3Ranker

Wynand Alkema



Information overload or filter failure

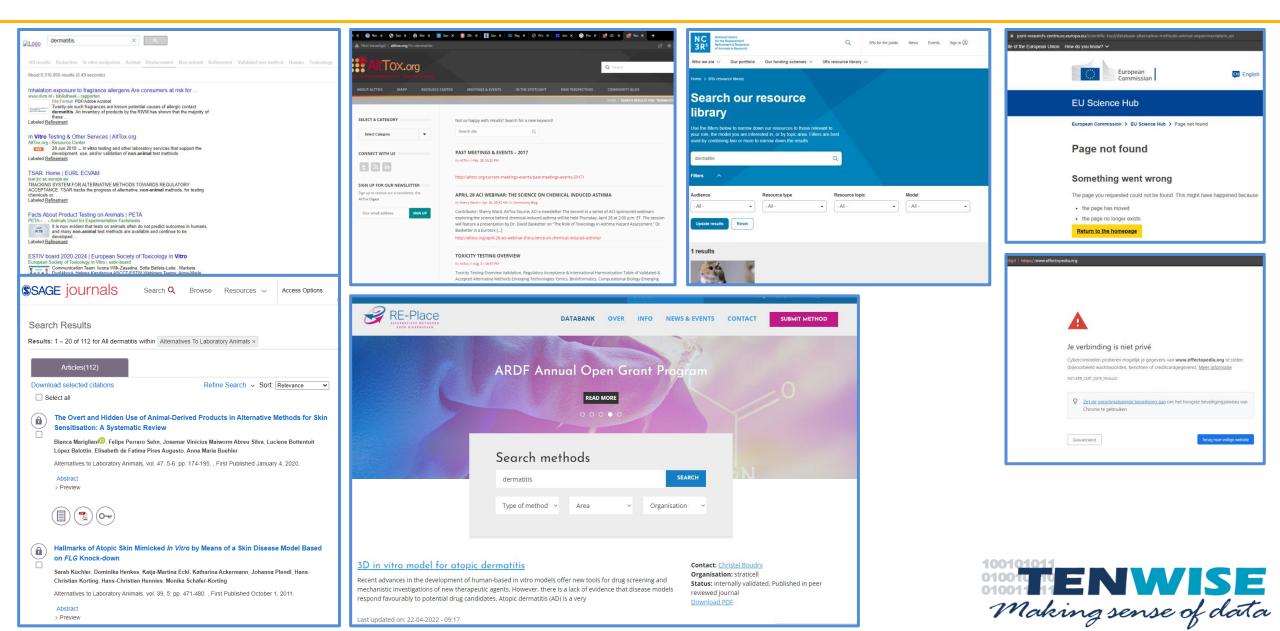




How can we identify literature and scientific articles that describe methods for **R**eplacement, **R**efinement and **R**eduction?



Search for dermatitis



A lot of information

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Making sense of data

The problem

- How can we identify articles that describe methods for Replacement, Refinement and Reduction?
 - Often not explicitly described as such.
 - Hard to define the correct search terms.
- As a consequence the search is
 - Elaborate
 - Time consuming
 - Biased
 - Incomplete
 - Not updated



EVALUATION OF STRATEGIES TO IMPROVE SCIENTIFIC QUALITY AND RESPONSIBLE ANIMAL USE IN RESEARCH

Main findings from a survey:

