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# SourceData – bridging scientific publishing and open science

Dr. Thomas Lemberger  
EMBO

1. Open Science
2. SourceData
3. Outlook

# 1. Open science



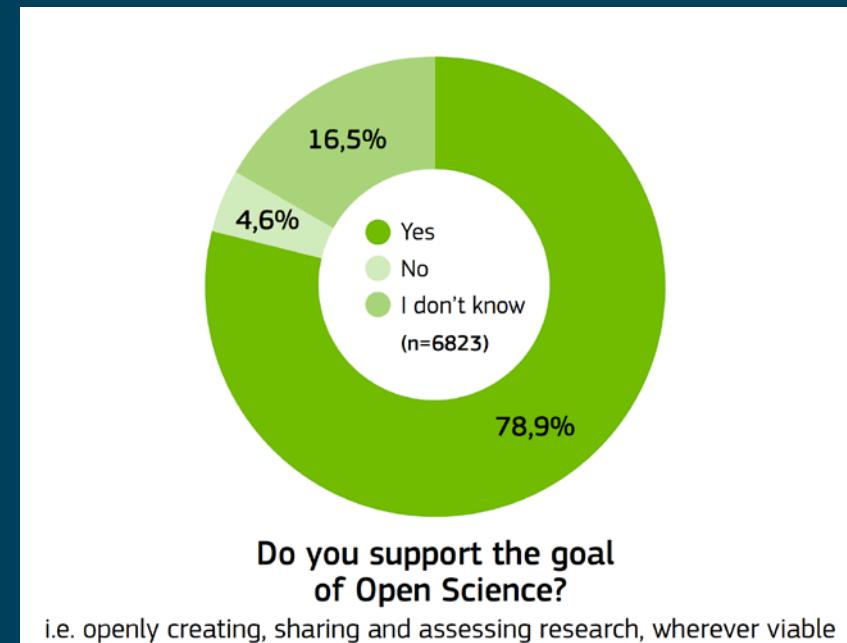
# Europe's Future: Open Innovation Open Science Open to the World

*Reflections of the RISE Group*



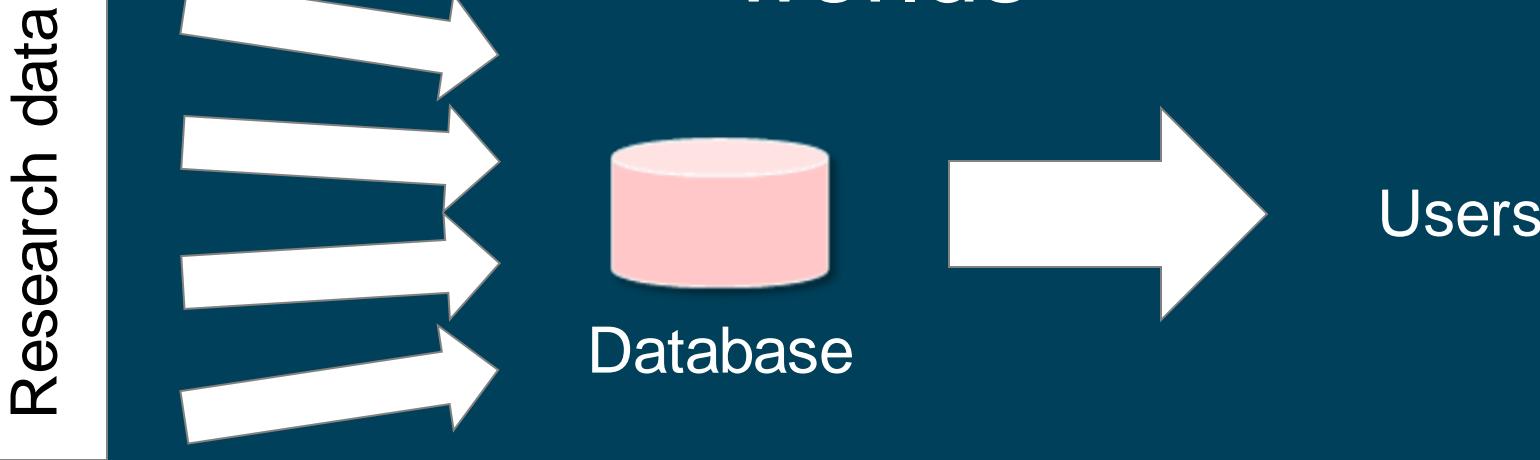
Research and  
Innovation

## Open Science



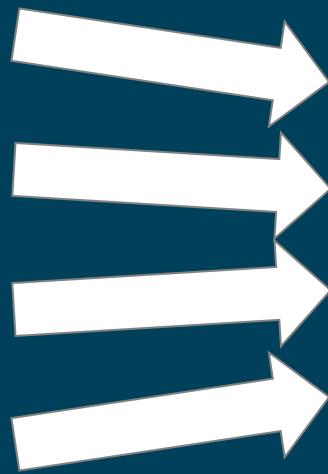
*Data are from the Survey of scholarly communication tool usage.  
<https://101innovations.wordpress.com/2016/04/04/support-for-open-science-in-eu-member-states/>*

# Data & publishing: separate worlds



# Data & publishing: separate worlds

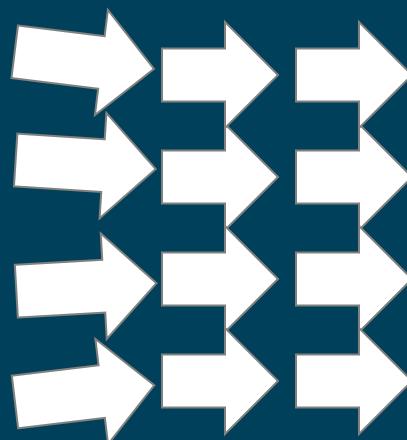
Research data



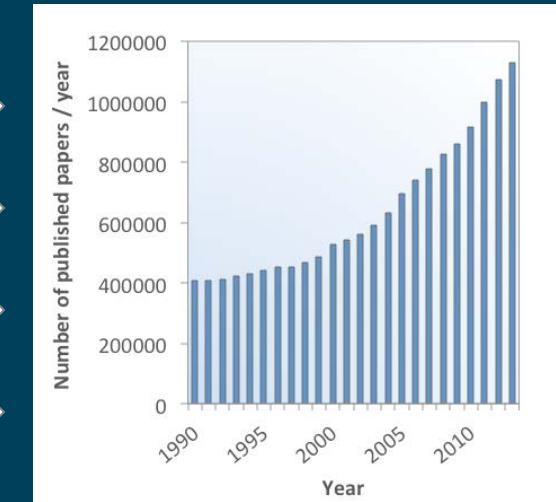
Database

Users

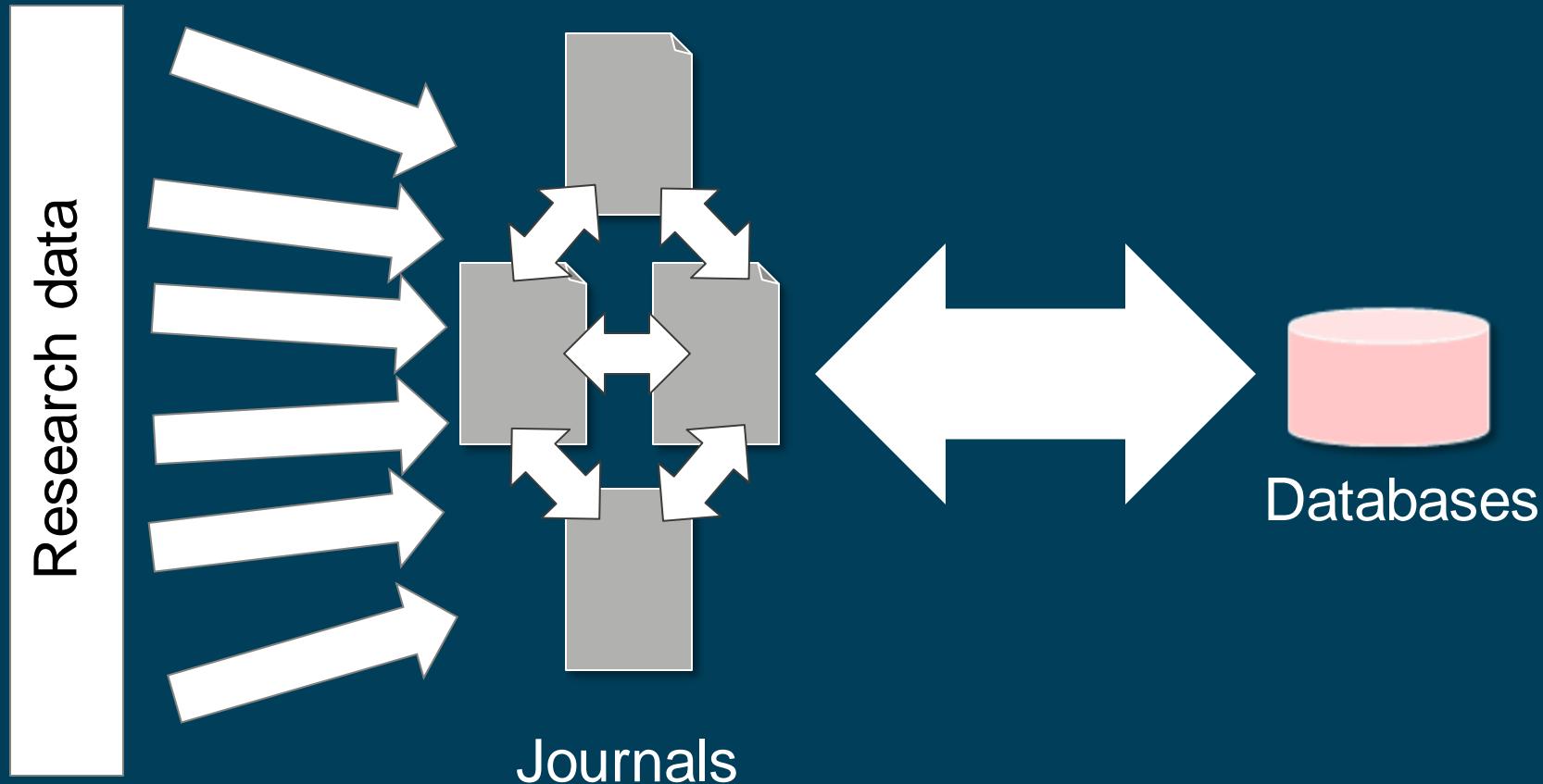
Research data



Journals



# Bridging publishing and open data



## ORIGINAL ARTICLE

## Improved Overall Survival in Melanoma with Combined Dabrafenib and Trametinib

Caroline Robert, M.D., Ph.D., Boguslawa Karaszewska, M.D., Jacob Schachter, M.D., Piotr Rutkowski, M.D., Ph.D., Andrzej Mackiewicz, M.D., Ph.D., Daniil Stroiakowski, M.D., Michael Lichinitser, M.D., Reinhard Dummer, M.D., Farrell 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.)

