
SourceData – bridging scientific publishing and open science

Dr. Thomas Lemberger
EMBO

1. Open Science
2. SourceData
3. Outlook

1. Open science



European
Commission

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Open **Science**

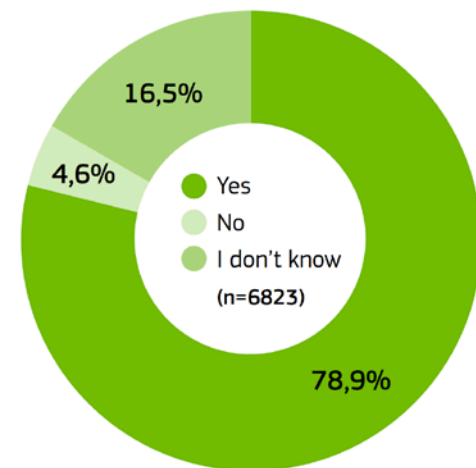
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Innovation

Open **Science**

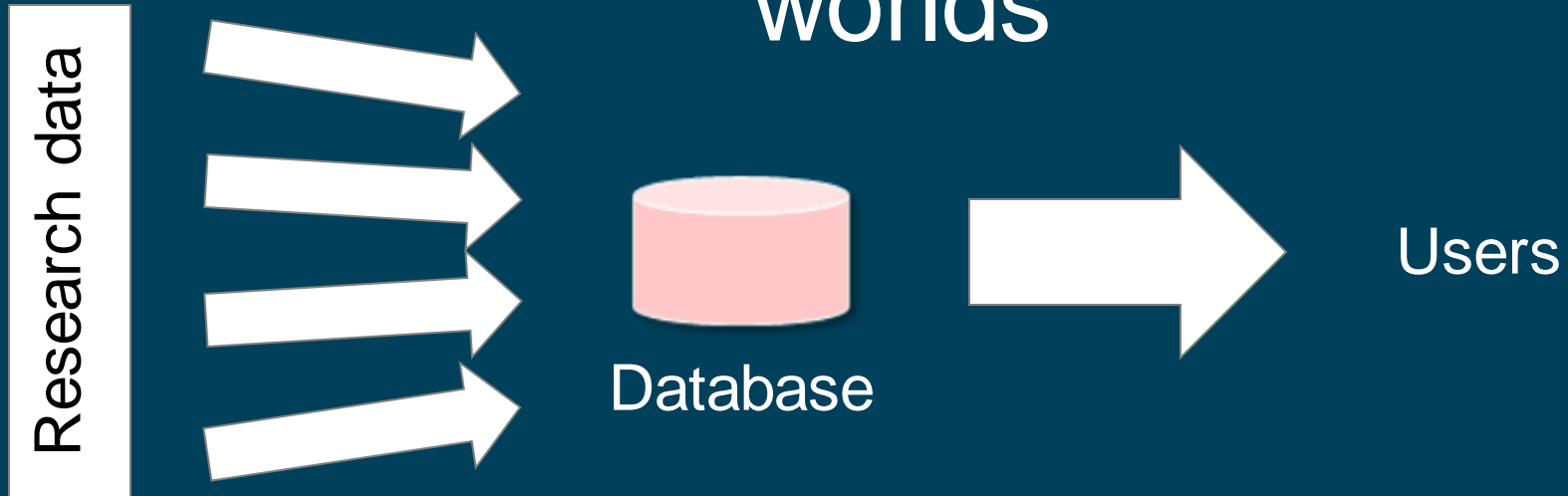


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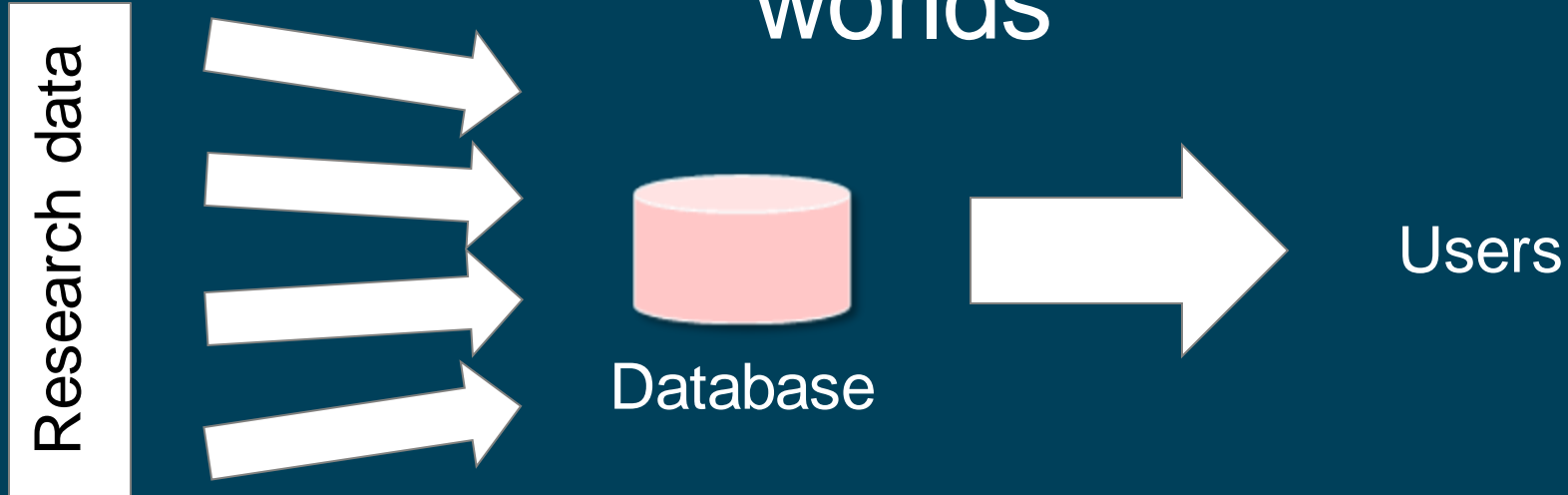
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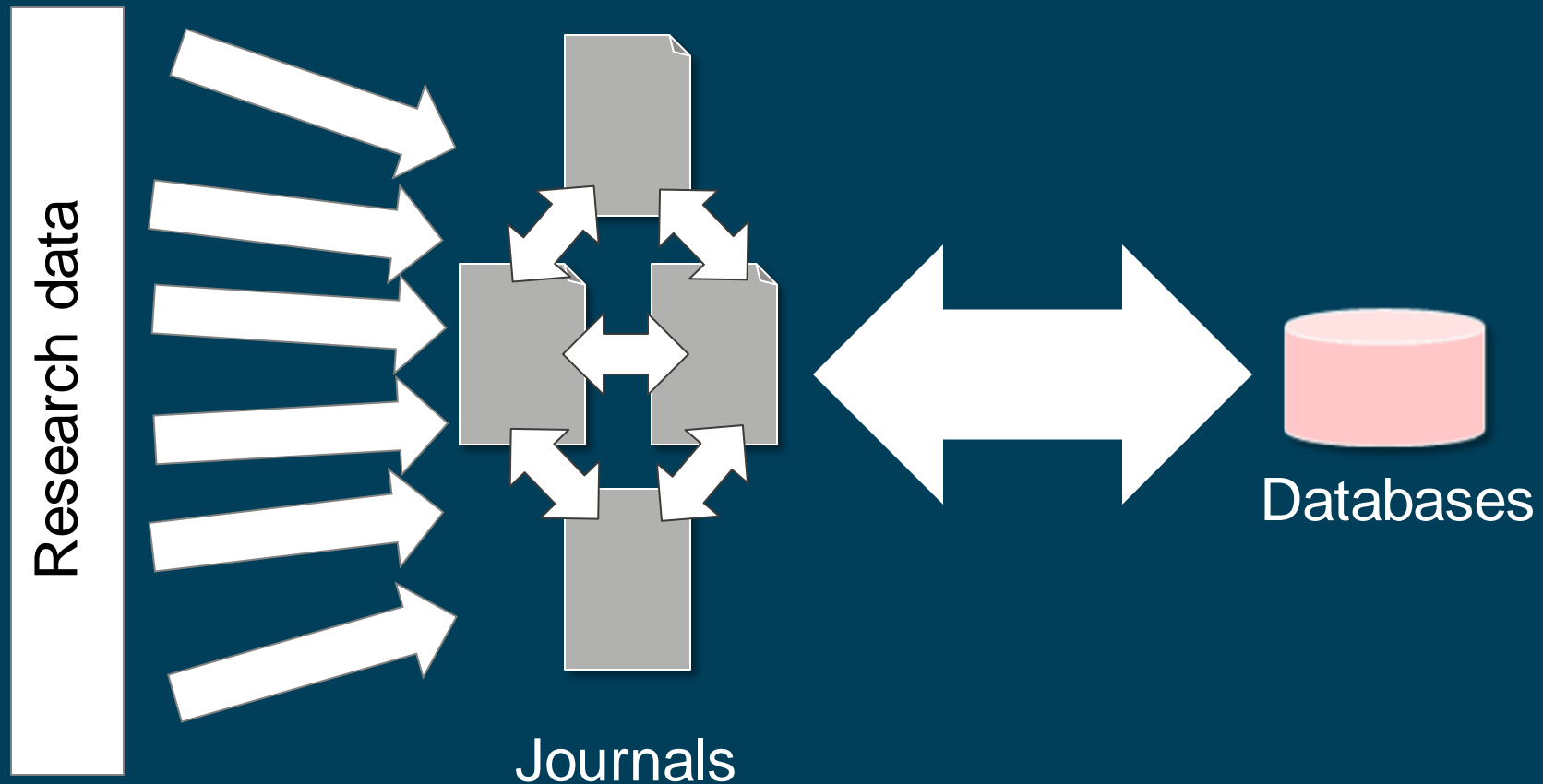
Data & publishing: separate worlds



Data & publishing: separate worlds



Bridging publishing and open data



ORIGINAL ARTICLE

Improved Overall Survival in Melanoma with Combined Dabrafenib and Trametinib

Caroline Robert, M.D., Ph.D., Bogusława Karaszewska, M.D., Jacob Schachter, M.D., Piotr Rutkowski, M.D., Ph.D., Andrzej Mackiewicz, M.D., Ph.D., Daniil Stroiakovski, M.D., Michael Lichinitser, M.D., Reinhard Dummer, M.D., Florent Grange, M.D., Ph.D., Laurent Mortier, M.D., Vanna Chiarion-Sileni, M.D., Kamil Drucis, M.D., Ph.D., Ivana Krajsova, M.D., Axel Hauschild, M.D., Ph.D., Paul Lorigan, M.D., Pascal Wolter, M.D., Georgina V. Long, M.D., Ph.D., Keith Flaherty, M.D., Paul Nathan, M.D., Ph.D., Antoni Ribas, M.D., Ph.D., Anne-Marie Martin, Ph.D., Peng Sun, Ph.D., Wendy Crist, B.A., Jeff Legos, Ph.D., Stephen D. Rubin, M.D., Shonda M. Little, M.P.H., and Dirk Schadendorf, M.D.