No budget/time for specific 3R search

Existing relevant 3R information not found / not used

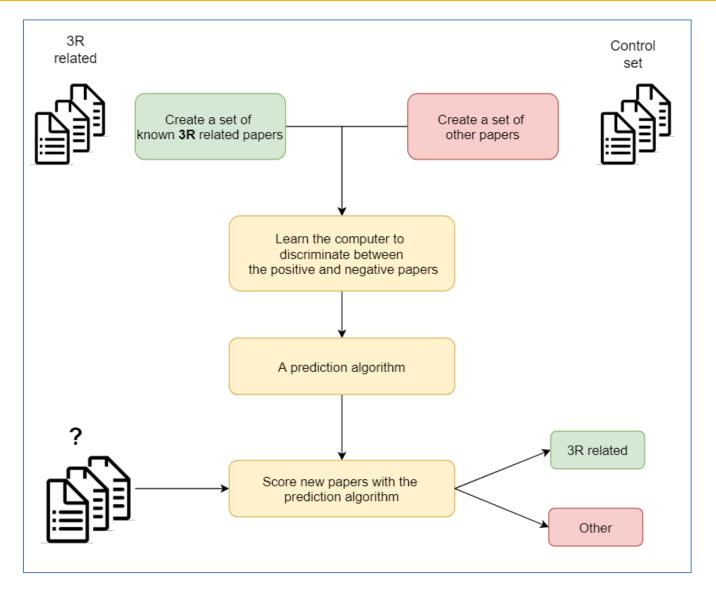


Solution: Mine the bibliome

EMBO reports viewpoint	Sage Journals Searce Browse by discipline v Information for v	ch this journal ~ Enter search terms Q Advanced search
Mining the bibliome: searching for a needle in a haystack? New computing tools are needed to effectively scan the growing amount of scientific literature for useful information • by Les Grivell	The 3Ranker: An Al-based Algorithm for	Impact Factor: 2.5 Journal Homepage Jublished online October 21, 2023 Journal Homepage Finding Non-animal Alternative Methods Sarun Ulfhake , Rafael Frias, Merel Ritskes-Hoitinga , and Wynand Alkema 9292231210777 Get access
Altern Lab Anim. 2021 Jul;49(4):133-136. doi: 10.1177/02611929211048447. Epub 2021 Sep 28. The Use of Artificial Intelligence for the Fast and Effective Identification of Three Rs-based Literature Merel Ritskes-Hoitinga ^{1 [2]} , Wynand Alkema ^{3 [4]} Affiliations + expand PMID: 34581190 DOI: 10.1177/02611929211048447	3Ranker, which is a fast, keyword-independent methods for use in biomedical research. The 3R	hensive structured databases and balanced uctured textual databases. In this paper we describe

Making sense of data

Machine Learning Approach



Based on a set of known positive and negative papers, a computer model is trained that can predict whether a paper is about a **3R** subject.

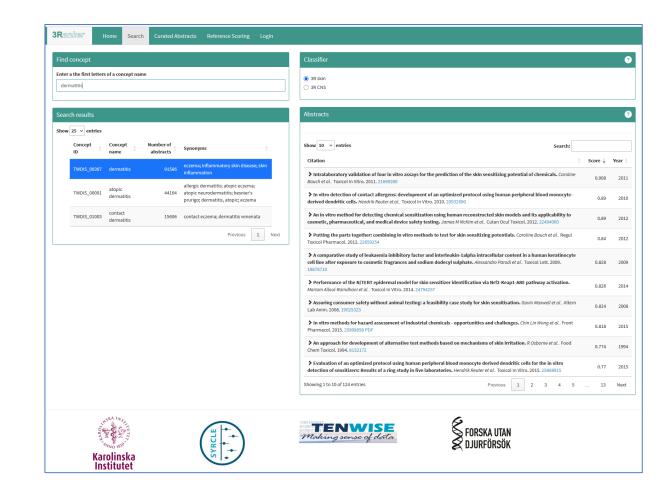
3865 papers describing Alternative Animal Tests (Mesh term)

A random abstract set



Currently available

- 40 million PubMed abstracts with a 3R score for **skin** or **central nervous system** ranging from 0 to 1.
- An **Applied Programming Interface** is available for plugging in into your own workflow.
- Searchable web interface with 500.000 predefined keywords (genes, pathways, diseases, drugs, products).

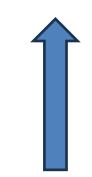




Access with an API

1	import requests	
2	import sys	
3		1
4	### Setting up the connection to the api ###	
5	# The valid APIKEY is read as the first argument from the command line	2
6	<pre>session = requests.Session()</pre>	
7	<pre>base_url = 'https://apimlqv2.tenwiseservice.nl/api/mlquery/'</pre>	3
8	<pre>session.headers['referer'] = 'https://apimlqv2.tenwiseservice.nl/'</pre>	
9	<pre>session.get(base_url + "start/")</pre>	4
10	<pre>payload = {'apikey': sys.argv[1],</pre>	_
11	<pre>'csrfmiddlewaretoken': session.cookies.get_dict()['csrftoken']}</pre>	5
12		
13	### Get some PMIDs	
14	payload['pmids'] = '33919317, 30671696, 21669280'	
15	results = session.post(base_url + "refset/class_scores/",	
16	payload)	
17	json_response = results.json()	
18		
19	### Print out scores	
20	for item in json_response['result']['class_scores']:	
21	<pre>print("\t".join(str(x) for x in [item['pmid'],</pre>	
22	item['classifier'],	
23	item['classifier_score']	
24		
25		
26		