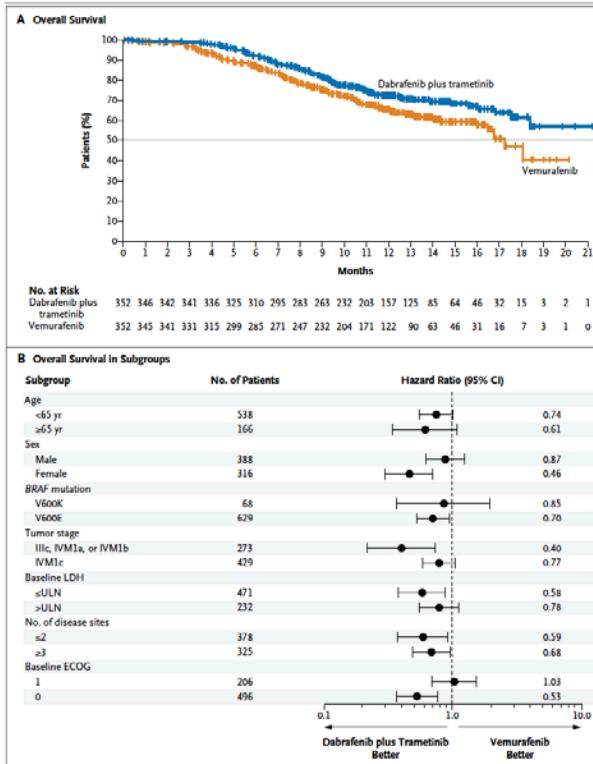
The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Robert at the Dermatology Service and INSERM Unité 981, Gustave Roussy, 114 rue Edouard Vaillant, 94 805 Villejuif-Paris Sud, France, or at caroline.robert@gustaveroussy.fr.

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

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

DOI:10.1056/NEJMoa1412690

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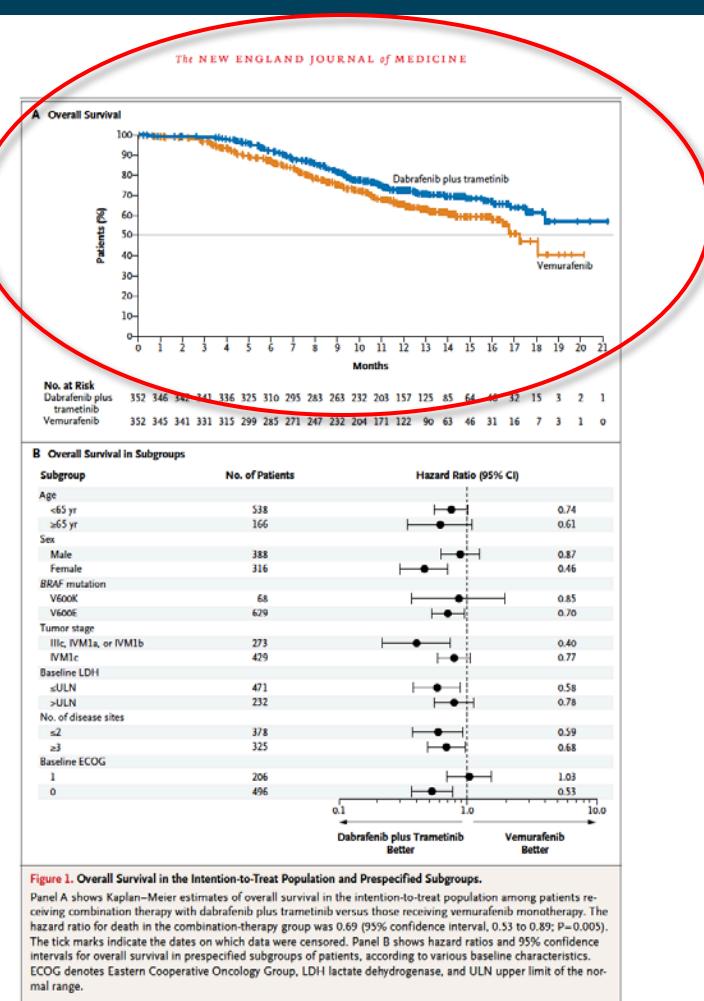
The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Robert at the Dermatology Service and INSERM Unité 981, Gustave Roussy, 114 rue Edouard Vaillant, 94 805 Villejuif-Paris Sud, France, or at caroline.robert@gustaveroussy.fr.

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

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

DOI:10.1056/NEJMoa1412690

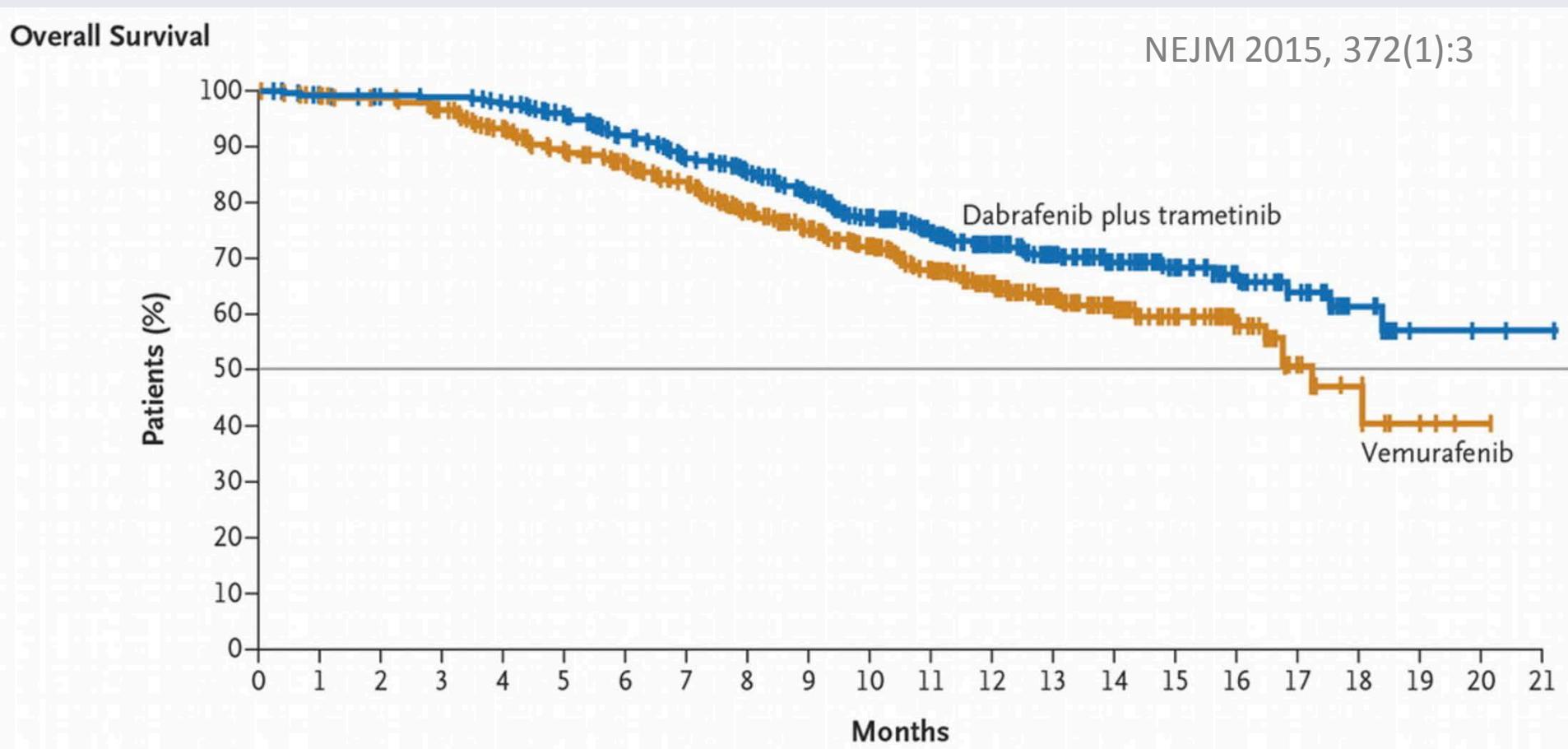
Copyright © 2014 Massachusetts Medical Society.