ABSTRACT

BACKGROUND

The BRAF inhibitors vemurafenib and dabrafenib have shown efficacy as monotherapies in patients with previously untreated metastatic melanoma with BRAF V600E or V600K mutations. Combining dabrafenib and the MEK inhibitor trametinib, as compared with dabrafenib alone, enhanced antitumor activity in this population of patients.

METHODS

In this open-label, phase 3 trial, we randomly assigned 704 patients with metastatic melanoma with a BRAF V600 mutation to receive either a combination of dabrafenib (150 mg twice daily) and trametinib (2 mg once daily) or vemurafenib (960 mg twice daily) orally as first-line therapy. The primary end point was overall survival.

RESULTS

At the preplanned interim overall survival analysis, which was performed after 77% of the total number of expected events occurred, the overall survival rate at 12 months was 72% (95% confidence interval [CI], 67 to 77) in the combination-therapy group and 65% (95% CI, 59 to 70) in the vemurafenib group (hazard ratio for death in the combination-therapy group, 0.69; 95% CI, 0.53 to 0.89; $P=0.005$). The prespecified interim stopping boundary was crossed, and the study was stopped for efficacy in July 2014. Median progression-free survival was 11.4 months in the combination-therapy group and 7.3 months in the vemurafenib group (hazard ratio, 0.56; 95% CI, 0.46 to 0.69; $P<0.001$). The objective response rate was 64% in the combination-therapy group and 51% in the vemurafenib group ($P<0.001$). Rates of severe adverse events and study-drug discontinuations were similar in the two groups. Cutaneous squamous-cell carcinoma and keratoacanthoma occurred in 1% of patients in the combination-therapy group and 18% of those in the vemurafenib group.

CONCLUSIONS

Dabrafenib plus trametinib, as compared with vemurafenib monotherapy, significantly improved overall survival in previously untreated patients with metastatic melanoma with BRAF V600E or V600K mutations, without increased overall toxicity. (Funded by GlaxoSmithKline; ClinicalTrials.gov number, NCT01597908.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Robert at the Dermatology Service and INSERM Unité 981, Gustave Roussy, 114 rue Edouard Vaillant, 94 805 Villejuif-Paris Sud, France, or at caroline.robert@gustaveroussy.fr.

This article was published on November 16, 2014, at NEJM.org.

N Engl J Med 2015;372:30-9.

DOI: 10.1056/NEJMoa1412699

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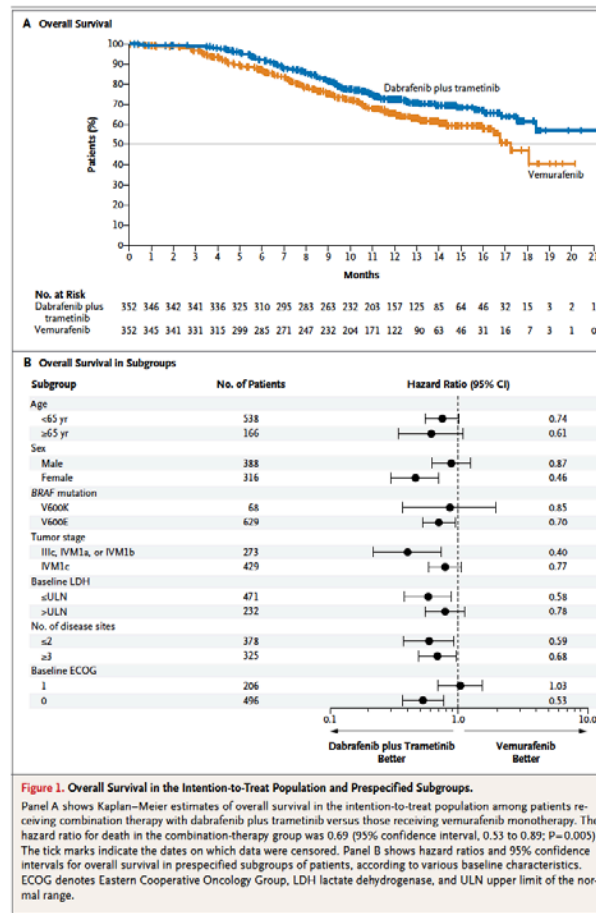


Figure 1. Overall Survival in the Intention-to-Treat Population and Prespecified Subgroups. Panel A shows Kaplan-Meier estimates of overall survival in the intention-to-treat population among patients receiving combination therapy with dabrafenib plus trametinib versus those receiving vemurafenib monotherapy. The hazard ratio for death in the combination-therapy group was 0.69 (95% confidence interval, 0.53 to 0.89; $P=0.005$). The tick marks indicate the dates on which data were censored. Panel B shows hazard ratios and 95% confidence intervals for overall survival in prespecified subgroups of patients, according to various baseline characteristics. ECOG denotes Eastern Cooperative Oncology Group, LDH lactate dehydrogenase, and ULN upper limit of the normal range.

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N Engl J Med 2015;372:30-9.

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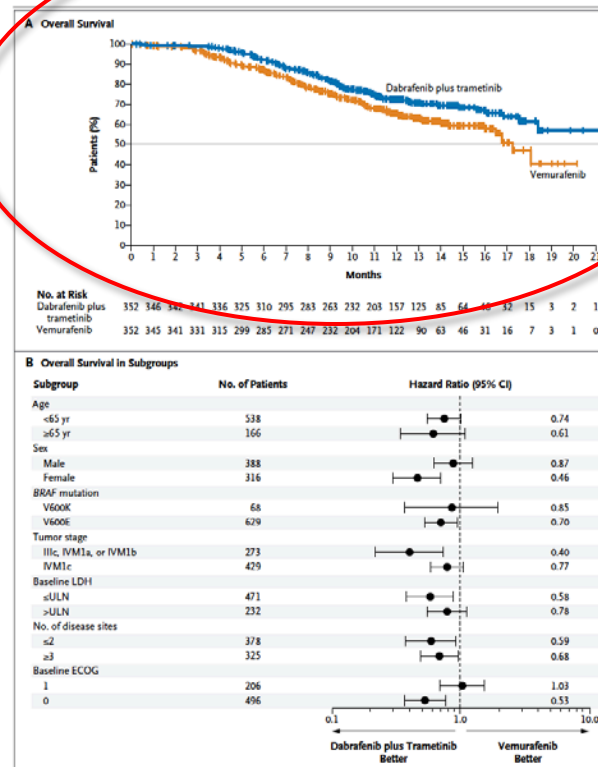
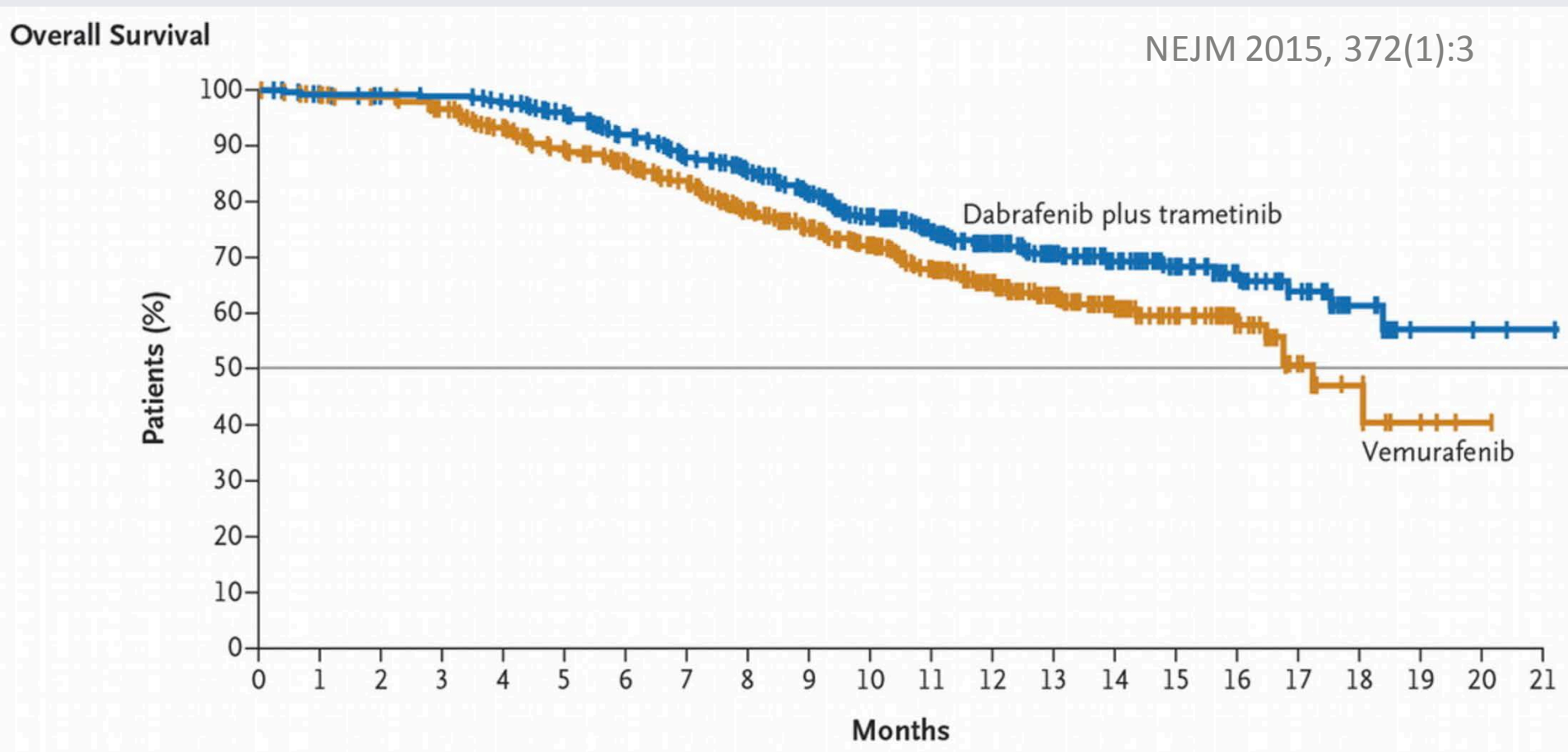