	A	В	С
1	PMID	Model	Score
2	21669280	3r_skin	0.908
3	30671696	3r_cns	0.562
4	30671696	3r_skin	0.506
5	33919317	3r_cns	0.772





	А	В	C
1	PMID	Model	Score
2	21669280	3r_skin	0.908
3	30671696	3r_cns	0.562
4	30671696	3r_skin	0.506
5	33919317	3r_cns	0.772

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	Share	Int J Mol Sci. 2021 Apr 21;22(9):4334. doi: 10.3390/ijms22094334. PMID: 33919317 Free PMC article. Review.						



	A	В	C
1	PMID	Model	Score
2	21669280	3r_skin	0.908
3	30671696	3r_cns	0.562
4	30671696	3r_skin	0.506
5	33919317	3r_cns	0.772





CNS: Parkinson's

Search 3R papers related to Parkinson's Disease:

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DIS_17683	Parkinsonism	19481			> Human stem cell models of neurodegeneration: a novel approach to study mechanisms of disease development. <i>Gunnar Hargus et al.</i> . Acta Neuropathol. 2013. 24306942	0.736	2013
			Previous 1 Next	t	> Modeling Parkinson's Disease and Atypical Parkinsonian Syndromes Using Induced Pluripotent Stem Cells. Takayasu Mishima et al Int J Mol Sci. 2018. 30518093 PDF	0.718	201
					> In Silico design of AVP (4-5) peptide and synthesis, characterization and in vitro activity of chitosan nanoparticles. Serda Kecel-Gunduz et al Daru. 2020. 31942695 PDF	0.706	202
					Chemically Induced Models of Parkinson's Disease: History and Perspectives for the Involvement of Ferroptosis. Shuheng Wen et al Front Cell Neurosci. 2021, 33424553 PDF	0.676	202



CNS: Parkinson's

Display only 3R papers that deal with induced Pluripotent Stem Cells (iPSC):

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Utilising Induced Pluripotent Stem Cells in Neurodegenerative Disease Research: Focus on Glia. Katral Int J Mol Sci. 2021. 33919317 PDF	rina Albert et	0.772	2021		
Modeling Parkinson's Disease and Atypical Parkinsonian Syndromes Using Induced Pluripotent Ster Takayasu Mishima et al Int J Mol Sci. 2018. 30518093 PDF	NIL National L	Library of N	Medicine Information		Log in
Modeling Human Neurological and Neurodegenerative Diseases: From Induced Placipotent Stem Concernance Neuronal Differentiation and Its Applications in Neurotrauma. Hisham Bahmad et al Front Mol Neurosc 28293168 PDF	Pub		317 d Create alert Create RSS		X Search User Guide
Human induced pluripotent stem cells and neurodegenerative disease: prospects for novel therapie Wook Jung et al Curr Opin Neurol. 2012. 22357218 PDF		. 2021 Apr 21;22(9);4334. doi: 10.3390/ijms22094334		FULL TEXT LINKS
Using induced pluripotent stem cell neuronal models to study neurodegenerative diseases. <i>Xinwen</i> Biochim Biophys Acta Mol Basis Dis. 2019. 30898538 PDF		ative Dise	otent Stem Cells i ease Research: Foc rală ² , Šárka Lehtonen ^{2–3}		Actions
> Application of human induced pluripotent stem cells for modeling and treating neurodegenerative Natalie L Payne et al N Biotechnol. 2014. 24815224		ells (iPSCs) are a s	II: 10.3390/ijms22094334 elf-renewable pool of cells derived d to other cell types, including neu		
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Citation

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International Journal of Molecular Sciences



Review

> Utilising Induced Pluripotent Stem Cells in Neurodegenerative Disease Research: Focus on Glia. *Katrina Albert et al.*. Int J Mol Sci. 2021. 33919317 PDF

Modeling Parkinson's Disease and Atypical Parkinsonian Syndromes Using Induced Pluripotent Stem Cells. Takayasu Mishima et al.. Int J Mol Sci. 2018. 30518093 PDF