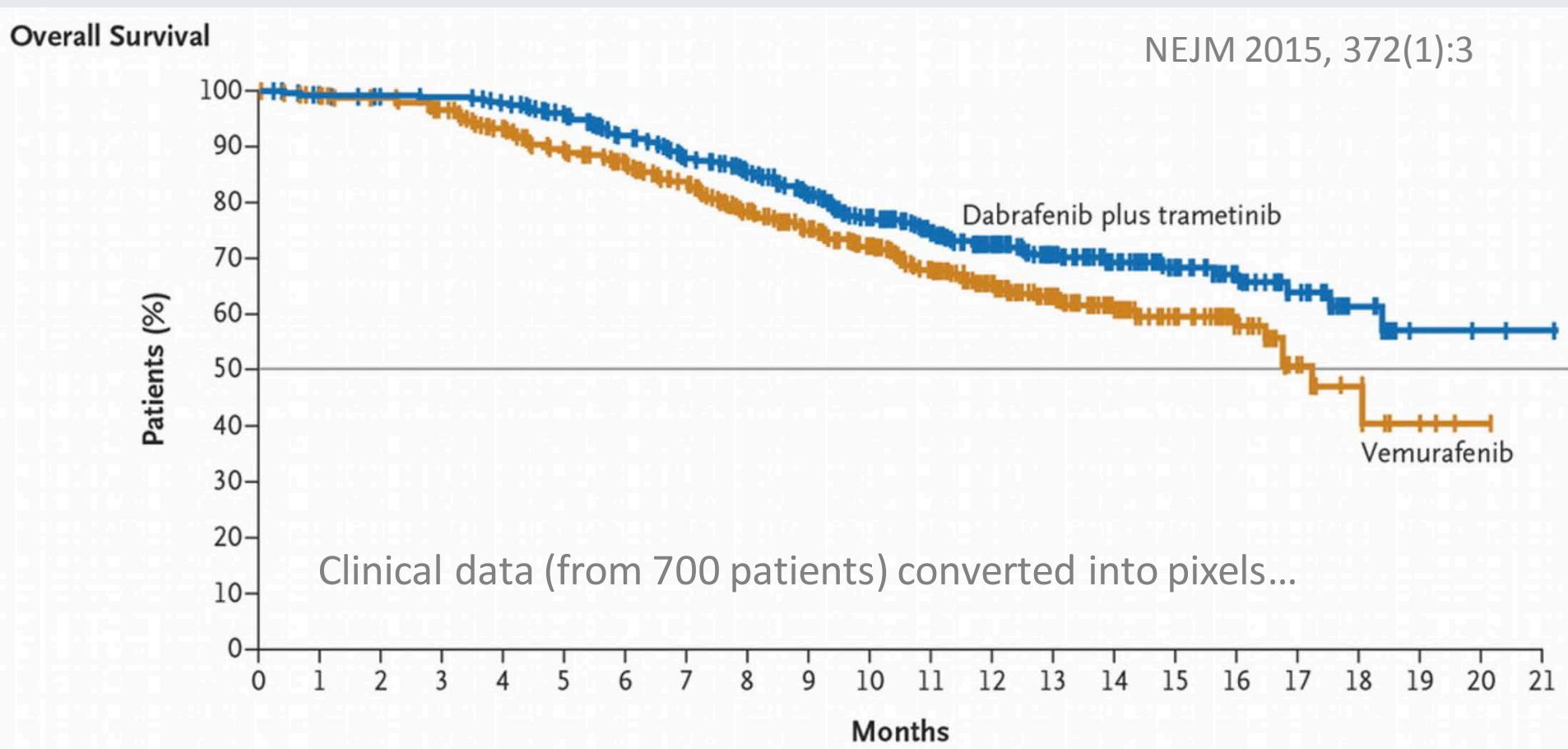
**Figure 1. Overall Survival in the Intention-to-Treat Population and Prespecified Subgroups.**

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.

# What is a figure?



# What is a figure?

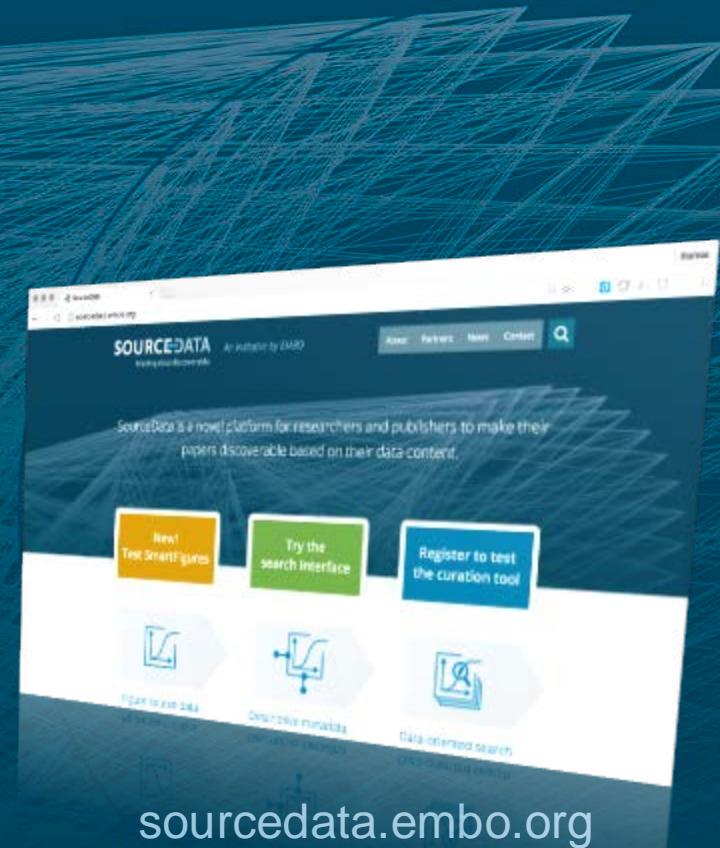


# 2. SourceData

# SOURCE•DATA

Making data discoverable

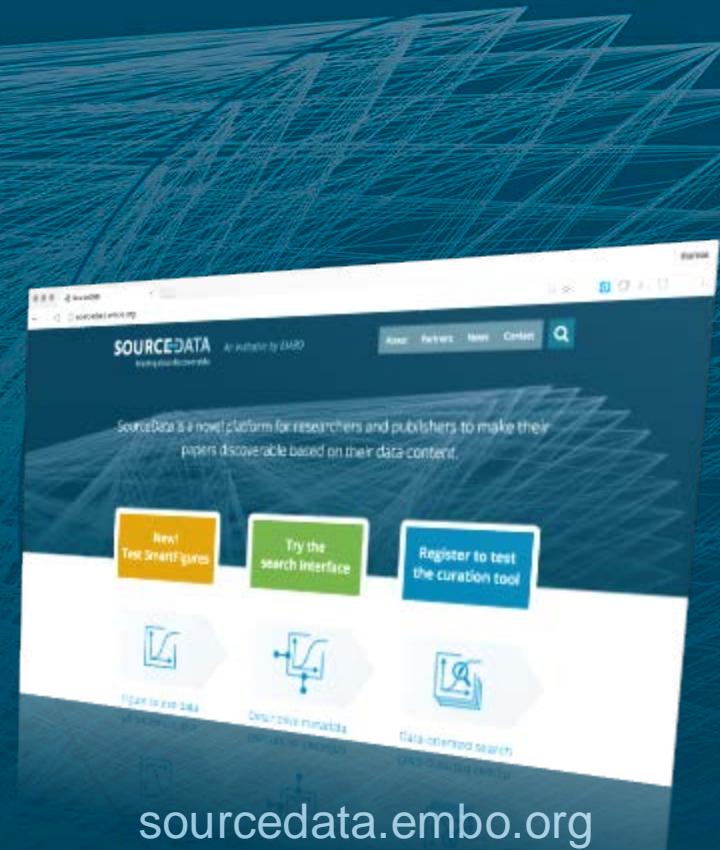
- Facilitate discovery and browsing of data and papers



# SOURCE•DATA

Making data discoverable

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



# SOURCE•DATA

Making data discoverable

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



[sourcedata.embo.org](http://sourcedata.embo.org)



# SOURCE DATA

Making data discoverable



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



## Directed Search

# Directed Search

Perturbation      Measured entity  
Does **Forskolin** influence **Huntingtin** ? 

## Search results



**Forskolin**

5 Experiments



**Y Huntingtin**

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

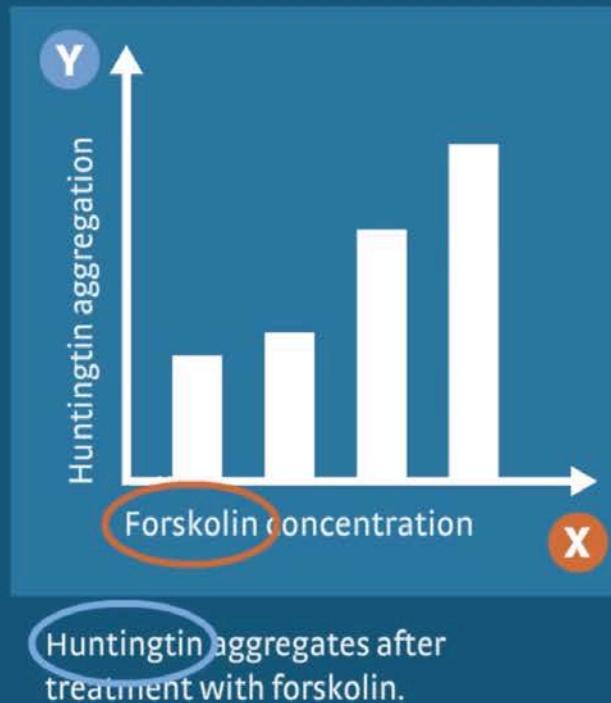
Williams E et al.

