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## Building Scholarly Knowledge Bases with Crowdsourcing and Text Mining

Markus Stocker

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**BASIC SCIENCE** 



#### Iron-regulatory proteins secure iron availability in cardiomyocytes to prevent heart failure

Saba Haddad<sup>1,2</sup>, Yong Wang<sup>1,2</sup>, Bruno Galy<sup>3,4</sup>, Mortimer Korf-Klingebiel<sup>1,2</sup>, Valentin Hirsch<sup>1,2</sup>, Abdul M. Baru<sup>1,2</sup>, Fatemeh Rostami<sup>1,2</sup>, Marc R. Reboll<sup>1,2</sup>, Jörg Heineke<sup>2</sup>, Ulrich Flögel<sup>5</sup>, Stephanie Groos<sup>6</sup>, André Renner<sup>7</sup>, Karl Toischer<sup>8</sup>, Fabian Zimmermann<sup>9</sup>, Stefan Engeli<sup>10</sup>, Jens Jordan<sup>10</sup>, Johann Bauersachs<sup>2</sup>, Matthias W. Hentze<sup>3</sup>, Kai C. Wollert<sup>1,2</sup>, and Tibor Kempf<sup>1,2</sup>\*

<sup>1</sup>Division of Molecular and Translational Cardiology, Hannover Medical School, Carl-Neuberg Straßle 1, 10625 Hannover, Germany, <sup>1</sup>Dopattment of Cardiology and Anglology, Hannover Medical School, Carl-Neuberg Straßle 1, 10625 Hannover, Germany, <sup>1</sup>Surpature Molecular Biology, Laboratory, Meun-Indentificational n. 691171 Heidelberg Germany Division of Virus-associated Cardinogenesis, German Cancer Research Centre, Im Neuenheimer Feld 280, 69120 Heidel University of Diazedorf, Universitäitostraße 1, 40225 Diazedorf, Germany, <sup>1</sup>Strattute of Cell Biology, Jamoner Medical Germany, <sup>1</sup>Dipatrement of Thoraciar Surger, University of Bohum, Gergeranito 11, 3255 Bail Olyn Piscumology, University of Gottagen, Robert Koch-Straße 4, 370/5 Gottagen, Germany, <sup>1</sup>Depattment of Analysical O

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See page 373 for the editorial comment on this article (doi: 10.1093/eurheartj/ehw386)

Aims	Iron deficiency (ID) is associated with adverse outcomes in heart failure (HF) but the underlying mechanisms are incompletely understood. Intracellular iron availability is secured by two mRNA-binding iron-regulatory proteins (IRPs), IRP1 and IRP2. Ve generated mice with a cardiomycotte-targeted deletion of Irp1 and Irp2 to explore the functional implications of ID in the heart independent of systemic ID and anaemia.
Methods and results	Iron content in cardiomyocytes was reduced in Irp-targeted mice. The animals were not anaemic and did not show a phenotype under baseline conditions. Irp-targeted mice, however, were unable to increase left ventricular (LV) systolic function in response to an acute dobutamine challenge. After myocardial infarction, Irp-targeted mice de- weloped more severe LV dysfunction with increased HF mortality. Mechanistically, the activity of the iron-sulphur cluster-containing complex I of the mitochondrial electron transport chain was reduced in left ventricles from Irp-targeted mice. As demonstrated by extracellular flux analysis in vitro, mitochondrial respiration was preserved at baseline but failed to increase in response to dobutamine in Irp-targeted cardiomyocytes. As shown by <sup>31</sup> P-magnetic resonance spectroscopy in vivo, LV phosphocreatine/ATP ratio declined during dobutamine stress in Irp-targeted mice but remained stable in control mice. Intravenous injection of ferric carboxymaltose replenished cardiac iron stores, restored mitochondrial respiratory capacity and inotropic reserve, and attenuated adverse remodelling after myocardial infarction in Irp-targeted mice but not in control mice. As shown by electrophoretic mobility shift asays, IRP activity was significantly reduced in LV tissue samples from patients with advanced HF and reduced LV tissue iron content.
Conclusions	ID in cardiomyocytes impairs mitochondrial respiration and adaptation to acute and chronic increases in workload. Iron supplementation restores cardiac energy reserve and function in iron-deficient hearts.
Keywords	Iron deficiency • Heart failure • Energy metabolism • Extracellular flux analysis • <sup>31</sup> P-Magnetic resonance spoctroscopy

\*Corresponding author: Tet: +49 (0)511 532-2229, Fax: +49 (0)511 532-3357, Email: kempf.tibor@mh-hannover.de

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## Scholarly knowledge?