Modeling Human Neurological and Neurodegenerative Diseases: From Induced Pluripotent Stem Cells to Neuronal Differentiation and Its Applications in Neurotrauma. *Hisham Bahmad et al.*. Front Mol Neurosci. 2017. 28293168 PDF

Human induced pluripotent stem cells and neurodegenerative disease: prospects for novel therapies. *Yong Wook Jung et al.*. Curr Opin Neurol. 2012. 22357218 PDF

Using induced pluripotent stem cell neuronal models to study neurodegenerative diseases. *Xinwen Zhang et al.*. Biochim Biophys Acta Mol Basis Dis. 2019. 30898538 PDF

Annlication of human induced nlurinotent stem cells for modeling and treating neurodegenerative

Modeling Parkinson's Disease and Atypical Parkinsonian Syndromes Using Induced Pluripotent Stem Cells

Takayasu Mishima, Shinsuke Fujioka, Jiro Fukae, Junichi Yuasa-Kawada and Yoshio Tsuboi *

Department of Neurology, Fukuoka University, Fukuoka 814-0180, Japan; mishima1006@fukuoka-u.ac.jp (T.M.); shinsuke@cis.fukuoka-u.ac.jp (S.F.); j-fukae@juntendo.ac.jp (J.F.); junkichi@marine.email.ne.jp (J.Y.-K.) * Correspondence: tsuboi@cis.fukuoka-u.ac.jp; Tel.: +81-92-801-1011 (ext. 3520)

Received: 3 September 2018; Accepted: 28 November 2018; Published: 4 December 2018



Abstract: Parkinson's disease (PD) and atypical parkinsonian syndromes are age-dependent multifactorial neurodegenerative diseases, which are clinically characterized by bradykinesia, tremor, muscle rigidity and postural instability. Although these diseases share several common clinical phenotypes, their pathophysiological aspects vary among the disease categories. Extensive animal-based approaches, as well as postmortem studies, have provided important insights into the disease mechanisms and potential therapeutic targets. However, the exact pathological mechanisms triggering such diseases still remain elusive. Furthermore, the effects of drugs observed in animal models are not always reproduced in human clinical trials. By using induced pluripotent stem cell (iPSC) technology, it has become possible to establish patient-specific iPSCs from their comatic cells and to effectively differentiate these iPSCs into different types of neurons, reproducing *Making sense of data*

Dermatitis

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atopic 44164	allergic dermatitis; atopic eczema; atopic neurodermatitis; besnier's	



Dermatitis

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TWDIS_00091	atopic dermatitis	44164	allergic dermatitis; atopic eczema; atopic neurodermatitis; besnier's prurigo; dermatitis, atopic; eczema	
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> In vitro detection of contact allergens: development of an optimized protocol using human peripheral blood monocyte-derived dendritic cells. <i>Hendrik Reuter et al.</i> . Toxicol In Vitro. 2010. 20932890	0.89	2010
An in vitro method for detecting chemical sensitization using human reconstructed skin models and its applicability to cosmetic, pharmaceutical, and medical device safety testing. <i>James M McKim et al.</i> . Cutan Ocul Toxicol. 2012. 22494060	0.89	2012
> Putting the parts together: combining in vitro methods to test for skin sensitizing potentials. Caroline Bauch et al Regul Toxicol Pharmacol. 2012. 22659254	0.84	2012
A comparative study of leukaemia inhibitory factor and interleukin-1alpha intracellular content in a human keratinocyte cell line after exposure to cosmetic fragrances and sodium dodecyl sulphate. Alessandro Parodi et al Toxicol Lett. 2009. 19878710	0.828	2009



Autophagy (pathway)

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A new approach for risk assessment of pulmonary toxicants: a preliminary study using didecyldimethylammonium chloride. Jun Woo Kim et al Environ Sci Pollut Res Int. 2024. 39266878		0.714	2024
The Current Understanding of Autophagy in Nanomaterial Toxicity and Its Implementation in Safety Assessment-Related Alternative Testing Strategies. <i>Rong-Jane Chen et al.</i> . Int J Mol Sci. 2020. 32235610 Pl		0.698	2020



P38 (gene)