Nature Chemical Biology 2008

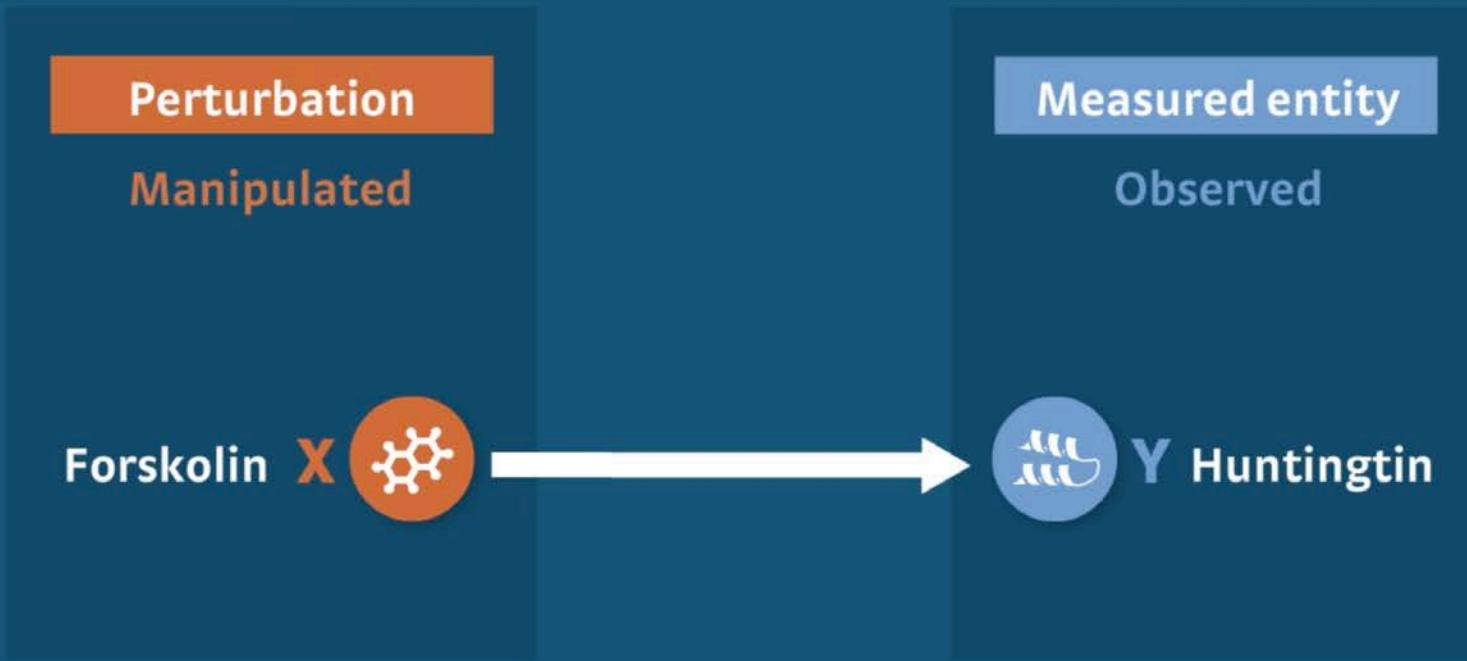
**Y**



# How it works

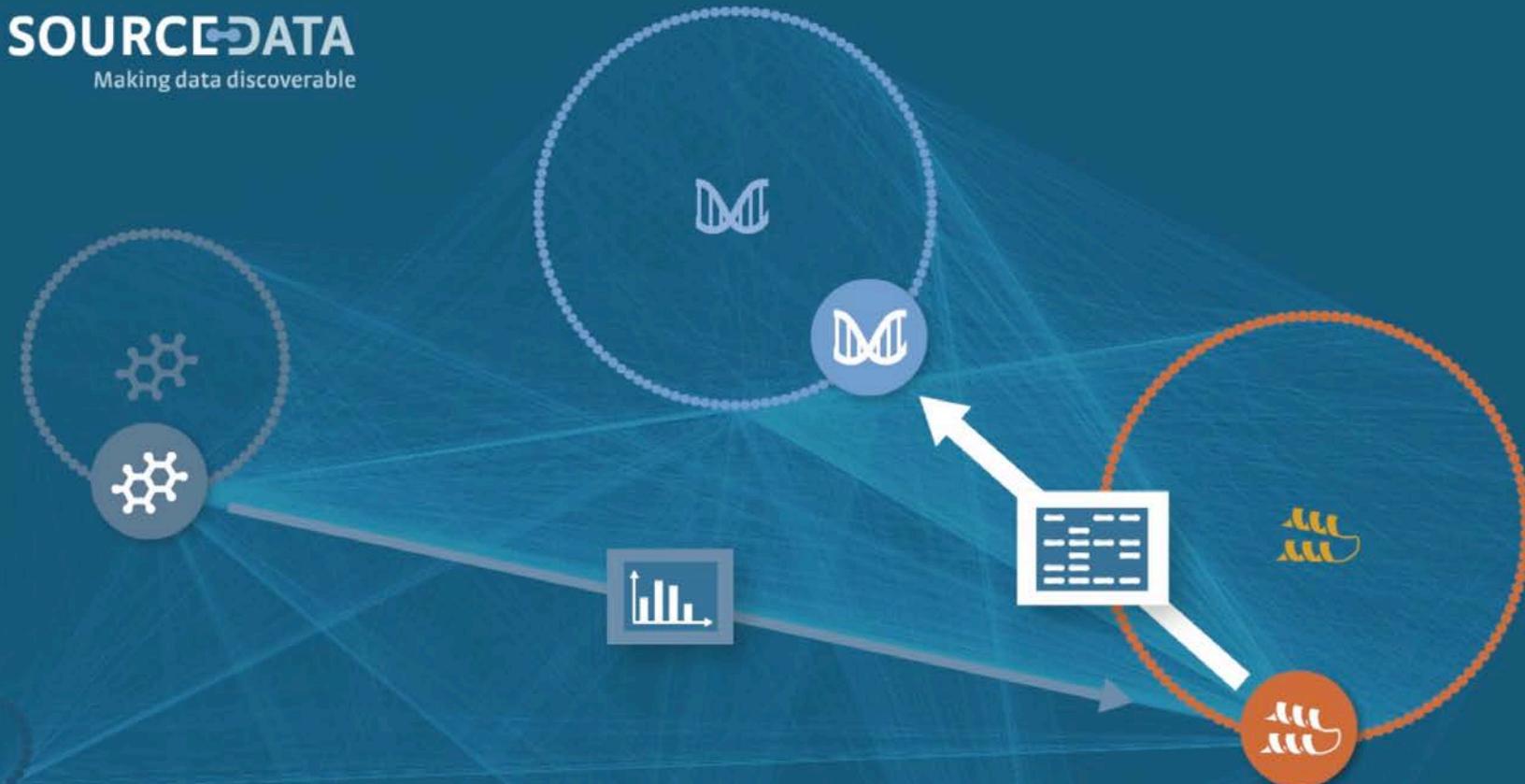


# How it works



# SOURCE DATA

Making data discoverable



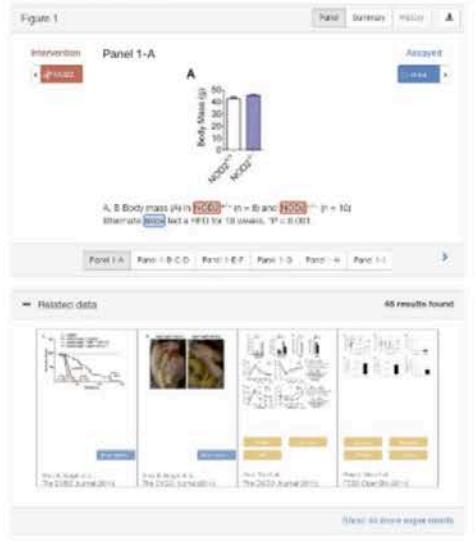
Liechti et al. (2017). *Nature Methods* 14:1021

## SmartFigures

[smartfigures.net](http://smartfigures.net)

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

Figure 1. <https://doi.org/10.1038/nmeth.2029>



## Data search

[sourcedata.vital-it.ch/public/#/search](https://sourcedata.vital-it.ch/public/#/search)

Perturbation      Measured entity

Does  influence  ?

## Curation interface

[sourcedata.vital-it.ch/#/login](https://sourcedata.vital-it.ch/#/login)



**EMBO**press



Swiss Institute of  
Bioinformatics

**SOURCE DATA**  
Making data discoverable



## Data search

Perturbation [?](#)

Does  affect

of type : [small molecule](#) [?](#)

Measured entity [?](#)

of type : [small molecule](#) [?](#)

[Simple search](#)

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

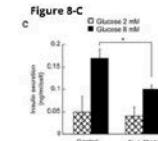
### Fission and selective fusion govern mitochondrial segregation and elimination by autophagy

Gilad Twig, Alvaro Elorza, Anthony J A Molina, Hibo Mohamed, Jakob D Wikström, Gil Walzer, Linsey Stiles, Sarah E Haigh, Steve Katz, Guy Las, Joseph Alroy, Min Wu, Bénédicte F Py, Junyong Yuan, Jude T Deeney, Barbara E Corkey, Orlan S Shriram  
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 fission, 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.

glucose 1 experiment insulin (human) (insulin)



[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](#)

glucose 1 experiment 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](#)

glucose 1 experiment insulin (human) (insulin)

[Show figures](#)

# DataSearch

## Data search

Perturbation [?](#)

Does  affect  ?

Measured entity [?](#)

Try: does [insulin](#) influence [glucose](#)? or does [glucose](#) influence [insulin](#)?

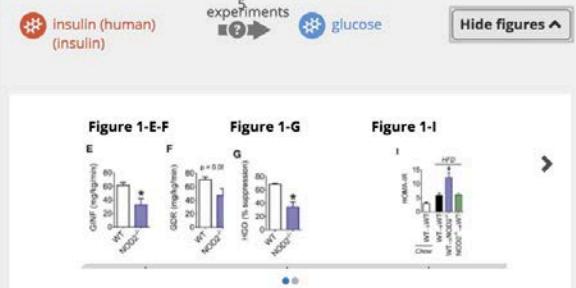
**Defective NOD2 peptidoglycan sensing promotes diet-induced inflammation, dysbiosis, and insulin resistance.**  
Denou E, Lolmède K, Garidou L, Pomici C, Chabo C, Lau TC, Fullerton MD, Nigro G, Zakaroff-Girard A, Luche E, Garret C, Serino M, Amar J, Courtney M, Cavallari JF, Henriksen BD, Barra NG, Foley KP, McPhee JB, Duggan BM, O'Neill HM, Lee AJ, Sansonetti P, Ashkar AA, Khan WI, 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](#)



**Fatty acid-induced NLRP3-ASC inflammasome activation interferes with insulin signaling**  
Haitao H Wen et al.  
Nature Immunology- 2011

[Show abstract](#)



Google  Microphone Search

All Images Videos Shopping News More Settings Tools

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](https://en.wikipedia.org/wiki/Blood_sugar_regulation)

? About this result Feedback

Google  Microphone Search

All Images Shopping News Videos More Settings Tools

About 58.100.000 results (0,49 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**.