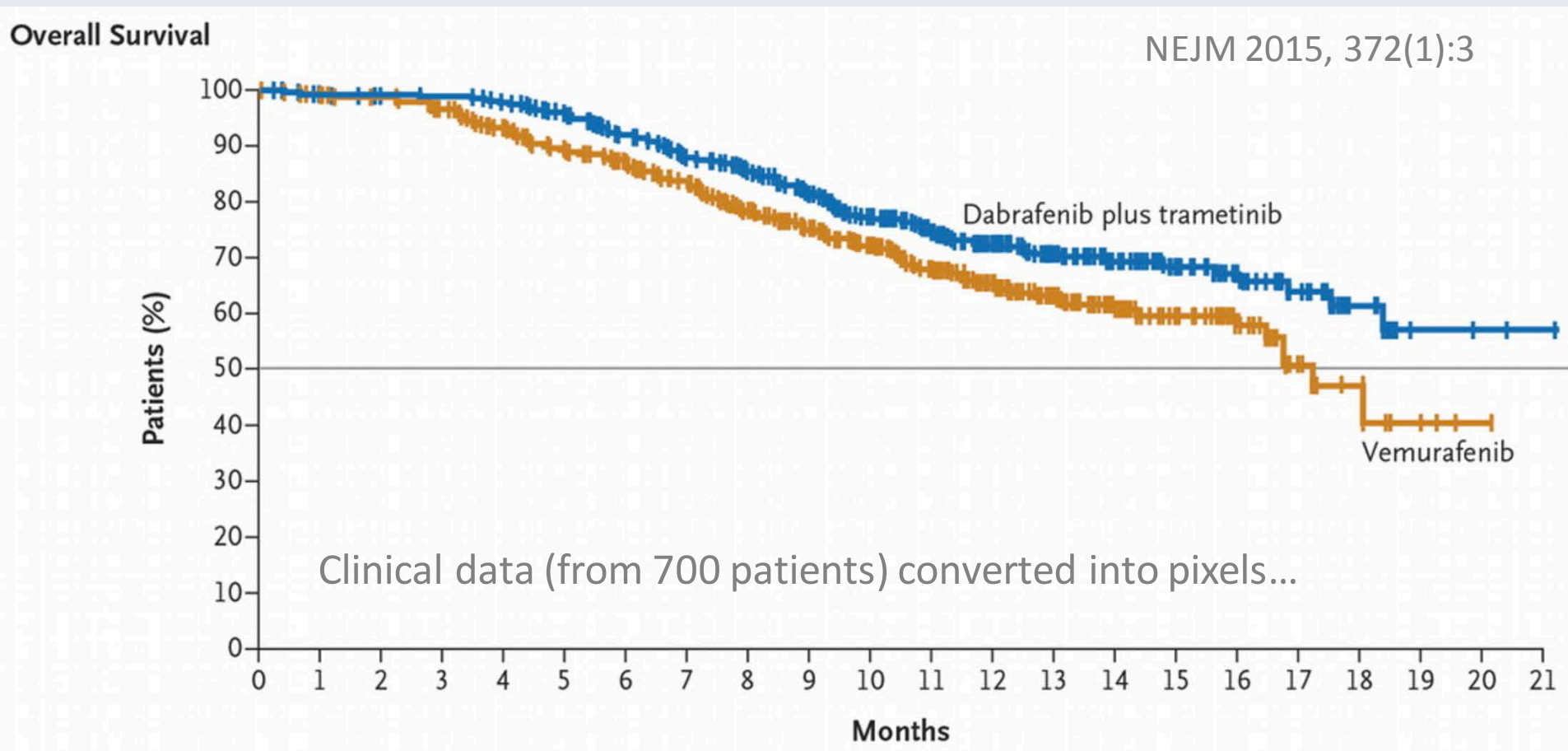
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What is a figure?

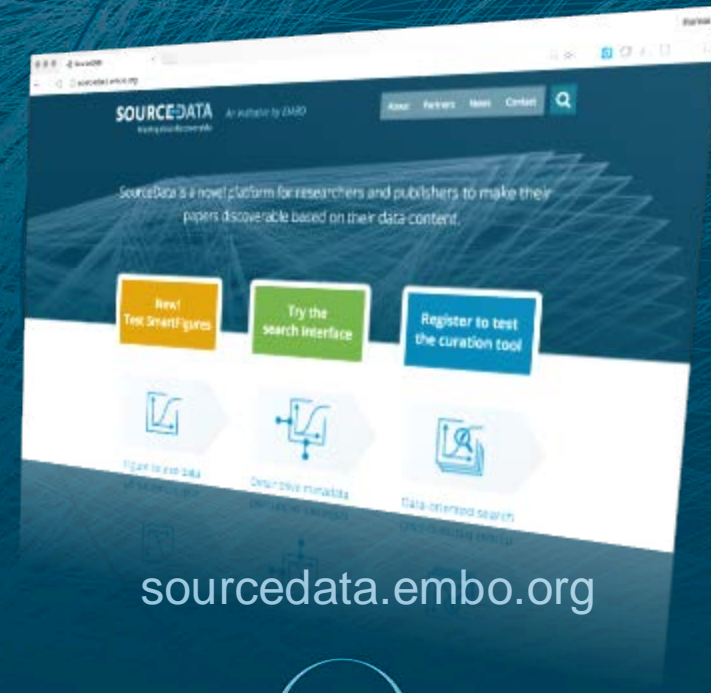


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2. SourceData

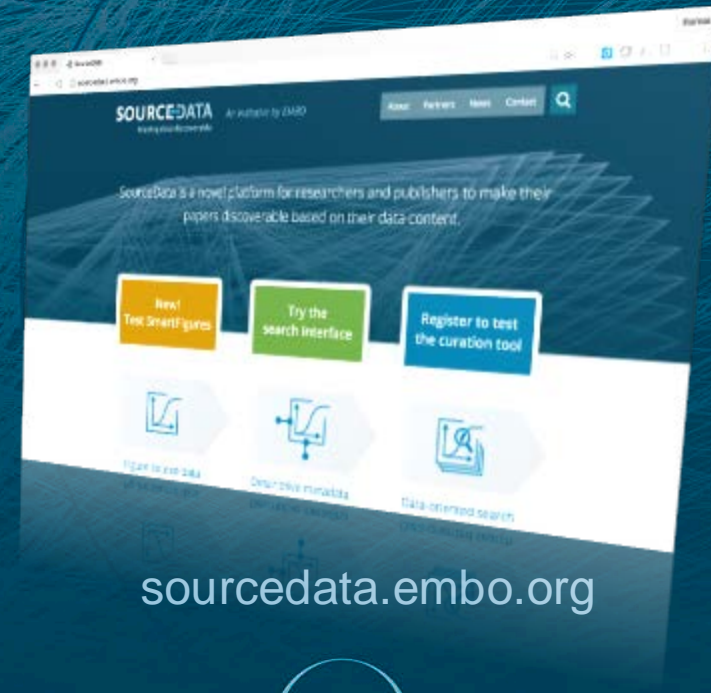
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SOURCE DATA

Making data discoverable

- Facilitate discovery and browsing of data and papers
- Couple discoverability with data availability



- Facilitate discovery and browsing of data and papers
- Couple discoverability with data availability
- Bridge scientific publishing with open science





Liechti et al. 2017
Nature Methods **14**:1021



Directed Search

Perturbation

Measured entity

Does

Forskolin

influence

Huntingtin

?



Directed Search

Perturbation **Measured entity**

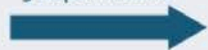
Does influence ? 

Search results



Forskolin

5 Experiments



Huntingtin

Novel targets for Huntington's disease in an mTOR-independent autophagy pathway

Williams E et al.

Nature Chemical Biology 2008

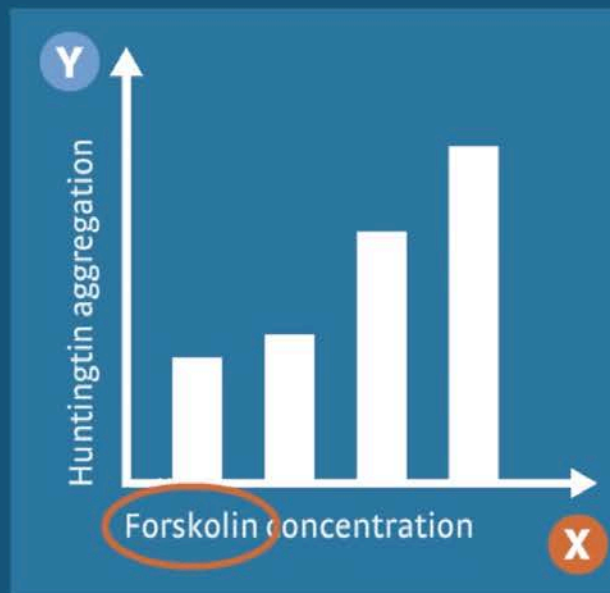
Y



X



How it works



Huntingtin aggregates after treatment with forskolin.