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MAP

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HGNC:6876	MAPK14	27818	CSBP1; CSBP2; CSPB1; Mxi2; PRKM14; PRKM15; p38			
PATH_001697	MAPK signalling	23864	MAP kinase signalling			
HGNC:6871	MAPK1	12470	ERK; ERK2; MAPK2; PRKM1; PRKM2; p41mapk			
HGNC:6881	MAPK8	6796	JNK; JNK1; PRKM8; SAPK1			
HGNC:6893	MAPT	4556	DDPAC; FLJ31424; FTDP-17; MAPTL; MGC138549; MSTD; MTBT1; MTBT2; PPND; PPP1R103: TAU: tau: tau-40			

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Role of p38 MAPK in the selective release of IL-8 induced by chemical allergen in naive THp-1 cells. Montserrat Mitjans et al Toxicol In Vitro. 2008. 18494145	v	0.582	2008
Studies of cell signaling in a reconstructed human epidermis exposed to sensitizers: IL-8 synthesis and release depend on EGFR activation. <i>Aurélie Frankart et al.</i> . Arch Dermatol Res. 2012. 22271211		0.524	2012
> The red wine polyphenol resveratrol shows promising potential for the treatment of nucleus pulposus- mediated pain in vitro and in vivo. Karin Wuertz et al Spine (Phila Pa 1976). 2011. 21587103		0.508	2011
Curcumin Alleviates Osteoarthritis Through the p38MAPK Pathway: Network Pharmacological Prediction and Experimental Confirmation. Xuan Wang et al J Inflamm Res. 2024. 39081871 PDF	on	0.508	2024



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Probiotic (product)

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probio

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● 3R skin ○ 3R CNS	

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Lactobacillus reuteri DSM 17938-A comparative study on the effect of probiotics and lysates on huma Ia Khmaladze et al Exp Dermatol. 2019. 31021014	an skin.	0.56	Year

★ Antioxidant Properties of Postbiotics: An Overview on the Analysis and Evaluation Methods. Negin

Hosseinzadeh et al.. Probiotics Antimicrob Proteins. 2024. 39395091

Antioxidants found naturally in foods have a significant effect on preventing several human diseases. However, the use of synthetic antioxidants in studies has raised concerns about their potential link to liver disease and cancer. The findings show that postbiotics have the potential to act as a suitable alternative to chemical antioxidants in the food and pharmaceutical sectors. Postbiotics are bioactive compounds generated by probiotic bacteria as they ferment prebiotic fibers in the gut. These compounds can also be produced from a variety of substrates, including nonprebiotic carbohydrates such as starches and sugars, as well as proteins and organic acids, all of which probiotics utilize during the fermentation process. These are known for their antioxidant, antibacterial, anti-inflammatory, and anti-cancer properties that help improve human health. Various methodologies have been suggested to assess the antioxidant characteristics of postbiotics. While there are several techniques to evaluate the antioxidant properties of foods and their bioactive compounds, the absence of a convenient and uncomplicated method is remarkable. However, cell-based assays have become increasingly important as an intermediate method that bridges the gap between chemical experiments and in vivo research due to the limitations of in vitro and in vivo assays. This review highlights the necessity of transitioning towards more biologically relevant cell-based assays to effectively evaluate the antioxidant activity of postbiotics. These experiments are crucial for assessing the biological efficacy of dietary antioxidants. This review focuses on the latest applications of the Caco-2 cell line in the assessment of cellular antioxidant activity (CAA) and bioavailability. Understanding the impact of processing processes on the biological properties of postbiotic antioxidants can facilitate the development of new food and pharmaceutical products.

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New development / disease areas