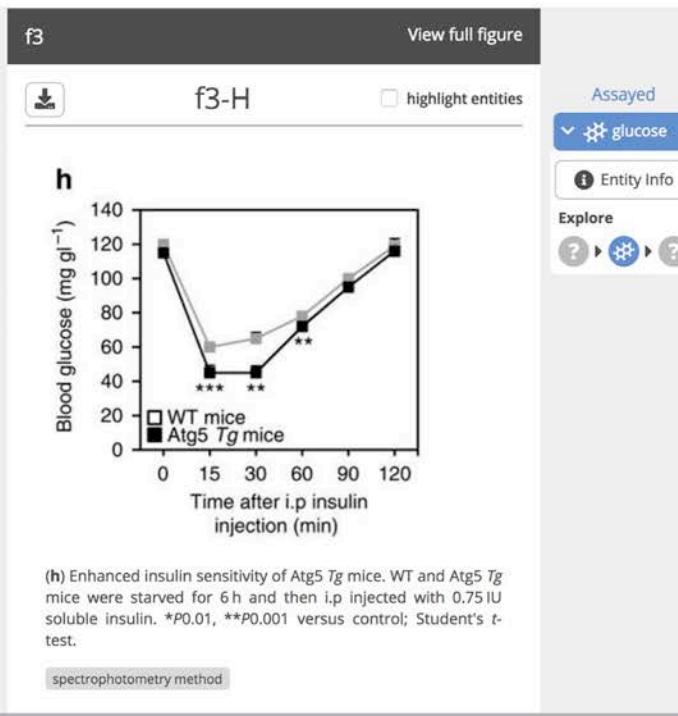
**Blood sugar regulation - Wikipedia**  
[https://en.wikipedia.org/wiki/Blood\\_sugar\\_regulation](https://en.wikipedia.org/wiki/Blood_sugar_regulation)

? About this result Feedback

Overexpression of Atg5 in mice activates autophagy and extends lifespan

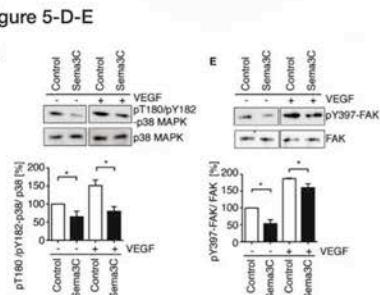
Pyo JO et al. *Nature communications* 2013

Reproduced from 10.1038/ncomms3300 with permissions



Semaphorin-3C signals through Neuropilin-1 and Neuropilin-2 to regulate pathological angiogenesis.  
Yang WJ et al. *EMBO molecular medicine* 2015

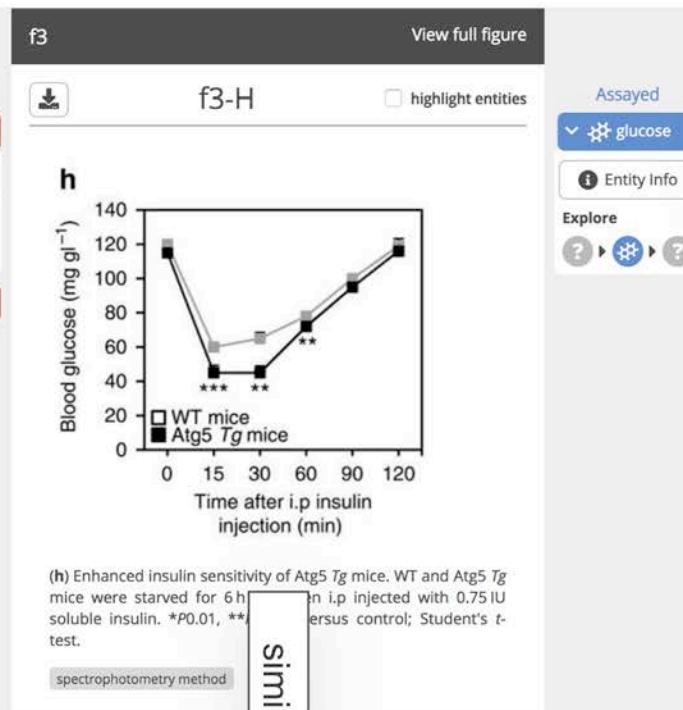
Figure 5



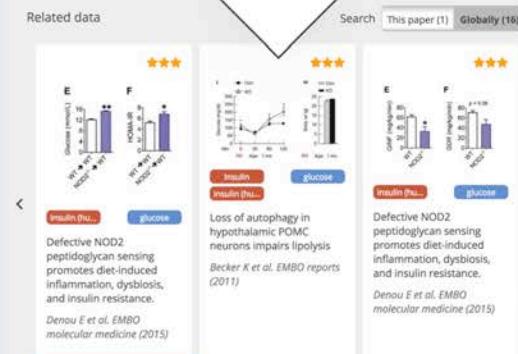
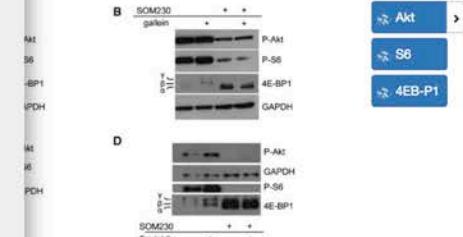
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Pyo JO et al. *Nature communications* 2013

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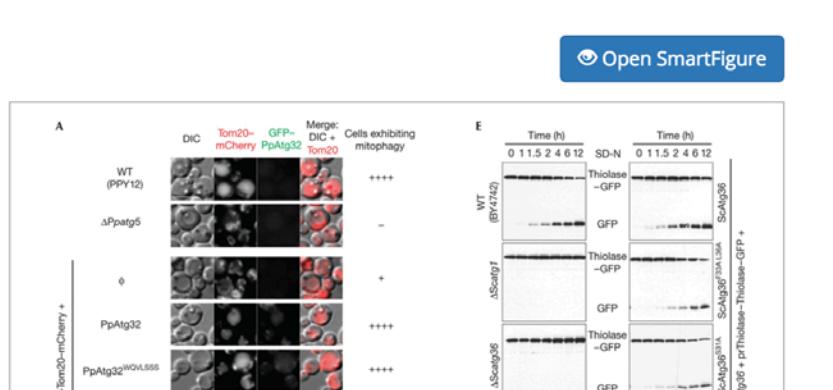
downstream  
protein synthesis TOR/4E-BP1 pathway in chemoresistance.



# A pilot implementation: smartfigures.net

## Common mechanisms for selective autophagy

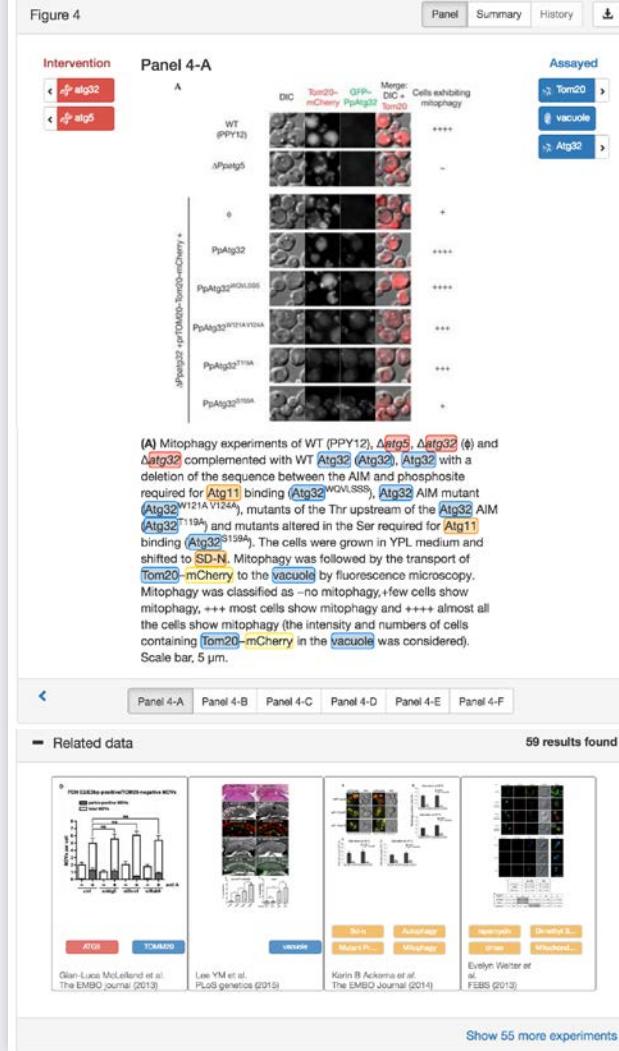
To extend the model of interaction proposed for Atg30 and the autophagic core machinery proteins, we subjected *P. pastoris* Atg32 mutants to mitophagy assays. Mitophagy was followed by Tom20 localization (Tom20-mCherry) and Tom20 degradation (free GFP appearance from Tom20-GFP). Atg32 and Tom20 colocalized to mitochondria during growth condition in YPL medium (mid-log growth phase) and were degraded only after cells had reached stationary phase or shifted to SD-N (Figs 4A,B; supplementary Fig S5 online). Tom20 degradation was depended on Ypt7, Atg5 and Atg32 (Figs 4A,B), as expected for mitophagy.