How it works

Perturbation

Manipulated

Forskolin

X



Measured entity

Observed

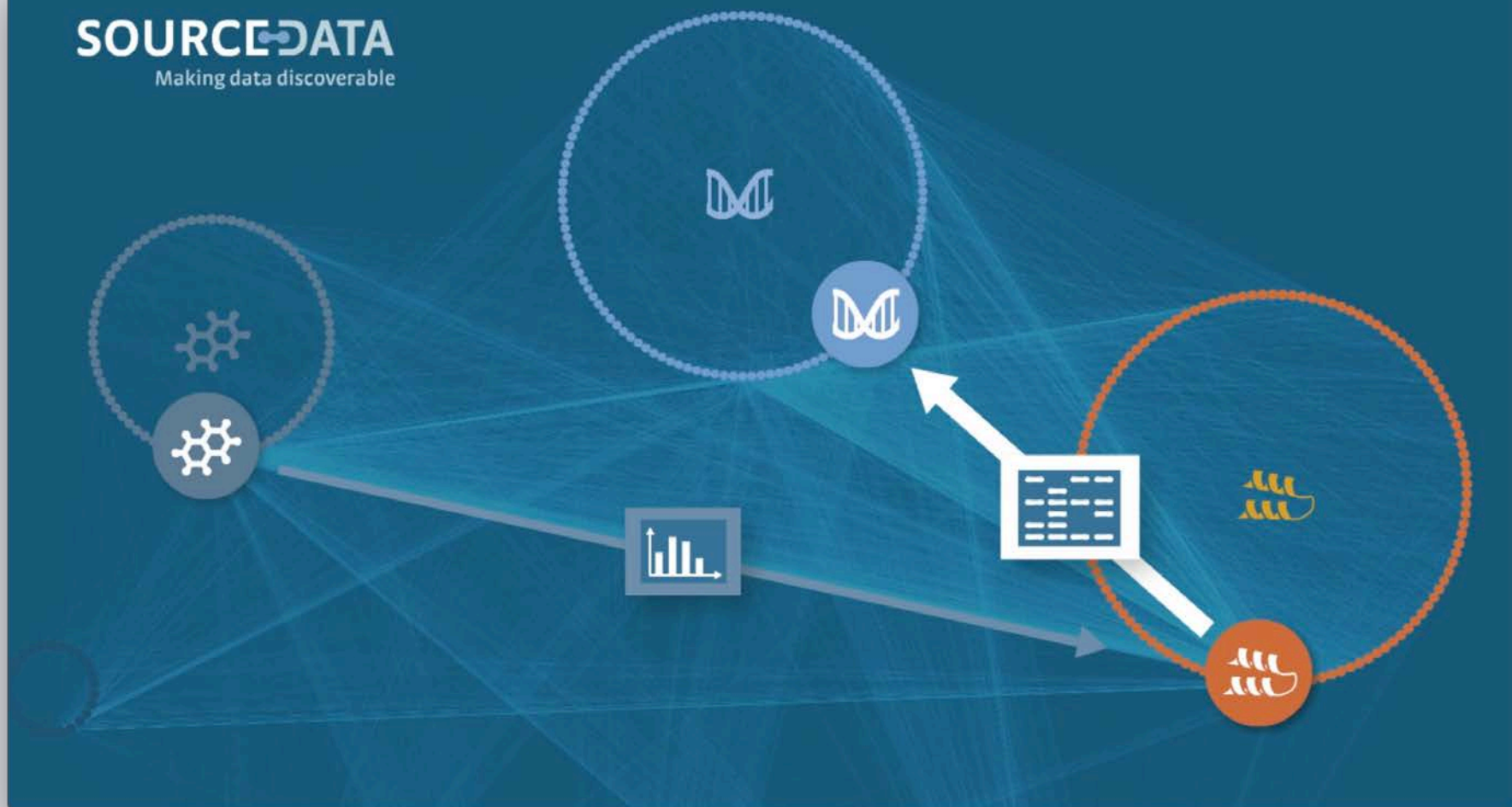


Y

Huntingtin



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Making data discoverable



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Defective NOD2 peptidoglycan sensing promotes diet-induced inflammation, dysbiosis, and insulin resistance.
Defective NOD2 peptidoglycan sensing promotes diet-induced inflammation, dysbiosis, and insulin resistance.

Dieber I et al. 2017 *Nature Medicine* 2017

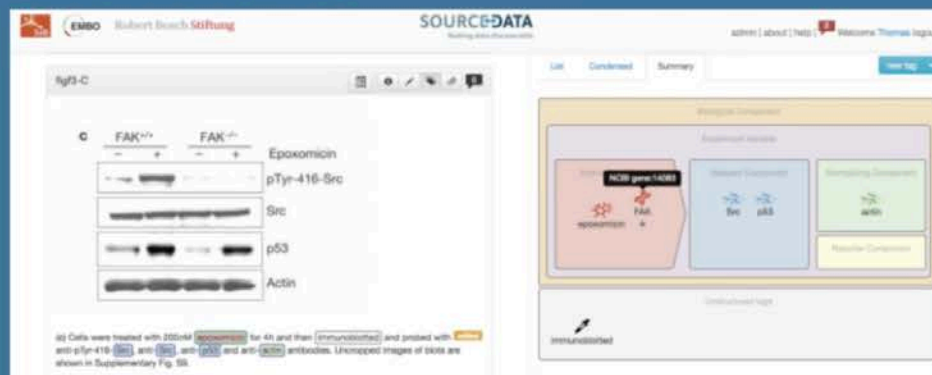


Data search sourcedata.vital-it.ch/public/#/search

Does **forskolin** influence **huntingtin** ?

Curation interface

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DataSearch

SOURCE DATA
Making data discoverable

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Data search

Perturbation ?

Does

of type : small molecule

Measured entity ?

affect

of type : small molecule

?

 **Reset**

Simple search

Fission and selective fusion govern mitochondrial segregation and elimination by autophagy
Glad Twig, Alvaro Elorza, Anthony J A Molina, Hibo Mohamed, Jakob D Wikstrom, Gill Walzer, Linsey Siles, Sarah E Haigh, Steve Katz, Guy Las, Joseph Alroy, Min Wu, Bénédicte F Py, Junying Yuan, Jude T Deeney, Barbara E Corkey, Orian S Shirihai
The EMBO journal- 2007

Hide abstract

Abstract:
Accumulation of depolarized mitochondria within beta-cells has been associated with oxidative damage and development of diabetes. To determine the source and fate of depolarized mitochondria, individual mitochondria were photolabeled and tracked through fusion and fission. Mitochondria were found to go through frequent cycles of fusion and fission in a 'kiss and run' pattern. Fission events often generated uneven daughter units: one daughter exhibited increased membrane potential ($\Delta\psi(m)$) and a high probability of subsequent fusion, while the other had decreased membrane potential and a reduced probability for a fusion event. Together, this pattern generated a subpopulation of non-fusing mitochondria that were found to have reduced $\Delta\psi(m)$ and decreased levels of the fusion protein OPA1. Inhibition of the fission machinery through DRP1(K38A) or FIS1 RNAi decreased mitochondrial autophagy and resulted in the accumulation of oxidized mitochondrial proteins, reduced respiration and impaired insulin secretion. Pulse chase and arrest of autophagy at the pre-proteolysis stage reveal that before autophagy mitochondria lose $\Delta\psi(m)$ and OPA1, and that overexpression of OPA1 decreases mitochondrial autophagy. Together, these findings suggest that fission followed by selective fusion segregates dysfunctional mitochondria and permits their removal by autophagy.

1 experiment

 glucose

 insulin (human)
(insulin)

Hide figures

Figure 8-C



Click on figure to view it in SmartFigure

Dual melanocortin-4 receptor and GLP-1 receptor agonism amplifies metabolic benefits in diet-induced obese mice.
Clemmensen C et al.
EMBO molecular medicine- 2015

Show abstract

1 experiment

 glucose

 insulin (human)
(insulin)

Show figures

Pharmacological correction of obesity-induced autophagy arrest using calcium channel blockers
Hwan-Woo H - W Park et al.
Nature communications- 2014

Show abstract

1 experiment

 glucose

 insulin (human)
(insulin)

Show figures

DataSearch

Data search

Perturbation ? **Measured entity** ?

Does affect ?

of type : small molecule

of type : small molecule

Reset

Simple search

Try: does **insulin** influence **glucose**? or does **glucose** influence **insulin**?

Defective NOD2 peptidoglycan sensing promotes diet-induced inflammation, dysbiosis, and insulin resistance.

Denou E, Lohmède K, Garidou L, Pomie C, Chabo C, Lau TC, Fullerton MD, Nigro G, Zakaroff-Girard A, Luche E, Garret C, Serino M, Amar J, Courtney M, Cavallari JF, Henriksbo BD, Barra NG, Foley KP, McPhee JB, Duggan BM, O'Neill HM, Lee AJ, Sansonetti P, Ashkar AA, Khan WJ, Surette MG, Bouloumié A, Steinberg GR, Burcelin R, Schertzer JD
EMBO molecular medicine- 2015

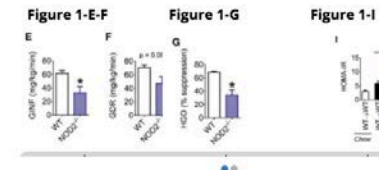
Hide abstract ^

Abstract:

Pattern recognition receptors link metabolite and bacteria-derived inflammation to insulin resistance during obesity. We demonstrate that NOD2 detection of bacterial cell wall peptidoglycan (PGN) regulates metabolic inflammation and insulin sensitivity. An obesity-promoting high-fat diet (HFD) increased NOD2 in hepatocytes and adipocytes, and NOD2(-/-) mice have increased adipose tissue and liver inflammation and exacerbated insulin resistance during a HFD. This effect is independent of altered adiposity or NOD2 in hematopoietic-derived immune cells. Instead, increased metabolic inflammation and insulin resistance in NOD2(-/-) mice is associated with increased commensal bacterial translocation from the gut into adipose tissue and liver. An intact PGN-NOD2 sensing system regulated gut mucosal bacterial colonization and a metabolic tissue dysbiosis that is a potential trigger for increased metabolic inflammation and insulin resistance. Gut dysbiosis in HFD-fed NOD2(-/-) mice is an independent and transmissible factor that contributes to metabolic inflammation and insulin resistance when transferred to WT, germ-free mice. These findings warrant scrutiny of bacterial component detection, dysbiosis, and protective immune responses in the links between inflammatory gut and metabolic diseases, including diabetes.

spectrophotometry method

insulin (human) (insulin) experiments glucose **Hide figures** ^



Click on figure to view it in SmartFigure

Fatty acid-induced NLRP3-ASC inflammasome activation interferes with insulin signaling

Haitao H Wen et al.
Nature Immunology- 2011

Show abstract v

insulin (human) (insulin) experiments glucose **Show figures** v



how does insulin regulate glucose



All

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About 36.400.000 results (0,56 seconds)

This hormone, **insulin**, causes the liver to convert more **glucose** into glycogen (this process is called glycogenesis), and to force about 2/3 of body cells (primarily muscle and fat tissue cells) to take up **glucose** from the blood through the GLUT4 transporter, thus decreasing **blood sugar**.