#### http://doi.org/10.1093/eurheartj/ehw333



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<sup>a</sup>Data Seal of Approval



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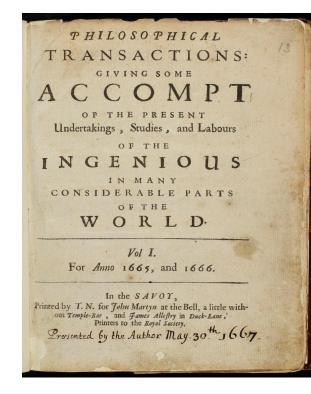
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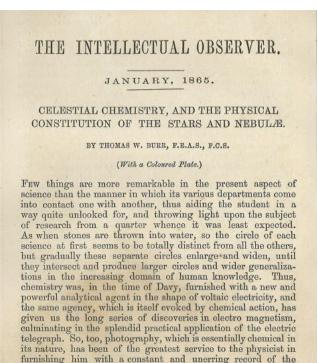


# **Digitization & Digitalization**

## **Digitization of scholarly communications**







European Heart Journal (2017) 38, 362–372 doi:10.1093/curhcarti/chw333 **BASIC SCIENCE** 

#### Iron-regulatory proteins secure iron availability in cardiomyocytes to prevent heart failure

Saba Haddad<sup>12</sup>, Yong Wang<sup>1,2</sup>, Bruno Galy<sup>1,4</sup>, Mortimer Korf-Klingebiel<sup>1,2</sup>, Valentin Hirsch<sup>1,2</sup>, Abdul M. Baru<sup>1,2</sup>, Fatemeh Rostam<sup>1,7</sup>, Marc R. Reboll<sup>1,2</sup>, Jörg Heineke<sup>3</sup>, Ulrich Flögel<sup>7</sup>, Stephanie Groos<sup>4</sup>, André Renner<sup>7</sup>, Kart Toischer<sup>8</sup>, Fablan Zimmermann<sup>7</sup>, Stefan Engell<sup>11</sup>, Jens Jordan<sup>8</sup>, Johann Bauersachs<sup>7</sup>, Matthias W. Hentze<sup>7</sup>, Kat C. Woller<sup>1,2</sup>, and Tibor Kemp<sup>1,6,4</sup>

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\*Corresponding author: Tet +49 (0)511 S32-3229, Fac +49 (0)511 S32-3357, Email: kempfotbor@inh-hannover.de Published on behalf of the European Society of Cardiology. All rights reserved 0 The Author 2016. For permissions please email: journals.permissions/flow

#### http://doi.org/10.1093/eurheartj/ehw333

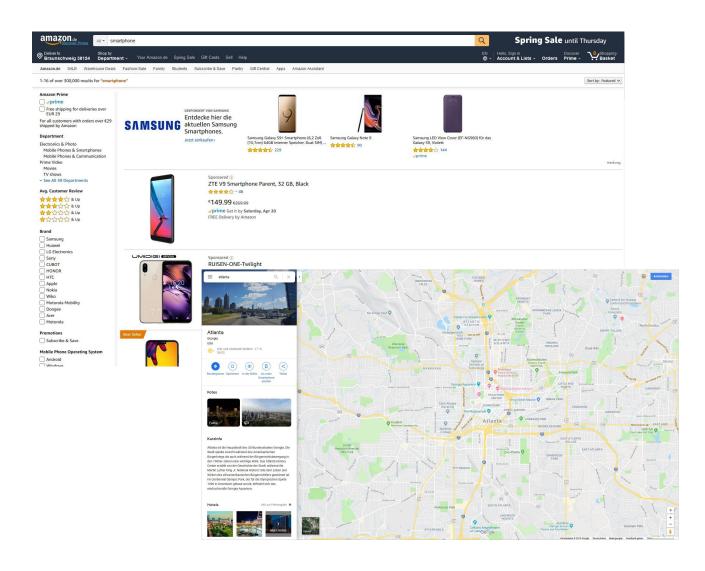
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## **Digitalization elsewhere**







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# Can we build a knowledge base?



# Can we build a knowledge base?

... or knowledge bases?



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equatorial circumference	4.371×10 <sup>6</sup> km (kilometers)		
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## **Compare Methods**

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Title	Analysis of Amphetamine in Blood by Gas chromatography	Analysis of <b>Methamphetamine</b> in Blood by Solid phase extraction	Analysis of 3,4- Methylenedioxymethamphetamine in Blood by Solvent extraction
CAS Method Number	1-125-CAS-235751	1-125-CAS-60925	1-125-CAS-12925
Method Category	Forensic Analysis; Addictive Drug Assay	Forensic Analysis; Active Pharmaceutical Ingredient and Metabolite Analysis	Forensic Analysis
Technique	Mass spectrometry; Gas chromatography; Extraction	Gas chromatography-mass spectrometry; Solid phase extraction	Mass spectrometry; Reversed phase liquid chromatography; Solvent extraction
Analyte	Amphetamine; Methamphetamine	Amphetamine; Methamphetamine	Tetrahydrocannabinol; 3,4- Methylenedioxyamphetamine; Amphetamine; 3,4- View All ~
Matrix	Hair; Liver; Lung; Spleen; Urine; Blood; Brain; Adipose tissue	Blood	Blood