## Phosphorylation of mitophagy and pexophagy receptors coordinates their interaction with Atg8 and Atg11

Phosphorylation of mitophagy and pexophagy receptors coordinates their interaction with Atg8 and Atg11

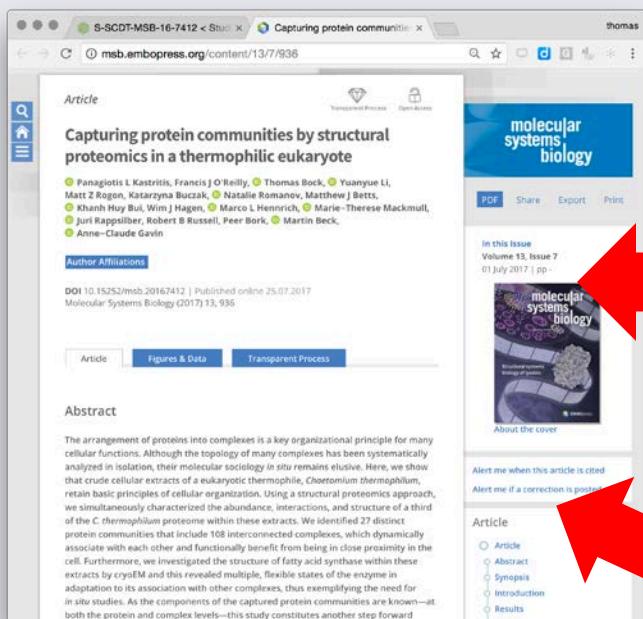
Jean-Claude Farré et al. EMBO reports 2013



Show 55 more experiments

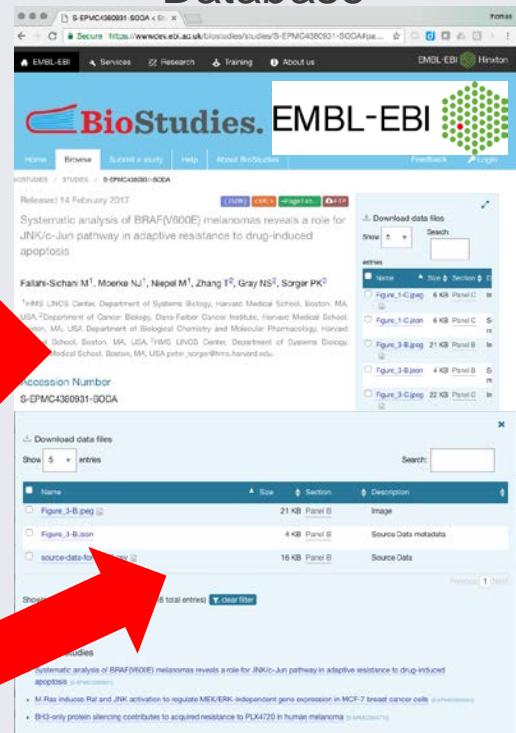
# Integration with data repositories

## Paper



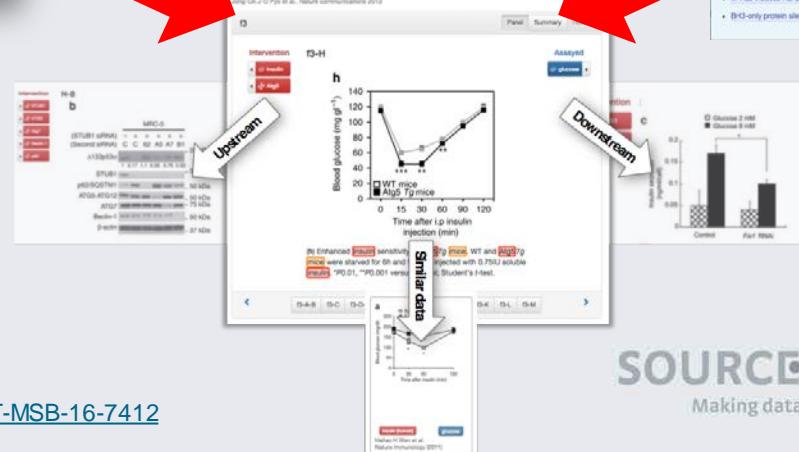
The screenshot shows the 'Capturing protein communities by structural proteomics in a thermophilic eukaryote' article from Molecular Systems Biology. The page includes the journal logo, author list, abstract, and a sidebar with navigation links like 'Article', 'Figures & Data', and 'Transparent Process'.

## Database



The screenshot shows a study entry in BioStudies titled 'Systematic analysis of BRAF(V600E) melanomas reveals a role for JNK-Jun pathway in adaptive resistance to drug-induced apoptosis'. It includes a table of contents, a list of authors, and a sidebar for 'Download data files'.

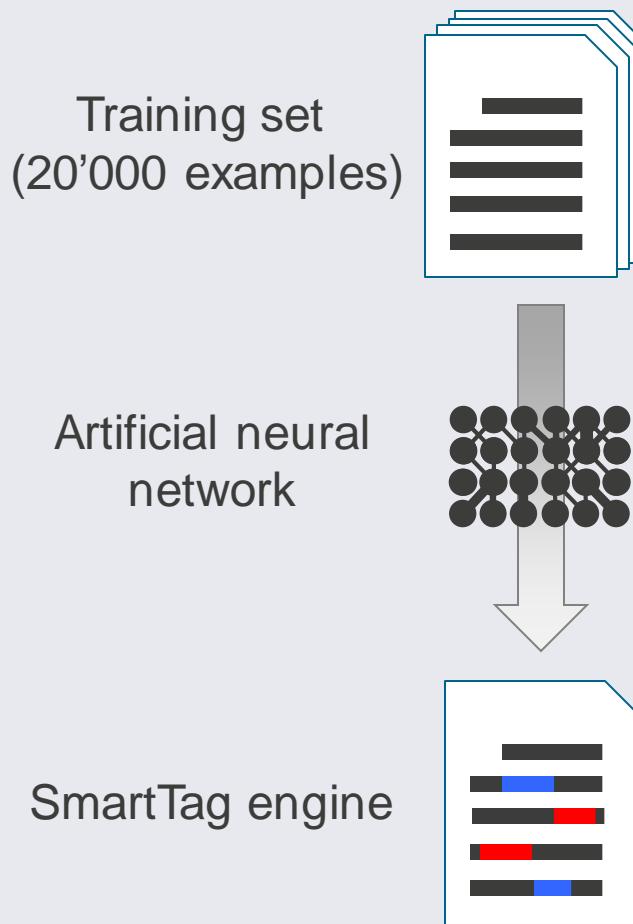
## SmartFigure



SOURCE DATA  
Making data discoverable

EMBO

# An AI approach to semantic analysis

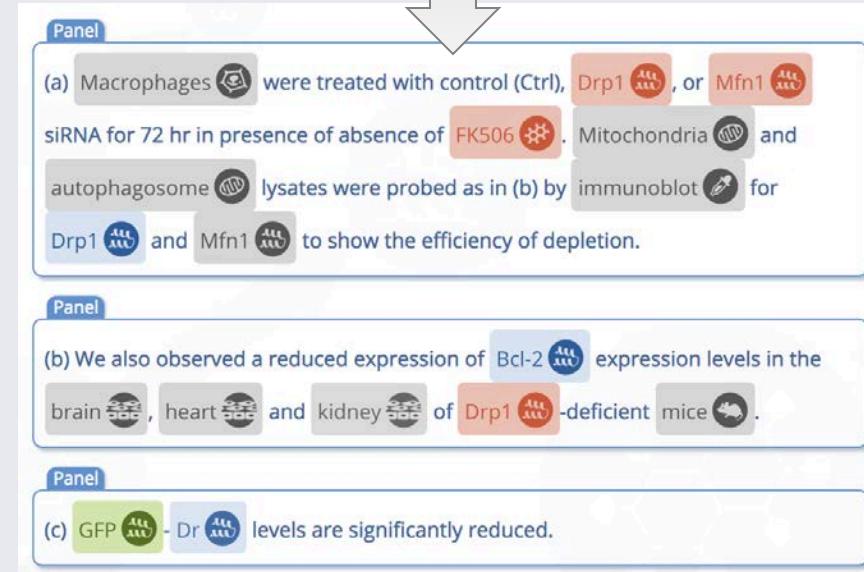
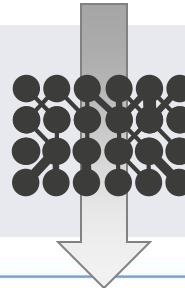


# An AI approach to semantic analysis

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



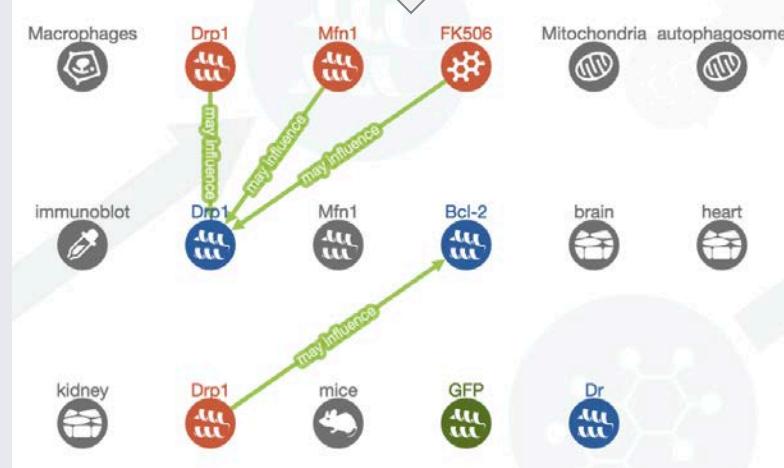
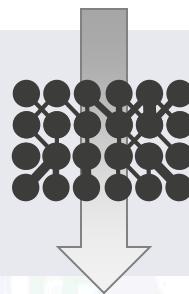
SmartTag:  
deep semantic  
interpretation

# An AI approach to semantic analysis

Plain text  
(figure legend)