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Reviewer 1 232	Only certified reviewers can contribute to the evaluation of abstracts. Interested? Contact us: nils.hijlkema@tenwise.nl/brun.ulfhake@ki.se
Reviewer 4 5	Frequency and characteristic features of REM sleep without atonia.
	OBJECTIVES: Isolated REM sleep without atonia (iRSWA) is regarded as prodromal phase of REM sleep behavior disorder (RBD) and synucleinopathies. Other factors, however, have also been described to cause RSWA, including sleep apnea, antidepressants use and narcolepsy. We investigated the frequency of RSWA and its different etiologies. METHODS: We investigated RSWA in patients that underwent a clinical video polysomnography. In iRSWA subjects, we examined polysomnography indication and two markers of prodromal Parkinson's disease: excessive daytime sleepiness and depressive symptoms, with a case-control design. RESULTS: Of the 864 included polysomnographies, 188 were positive for RSWA (21.8%), 17 for RBD (2.0%) and 48 for iRSWA (5.6%). Mean Epworth Sleepiness Scale scores were 9.8 ± 4.8 (iRSWA subjects) and 7.5 ± 4.9 (controls), p = 0.014. Mean Beck Depression Inventory-II scores were 11.3 ± 7.9 (iRSWA subjects) and 9.5 ± 8.4 (controls), p = 0.229. Excessive daytime sleepiness was more often the polysomnography indication in the iRSWA group (p = 0.006). CONCLUSIONS: RSWA is a frequent finding in the context of antidepressant use or synucleinopathies. iRSWA subjects reported increased excessive daytime sleepiness and more often had excessive daytime sleepiness as polysomnography indication. SIGNIFICANCE: Our study provides evidence for high frequency of RSWA, underscoring the need for longitudinal studies in iRSWA patients, with interest for conversion to synucleinopathies.



Take home messages

3Ranker provides a versatile AI algorithm that can be

- **Extended** towards new research fields
- Incorporated in other tools via the API
- **Updated** automatically with new PubMed data
- **Applied** towards new text sources

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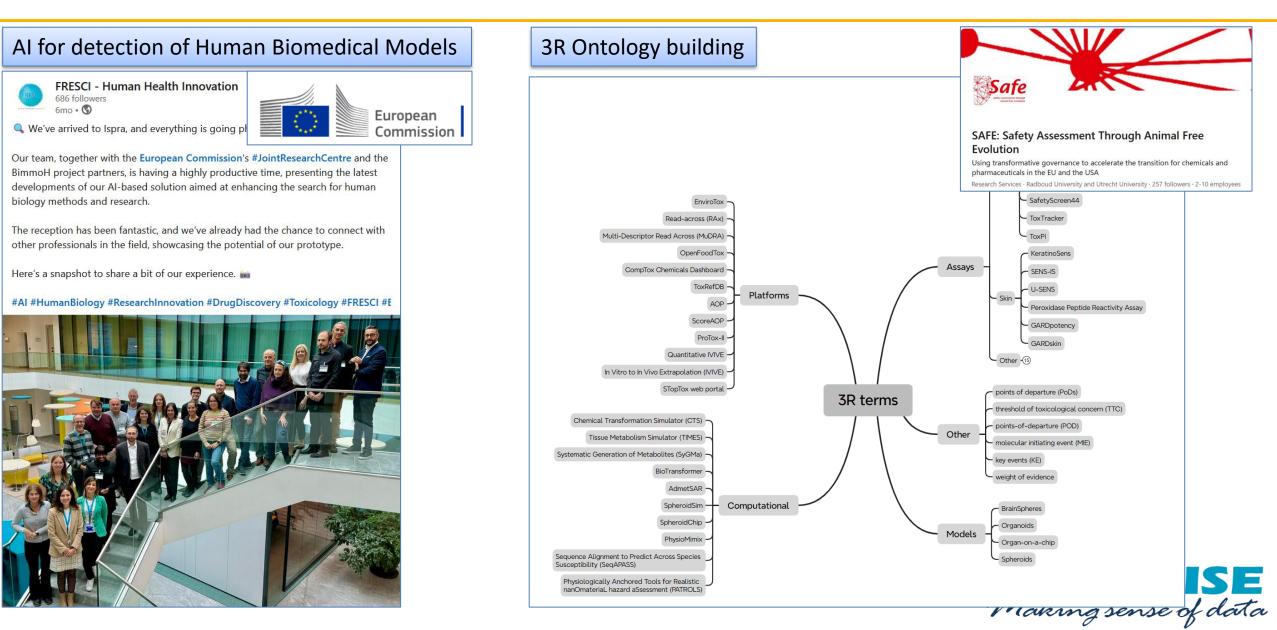
The 3D skin reconstructions used in the study represent an important research tool, added Gitali Indra.

"It's very important to not use animal models in the testing of cosmetics and skin care products," she said. "People don't like to see animal testing data, especially in Europe, where they'll put a picture of a bunny rabbit on a product so people know animals weren't used in the testing. This is a very good model that we can use to test many kinds of drugs by using different assays."



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