[Blood sugar regulation - Wikipedia](#)

https://en.wikipedia.org/wiki/Blood_sugar_regulation

About this result Feedback



how does glucose regulate insulin?



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[Blood sugar regulation - Wikipedia](#)

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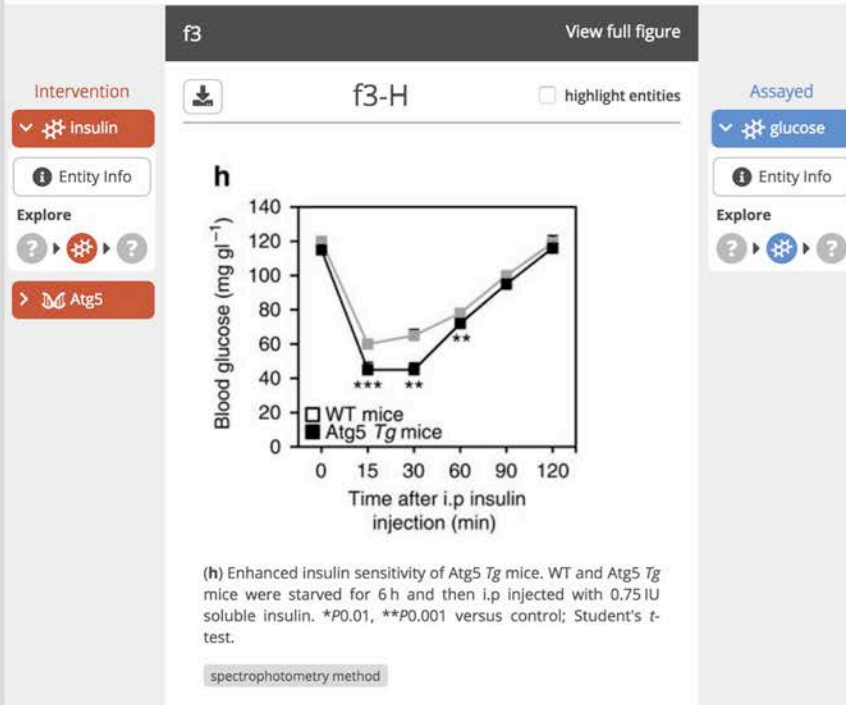
About this result Feedback



Overexpression of Atg5 in mice activates autophagy and extends lifespan

Pyo JO et al. *Nature communications* 2013

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Overexpression of Atg5 in mice activates autophagy and extends lifespan

Pyo JO et al. *Nature communications* 2013

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f3

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Intervention

Insulin

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Atg5

f3-H

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Assayed

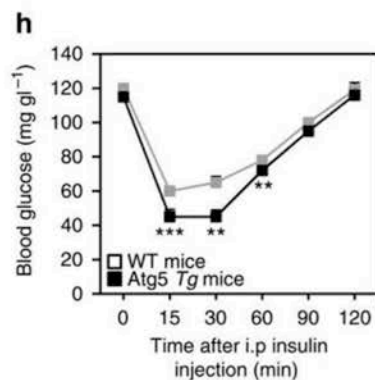
glucose

Entity Info

Explore

glucose

downstream



(h) Enhanced insulin sensitivity of Atg5 Tg mice. WT and Atg5 Tg mice were starved for 6 h and then i.p. injected with 0.75 IU soluble insulin. *P<0.01, **P<0.001 versus control; Student's t-test.

spectrophotometry method

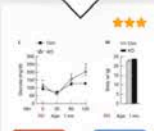
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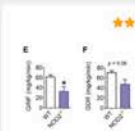
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Defective NOD2 peptidoglycan sensing promotes diet-induced inflammation, dysbiosis, and insulin resistance. Denou E et al. *EMBO molecular medicine* (2015)

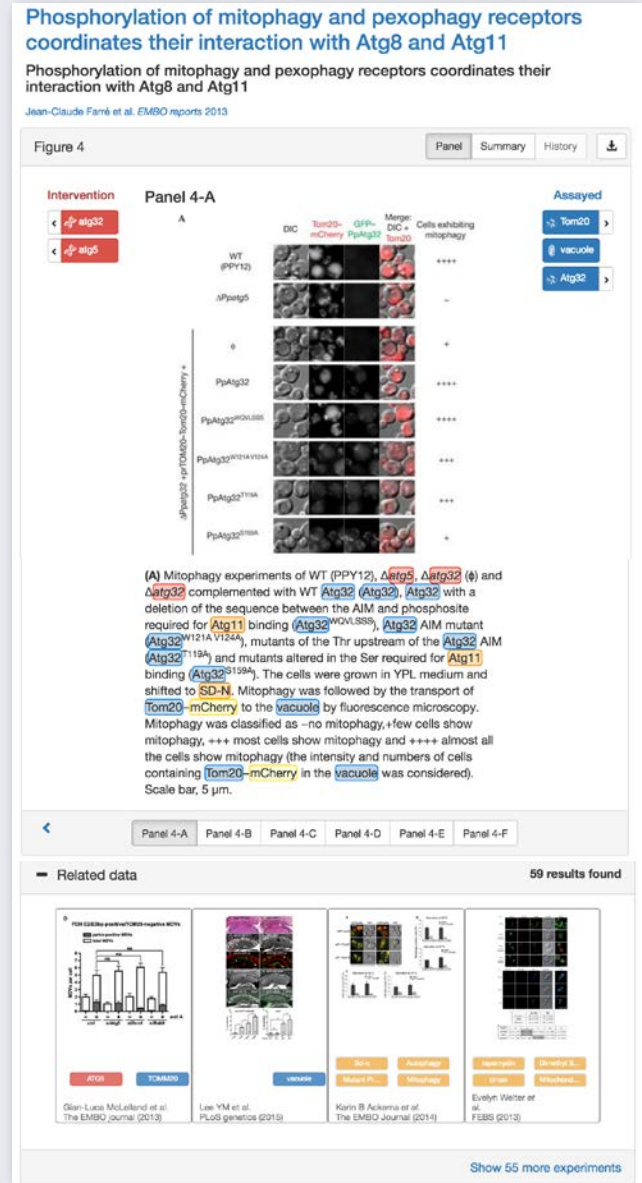
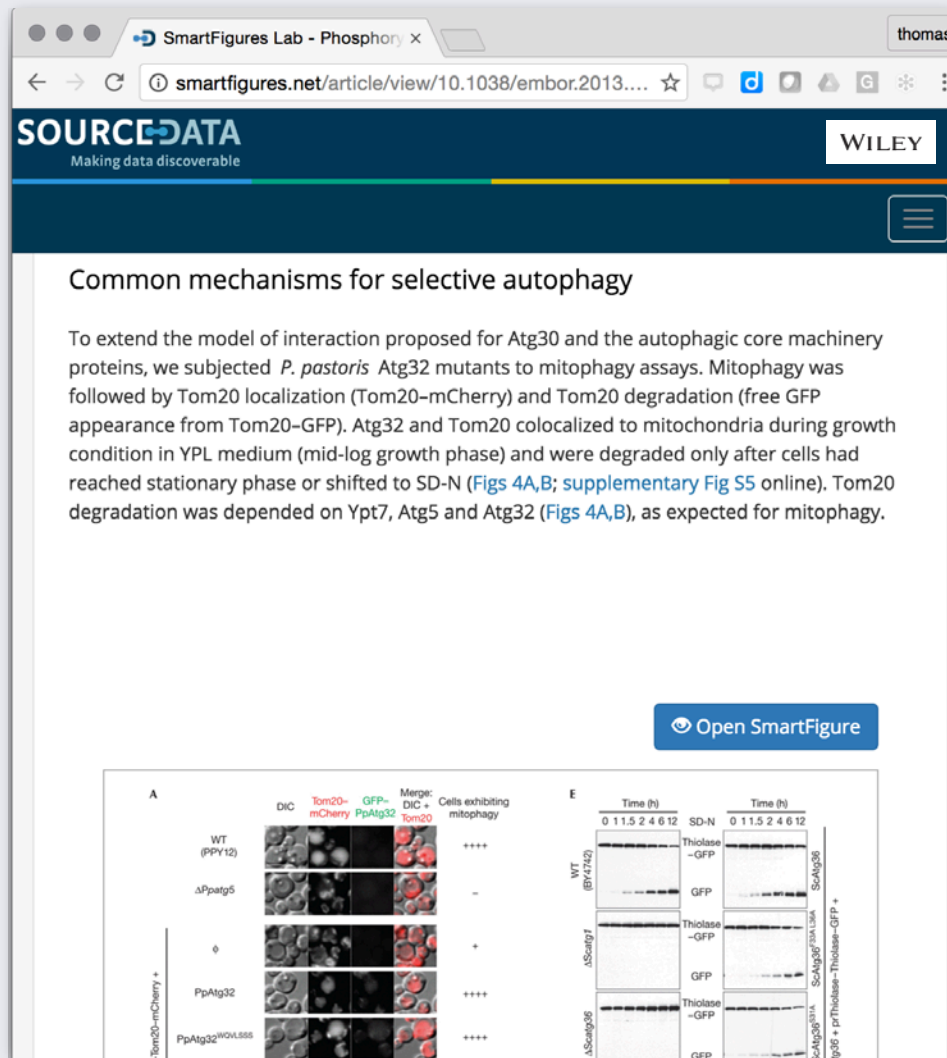


Loss of autophagy in hypothalamic POMC neurons impairs lipolysis. Becker K et al. *EMBO reports* (2011)



Defective NOD2 peptidoglycan sensing promotes diet-induced inflammation, dysbiosis, and insulin resistance. Denou E et al. *EMBO molecular medicine* (2015)