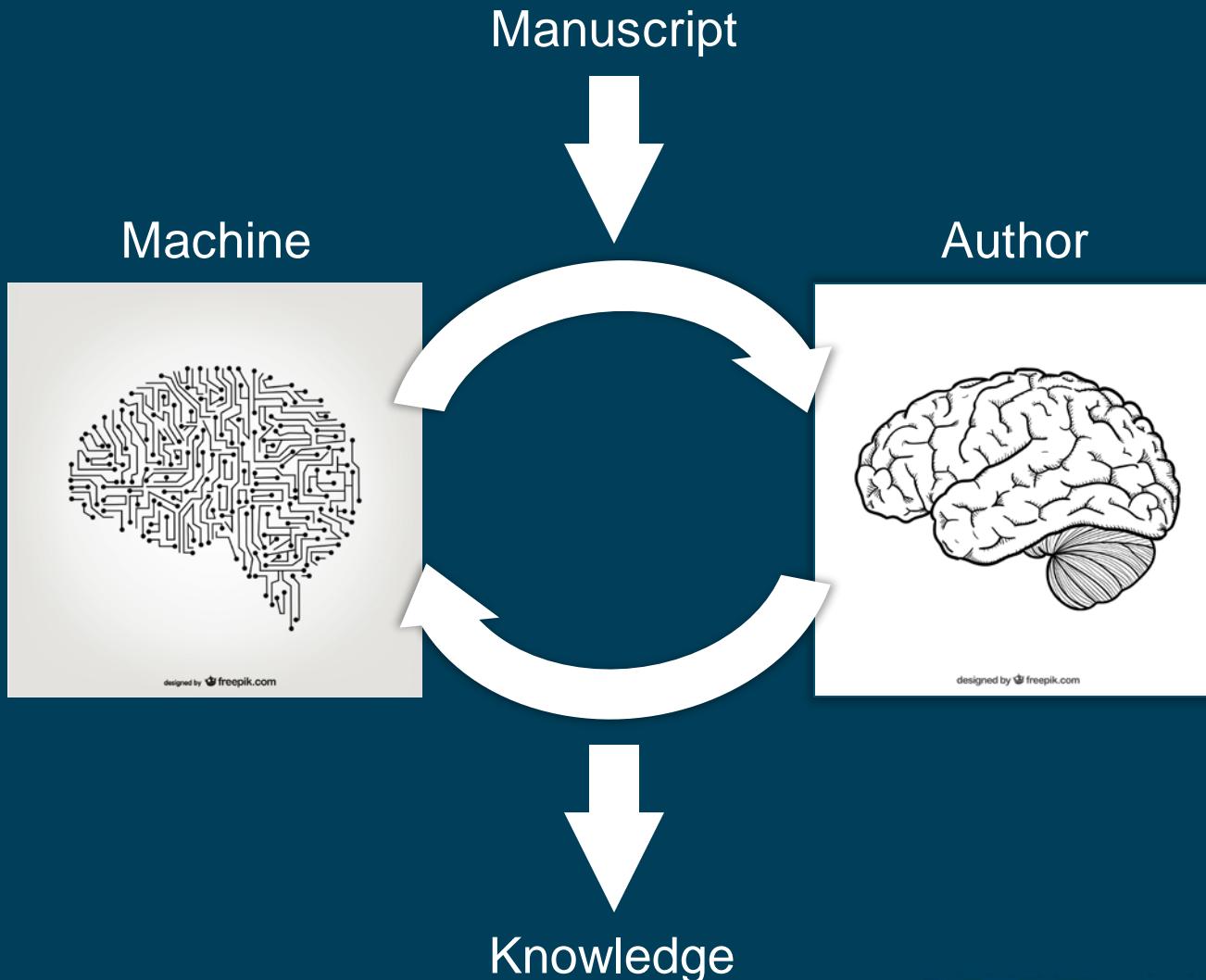
(a) Macrophages were treated with control (Ctrl), Drp1, or Mfn1 siRNA for 72 hr in presence or absence of FK506. Mitochondria and autophagosome lysates were probed as in (b) by immunoblot for Drp1 and Mfn1 to show the efficiency of depletion. (b) We also observed a reduced expression of Bcl-2 expression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

