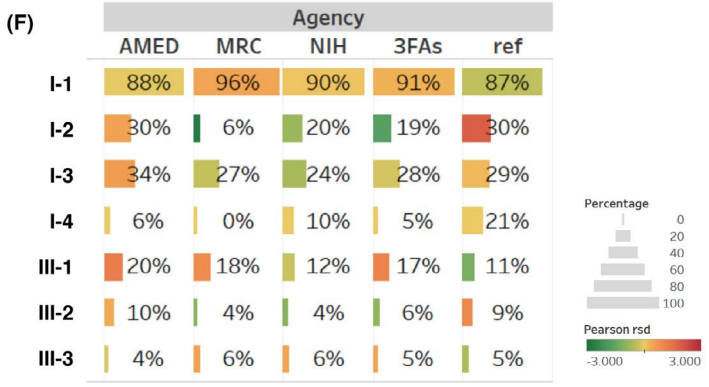




(D)

No.	Area of research	AMED-PPAI	MRC-HIU	NIH-HAI	Others					
					2015-2019	2015	2016	2017	2018	2019
0	Hosts and microbiota	22%	6%	16%	12%	8%	9%	17%	7%	17%
1	Extracellular signals and immune responses	10%	26%	14%	22%	32%	23%	23%	21%	12%
2	Asthma/Atopic dermatitis and innate lymphoid cells	14%	8%	22%	6%	8%	7%	4%	3%	10%
3	Clinical management of immunological diseases	12%	4%	10%	9%	6%	6%	12%	8%	12%
4	Basic research for cancer immunotherapy	4%		8%	10%	7%	9%	10%	16%	8%
5	Infectious diseases including HIV	6%	12%		5%	4%	6%	4%	7%	5%
6	Lymphocyte subsets and functions		10%	10%	10%	15%	13%	6%	6%	11%
7	Macrophages, monocytes, dendritic cells and neutrophils	2%	2%	4%	6%	6%	9%	3%	5%	7%
8	Clinical management of allergic diseases	18%	18%		4%	4%	2%	5%	6%	2%
9	Omics and single cell analysis	10%	14%	6%	2%		1%		4%	6%
10	Clinical research for cancer immunotherapy				10%	7%	11%	9%	12%	10%
11	Neuroinflammation and central nervous system	2%		10%	4%	3%	4%	7%	5%	





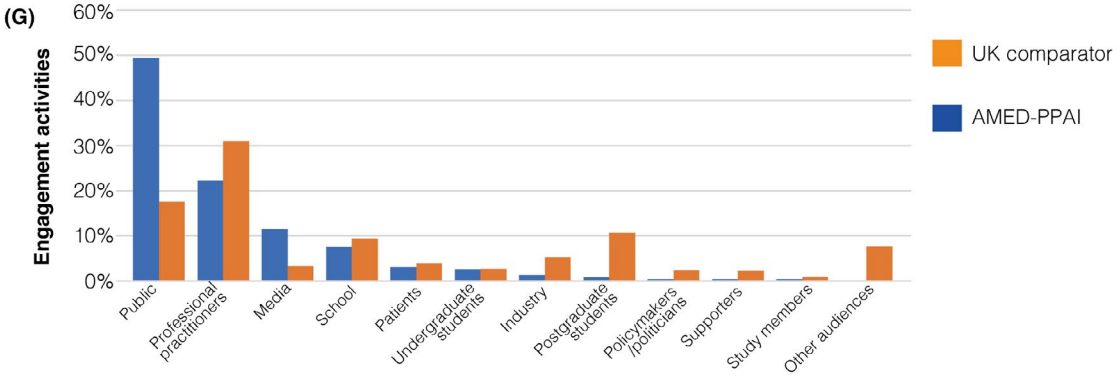


FIGURE 1 Comparison of research impact of international funding agencies (FAs). Scholarly outputs from AMED-PPAI, MRC-HIU, and NIH-HAI were analyzed using FWCI (A) and international co-authorship ratio (B). UMAP with spectral clustering for dimension reduction of top 50 FWCI papers from three FAs (C, D) and relevance of each FA against twelve clusters (E). Cross-tabulation of MeSH headings' list of Actions of Strategy 2030 with list of top 50 papers from each FA (F) (box size: the percentage of papers with related MeSH; box color: standardized Pearson residuals). Objectives of engagement activities were listed for AMED-PPAI and UK comparator (G)

CONFLICT OF INTEREST

TF and AI are employees of the AMED. YO and KA are scientific advisors of AMED. MTa is the Program Officer, and HI is the Program Supervisor of the AMED-PPAI. TA (2015–2020) and YO (2018–2020) were employees of the AMED. SNi was the former Program Supervisor of the AMED-PPAI (2015–2018). The other details about competing interests are provided separately.