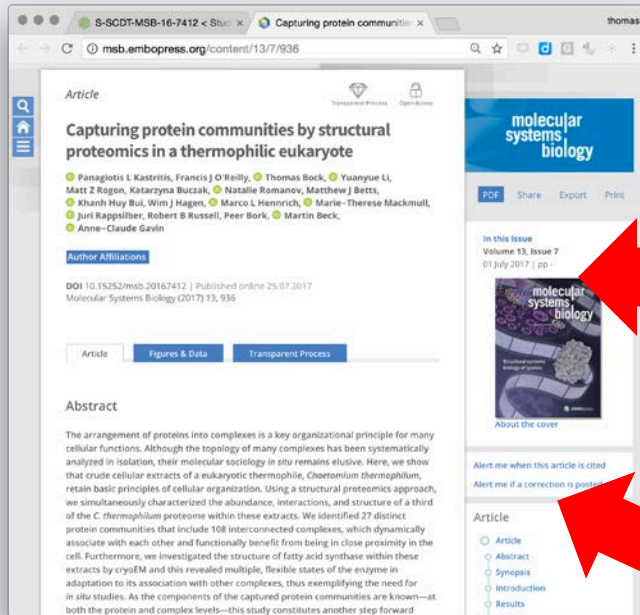
A pilot implementation: smartfigures.net



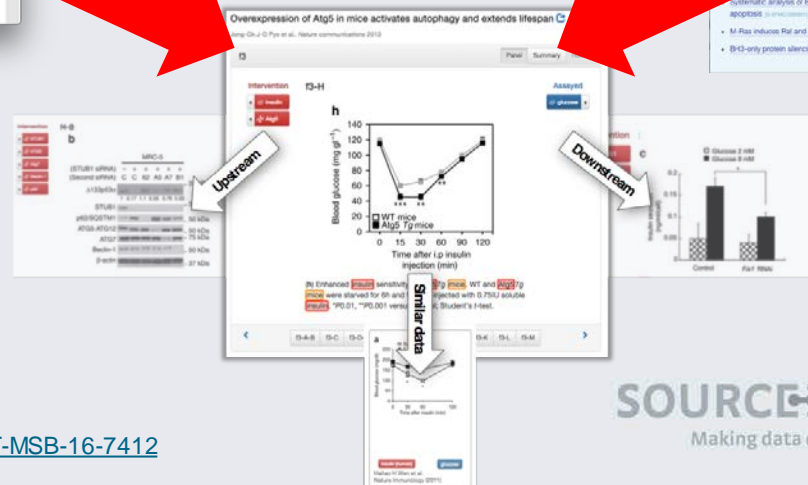
Integration with data repositories

Paper

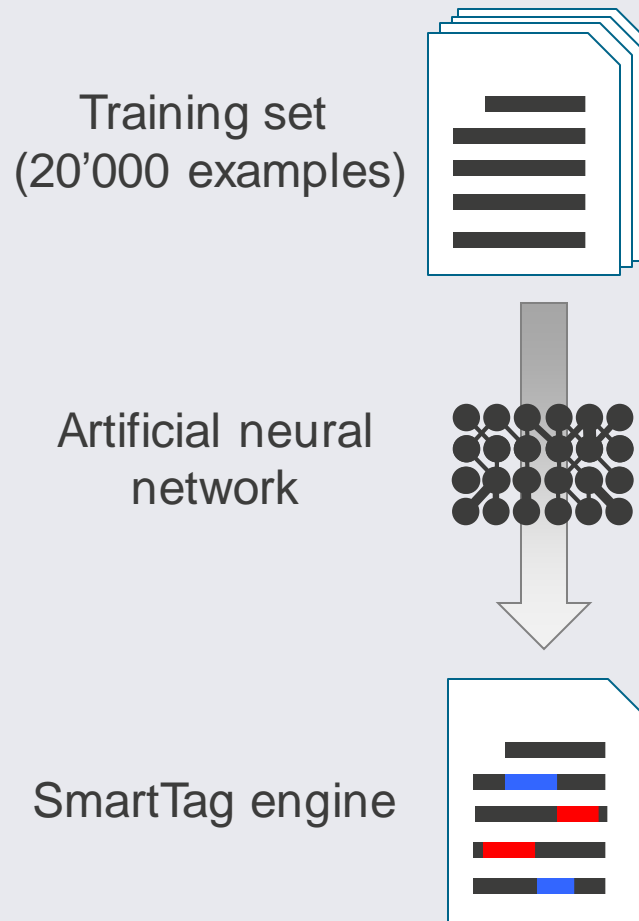
Database



SmartFigure



An AI approach to semantic analysis

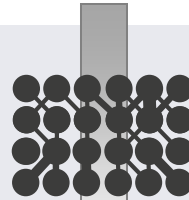


An AI approach to semantic analysis

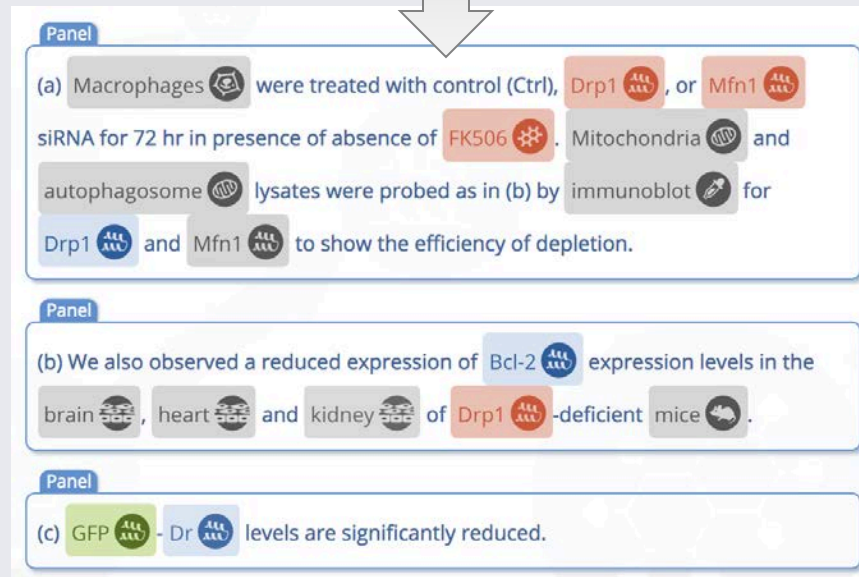
Plain text
(figure legend)

(a) Macrophages were treated with control (Ctrl), Drp1, or Mfn1 siRNA for 72 hr in presence of absence of FK506. Mitochondria and autophagosome lysates were probed as in (b) by immunoblot for Drp1 and Mfn1 to show the efficiency of depletion. (b) We also observed a reduced expression of Bcl-2 expression levels in the brain, heart and kidney of Drp1-deficient mice. (c) GFP-Dr levels are significantly reduced.

Artificial neural
network



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deep semantic
interpretation

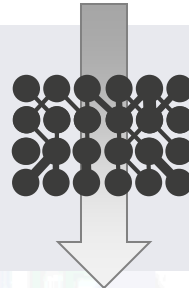


An AI approach to semantic analysis

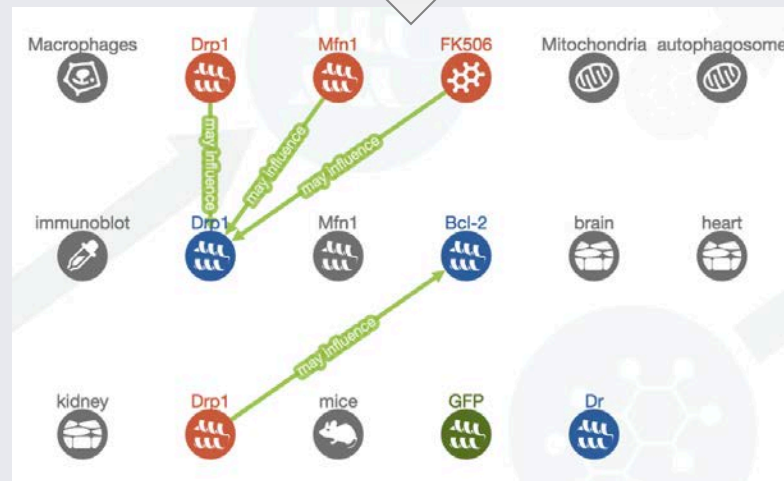
Plain text
(figure legend)

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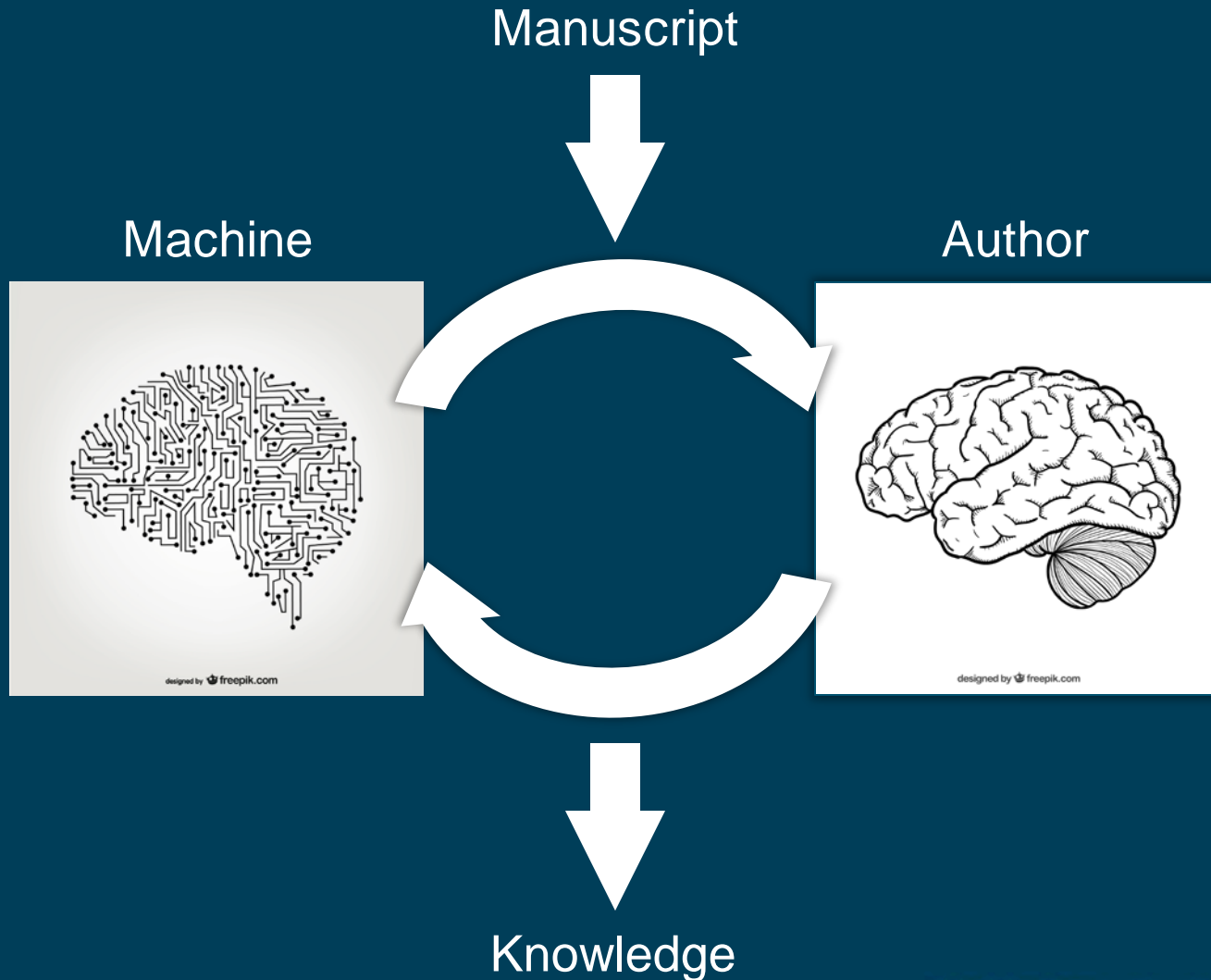
Artificial neural
network