Artificial neural  
network



SmartTag:  
deep semantic  
interpretation

# Disseminating knowledge



# 3. Outlook

# 'Smart' papers

Title

Abstract

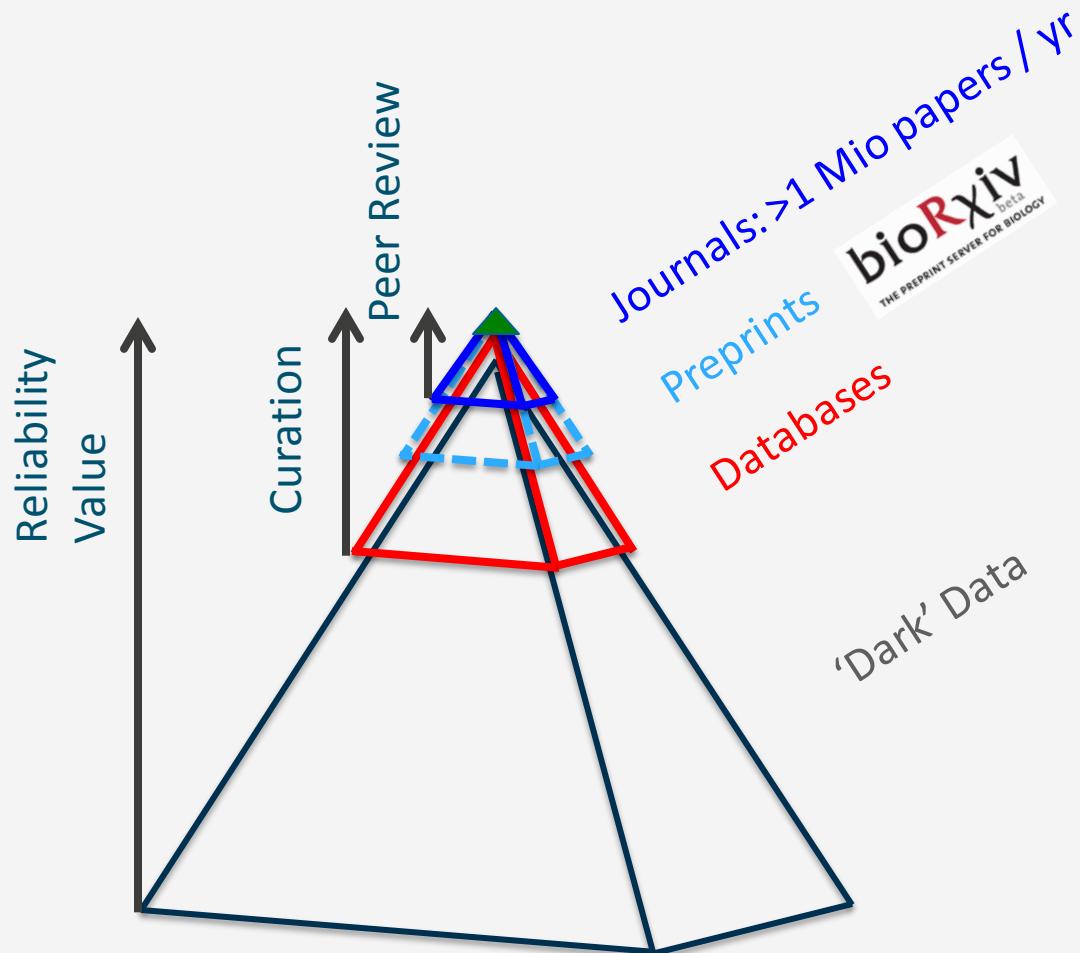
Main paper

SmartFigures

Datasets & code

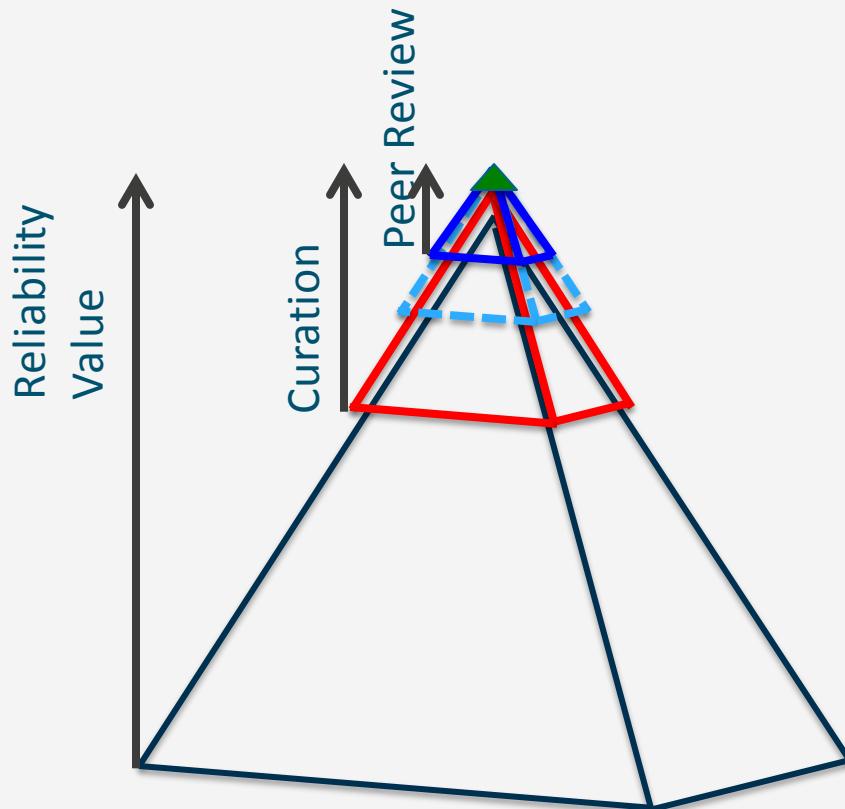


# Accelerating science with Open Science

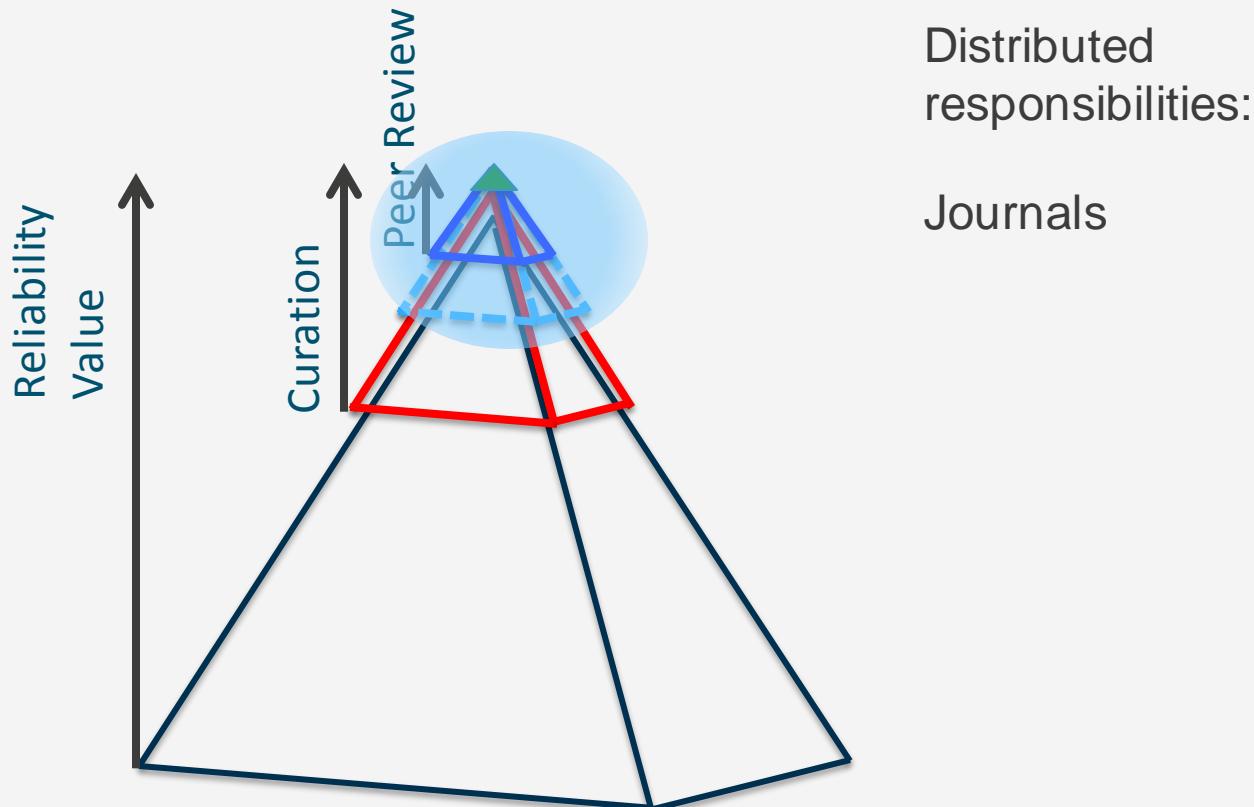




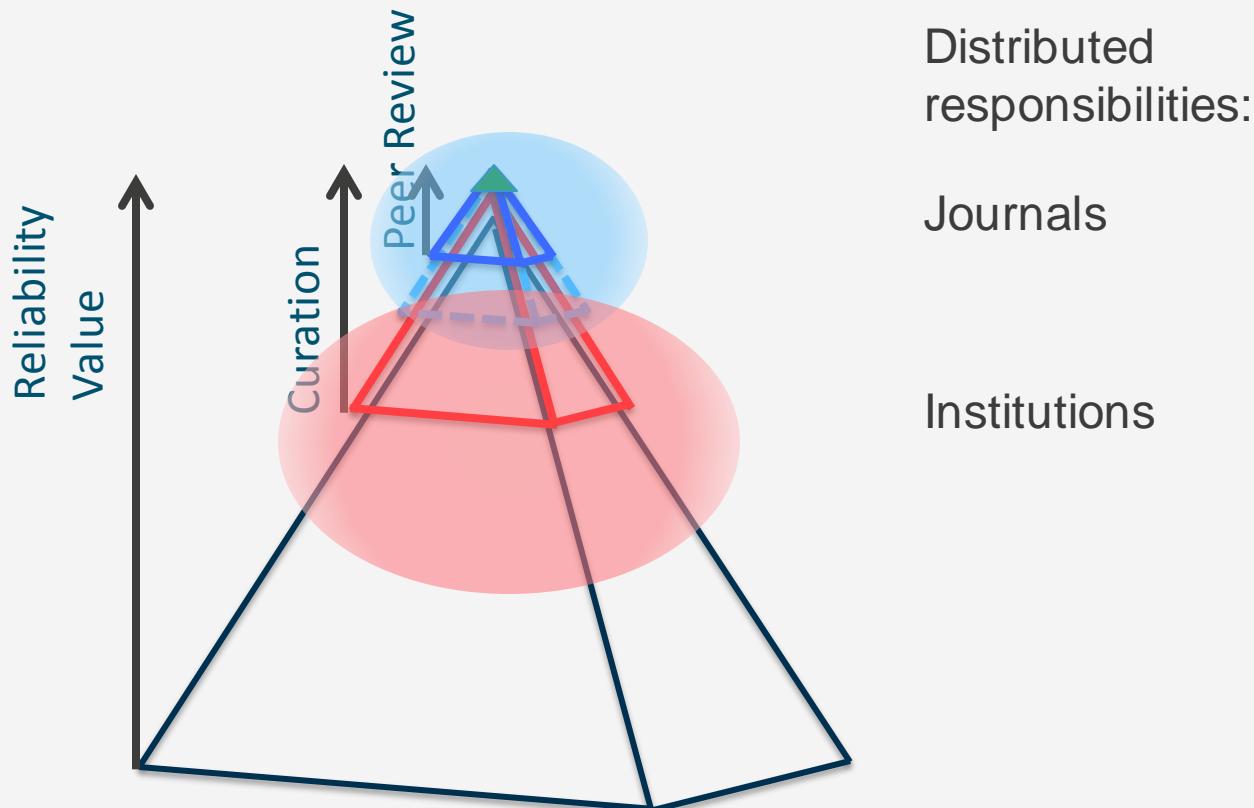
# *Quality* Open Science: how to make it work?



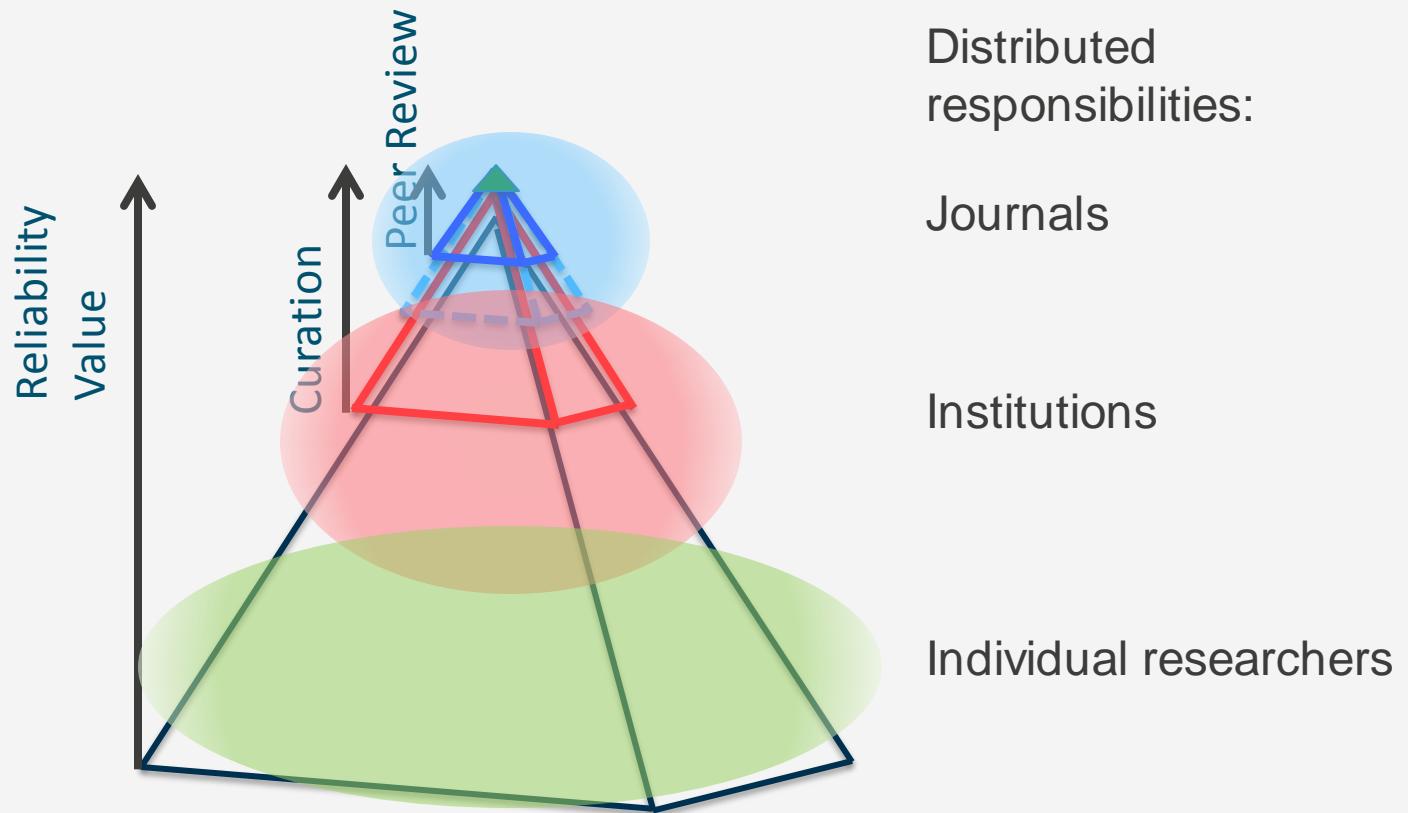
# *Quality* Open Science: how to make it work?



# *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*



Brussels, 27 May 2016  
(OR. en)

9526/16

RECH 208  
TELECOM 100

## OUTCOME OF PROCEEDINGS

From: General Secretariat of the Council

To: Delegations

No. prev. doc.: 8791/16 RECH 133 TELECOM 74

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

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# THANK YOU!

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