Takeya Adachi[1,2,3,4]
Yasushi Ogawa[5,6]
Tamami Fukushi[7]
Kei Ito[8]
Amane Koizumi[9]
Masashi Shirabe[10]
Masako Toriya[11]
Jun Hirako[12]
Takenori Inomata[1,13,14]
Katsunori Masaki[1,15]
Ryohei Sasano[12]
Sakura Sato[1,16]
Keigo Kainuma[17]
Masaki Futamura[1,18]
Keiko Kan-o[1,19]
Yosuke Kurashima[1,20]
Saeko Nakajima[1,21]
Masafumi Sakashita[1,22]
Hideaki Morita[1,23,24]
Aikichi Iwamoto[7]
Sankei Nishima[25]
Mayumi Tamari[7,26]
Hajime Iizuka[7,27]

[1]*ENGAGE-Task Force, Tokyo, Japan*
[2]*Keio Frontier Research & Education Collaborative Square (K-FRECS) at Tonomachi, Keio University, Kanagawa, Japan*
[3]*Department of Medical Regulatory Science, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, Kyoto, Japan*
[4]*Department of Dermatology, Tachikawa Hospital, Federation of National Public Service Personnel Mutual Aid Associations, Tokyo, Japan*
[5]*Department of Advanced Medicine, Nagoya University, Nagoya, Japan*
[6]*Department of Dermatology, Nagoya University, Nagoya, Japan*
[7]*Japan Agency for Medical Research and Development (AMED), Tokyo, Japan*
[8]*Accenture Inc., Tokyo, Japan*
[9]*National Institutes of Natural Science (NINS), Tokyo, Japan*
[10]*Tokyo Institute of Technology, Tokyo, Japan*
[11]*Global Research Institute, Keio University, Tokyo, Japan*
[12]*Graduate School of Informatics, Nagoya University, Nagoya, Japan*
[13]*Department of Ophthalmology, Juntendo University Graduate School of Medicine, Tokyo, Japan*
[14]*Department of Digital Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan*
[15]*Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, Tokyo, Japan*
[16]*Department of Allergy, Clinical Research Center for Allergy and Rheumatology, National Hospital Organization Sagamihara National Hospital, Kanagawa, Japan*
[17]*Institute for Clinical Research, National Hospital Organization Mie National Hospital, Mie, Japan*
[18]*Division of Pediatrics, National Hospital Organization Nagoya Medical Center, Nagoya, Japan*
[19]*Research Institute for Diseases of the Chest, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*
[20]*Department of Innovative Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan*
[21]*Department of Drug Discovery for Inflammatory Skin Diseases, Kyoto University Graduate School of Medicine, Kyoto, Japan*
[22]*Department of Otorhinolaryngology Head and Neck Surgery, University of Fukui, Fukui, Japan*
[23]*Department of Allergy and Clinical Immunology, National Research Institute for Child Health and Development, Tokyo, Japan*
[24]*Allergy Center, National Center for Child Health and Development, Tokyo, Japan*
[25]*National Hospital Organization Fukuoka National Hospital, Fukuoka, Japan*
[26]*Division of Molecular Genetics, The Jikei University School of Medicine, Research Center for Medical Science, Tokyo, Japan*
[27]*Research Institute of Psoriasis, Housui General Medical Clinic, Sapporo, Japan*

Correspondence
Takeya Adachi, Department of Medical Regulatory Science, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, 465 Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, 602-8566 Kyoto, Japan.
Email: jpn4156@me.com