SmartTag:
deep semantic
interpretation



Disseminating knowledge



3. Outlook

'Smart' papers

Title

Abstract

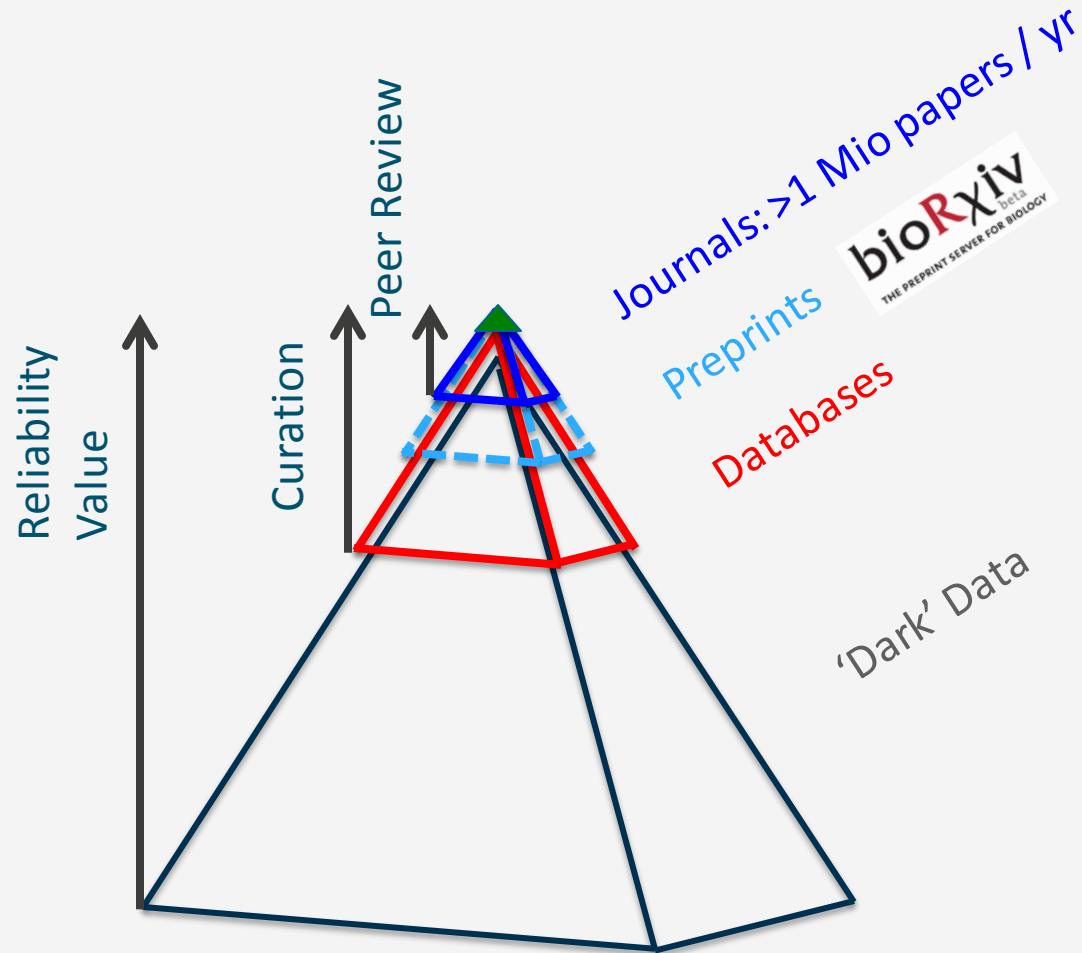
Main paper

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Datasets & code



Accelerating science with Open Science



The Economist

OCTOBER 19TH-25TH 2013

Economist.com

Washington's lawyer surplus

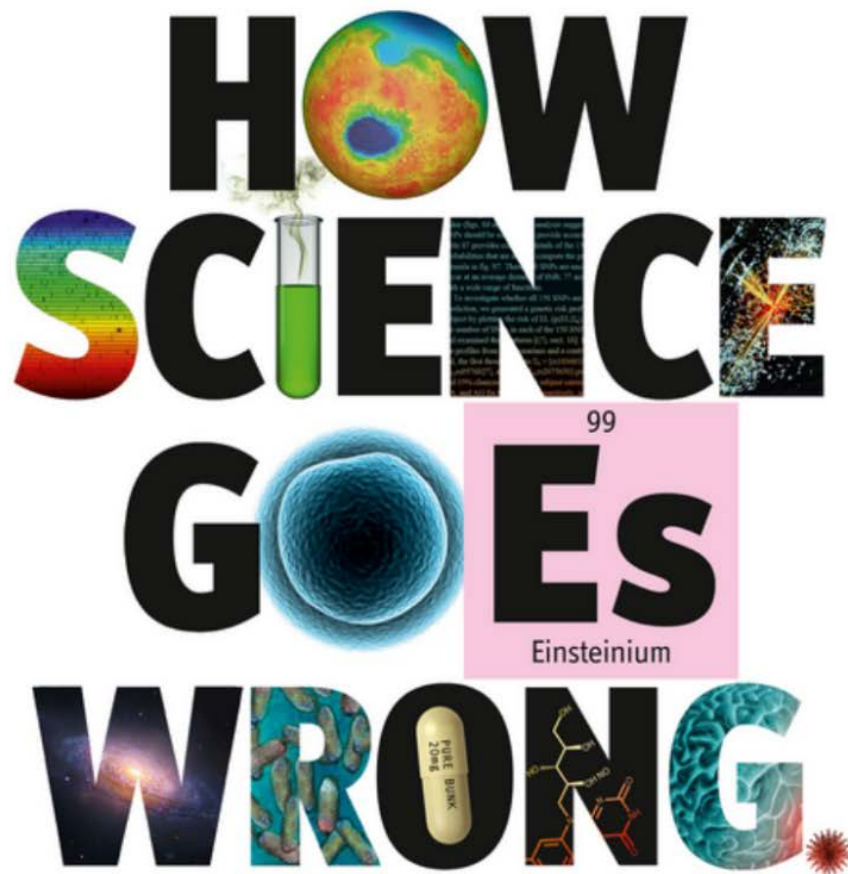
How to do a nuclear deal with Iran

Investment tips from Nobel economists

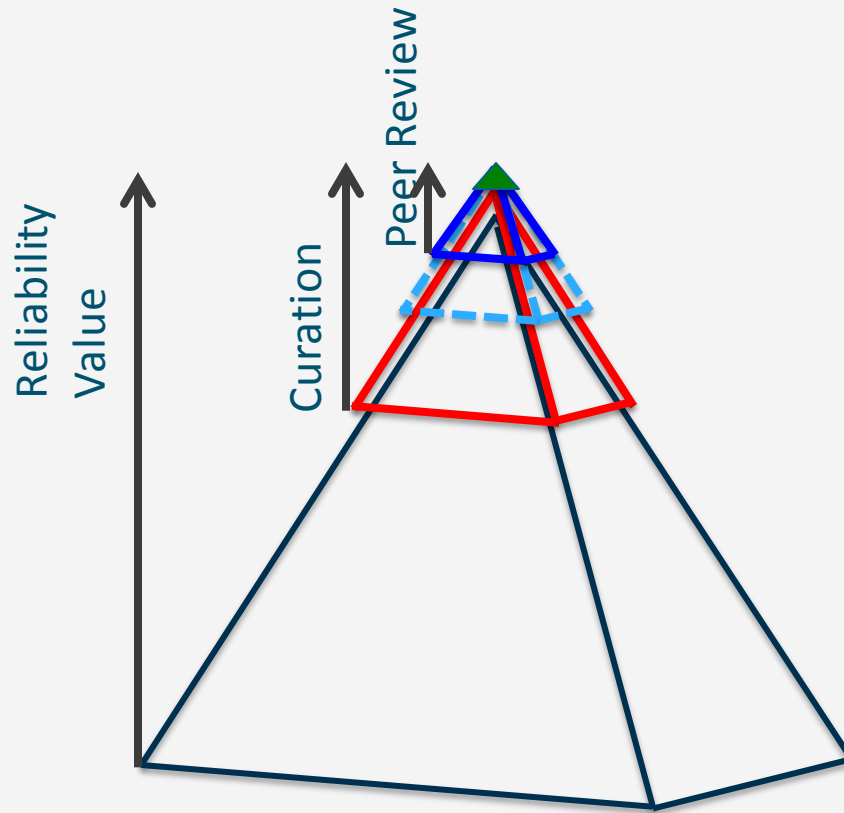
Junk bonds are back

The meaning of Sachin Tendulkar

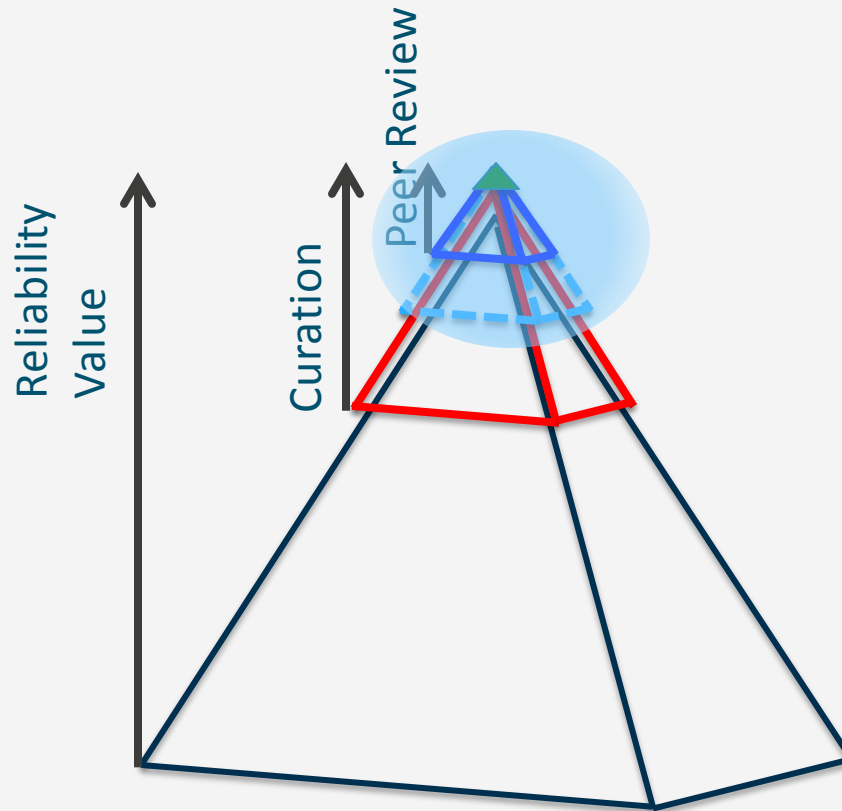
HOW SCIENCE GOES WRONG



Quality Open Science: how to make it work?



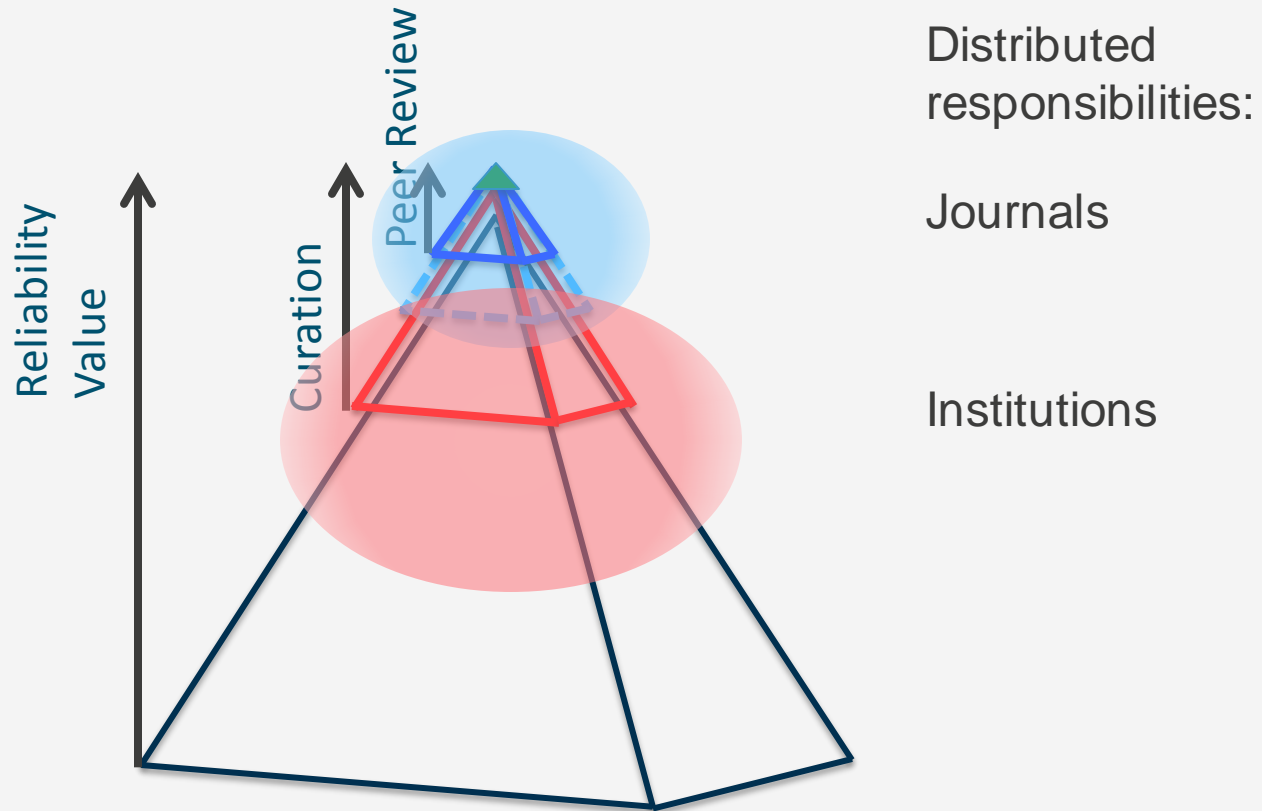
Quality Open Science: how to make it work?



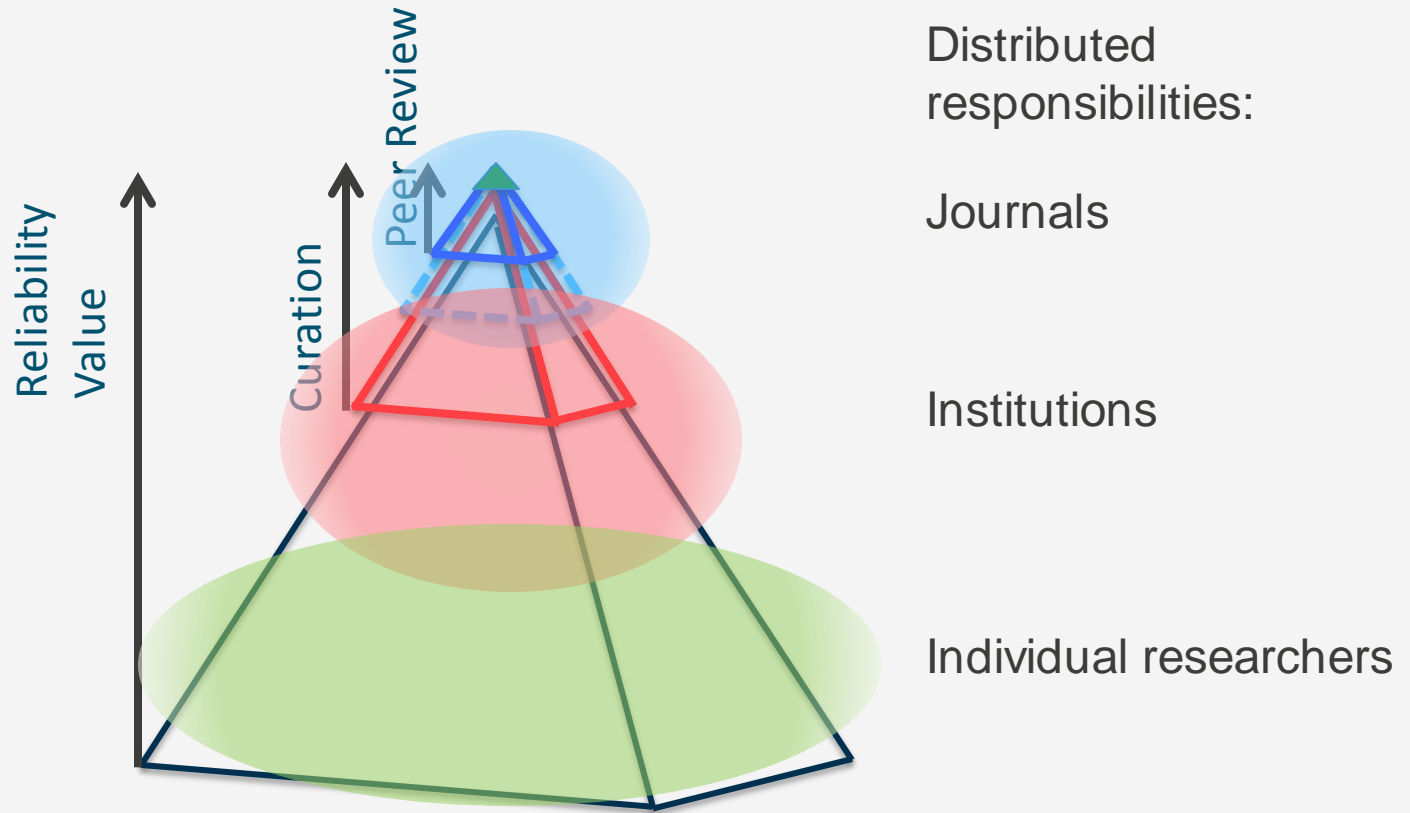
Distributed
responsibilities:

Journals

Quality Open Science: how to make it work?



Quality Open Science: how to make it work?





Open Innovation Open Science Open to the World

– a vision for Europe



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RECH 208
TELECOM 100

OUTCOME OF PROCEEDINGS

From:	General Secretariat of the Council
To:	Delegations
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Subject:	The transition towards an Open Science system - Council conclusions (adopted on 27/05/2016)

CALLS on the Commission, the Member States and the stakeholders to take the necessary actions needed for making open science a reality and to advocate the need for concerted actions in relevant national, EU, multilateral and international fora; **CALLS on the**

THANK YOU!

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