Takeya Adachi and Yasushi Ogawa authors contributed equally to this work

ORCID

Takeya Adachi https://orcid.org/0000-0002-5289-5980
Yasushi Ogawa https://orcid.org/0000-0003-3553-9607
Tamami Fukushi https://orcid.org/0000-0003-4599-2413
Amane Koizumi https://orcid.org/0000-0003-1177-0185
Masashi Shirabe https://orcid.org/0000-0003-4569-6171
Masako Toriya https://orcid.org/0000-0002-8955-0353
Takenori Inomata https://orcid.org/0000-0003-3435-1055
Katsunori Masaki https://orcid.org/0000-0003-0909-9409
Sakura Sato https://orcid.org/0000-0003-3674-0759
Masaki Futamura https://orcid.org/0000-0002-7442-9649
Keiko Kan-o https://orcid.org/0000-0002-7736-588X
Yosuke Kurashima https://orcid.org/0000-0001-8588-4033
Saeko Nakajima https://orcid.org/0000-0003-0831-1447
Hideaki Morita https://orcid.org/0000-0003-0928-8322
Aikichi Iwamoto https://orcid.org/0000-0001-5868-7499
Mayumi Tamari https://orcid.org/0000-0002-5755-9177

REFERENCES

1. Kamenetzky A, Hinrichs-Krapels S. How do organizations implement research impact assessment (RIA) principles and good practice? A narrative review and exploratory study of four international research funding and administrative organizations. *Health Res Policy Systs*. 2020;18:6.
2. Shirabe M, Koizum A. Substantiality: a construct indicating research excellence to measure university research performance. *J Data Inf Sci*. 2021;6:1.
3. Adachi T, Kainuma K, Asano K, et al. Strategic outlook toward 2030: Japan's research for allergy and immunology - secondary publication. *Allergol Int*. 2020;69:561.
4. Cohan A, Feldman S, Beltagy I, Downey D, Weld DS, Assoc Computat L, SPECTER: document-level representation learning using citation-informed transformers. 58th Annual Meeting of the Association for Computational Linguistics (Acl 2020). 2020;2270.
5. Boulding H, Kamenetzky A, Ghiga I, et al. Mechanisms and pathways to impact in public health research: a preliminary analysis of research funded by the national institute for health research (NIHR). *BMC Med Res Methodol*. 2020;20:34.
6. The Swedish Foundation for International Cooperation in Research and Higher Education: Public Research and Innovation Funding Actors in China. https://www.stint.se/wp-content/uploads/2020/09/23087_STINT_rapport_Public_Research_and_Innovation_Funding_Actors_in_China_webb.pdf. Accessed January 13, 2022.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

DOI: 10.1111/all.15250

Gastrointestinal γδ T cells reveal differentially expressed transcripts and enriched pathways during peanut oral immunotherapy

To the Editor,

Oral immunotherapy (OIT) has been successful in desensitizing patients to offending food allergens,[1] although the identification of tissue-resident T-cell subsets and cognate pathways leading to desensitization has been challenging. The γδ T cells are a major T-cell subset of mucosal intraepithelial lymphocytes (IELs) and play a significant role in tissue homeostasis and repair.[2] In addition to aiding mucosal barrier function, γδ T cells have also been recently discovered to be pivotal to cellular adaptations in response to nutrient sensing.[3] In the broader context of atopy, γδ T cells have been implicated both in IgE- and Th2-enhancing and IgE-suppressive effects.[4,5] However, specifically with regard to peanut allergy, γδ T cells were shown to be IgE-suppressive and thus protective in a study employing mouse models.[6] In a recent study, peripheral γδ Treg cells from patients analyzed over 24 weeks of peanut OIT were shown to undergo dynamic changes in expression profiles, implicating pathways involved in immune homeostasis.[7] To the best of our knowledge, the role of γδ T cells in the intestinal mucosa of food allergic patients during immunotherapy has not been examined. To this end, we investigated whether γδ T cells in the gastrointestinal (GI) tract exhibited changes during peanut OIT. We hypothesized that GI-resident γδ T cells in peanut allergic patients would increase during the course of peanut OIT and might reveal transcripts and pathways relevant to the mechanisms of peanut desensitization.

Participants were recruited from a randomized, double-blind, placebo-controlled, phase II clinical trial of peanut OIT (POISED; NCT02103270).[1] Informed consent was obtained from all participants. Following dosage build-up over ~52 weeks, peanut-allergic

Nadeau, Manohar, DeKruyff and Chinthrajah are Co-senior authors.