#### 



S Derivation of organoids from primary tumour tissue

Hazel Rogers<sup>1</sup>, Laura Letchford<sup>1</sup>, Sara Vieira<sup>1</sup>, Maria Garcia-Casado<sup>1</sup>, Mya Fekry-Troll<sup>1</sup>, Charlotte Beaver<sup>1</sup>, Rachel Nelson<sup>1</sup>, Hayley Francies<sup>1</sup>, Mathew Garnett<sup>1</sup> <sup>1</sup>Wellcome Sanger Institute

Jul 07, 2020	1 Works for me	dx.doi.org/10.17504/protocols.io.bfvnjn5e
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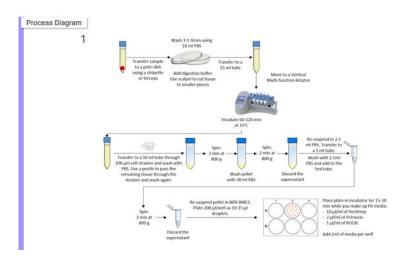
BEFORE STARTING

- Thaw BME2 aliquot overnight at 👌 4 °C and dilute 4:1 with appropriate organoid media (tissue specific) to
- make an 80% stock
- Ensure cell culture plates have been stored overnight in 8 37 °C incubator
- · Pre-warm organoid culture media to room temperature
- Prepare 100 mg/ml collagenase stock. Re-suspend 3 g collagenase II in 3 10 mL PBS. Aliquots can be

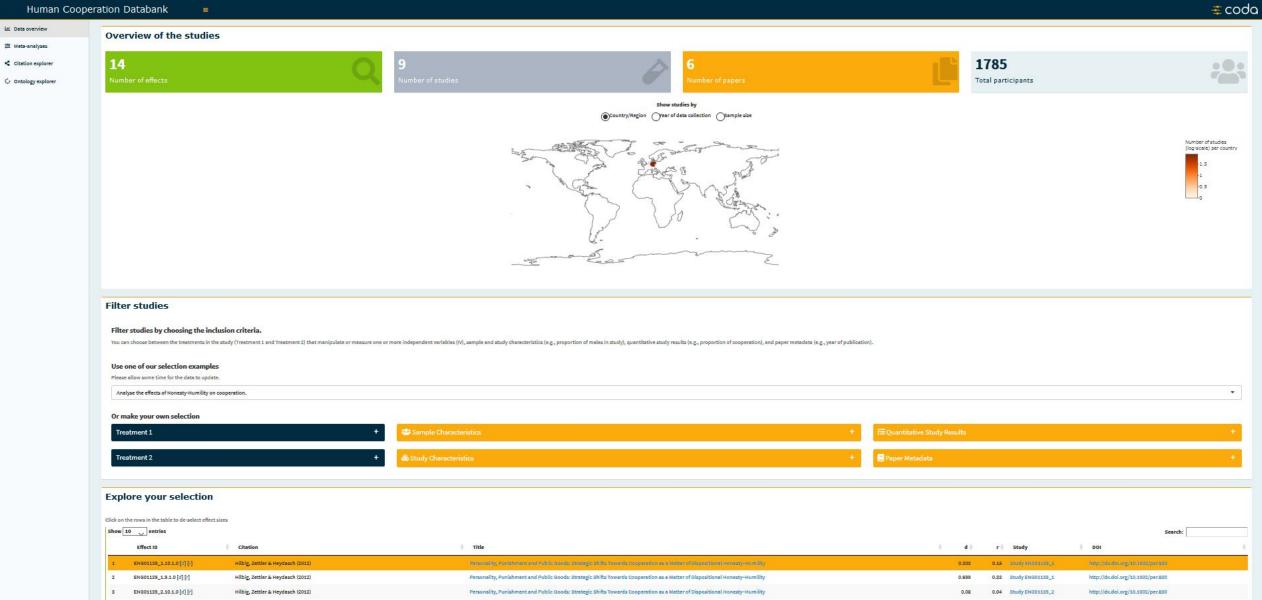
stored at & -20 °C for up to one year.

Prepare digestion buffer:

Reagent	Stock Concentration	Volume	
Organoid Media	-	9.5 ml	
Collagenase	100 mg/ml	0.5 ml	
Primocin	50 mg/ml	0.02 ml	
Penicillin Streptomycin	100X	0.1 ml	
Rock inhibitor (Y-27632) (10 mM)	10 mM	0.01 ml	







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ENG01139_1.10.1.0 [d] [r]	Hilbig, Zettler & Heydaach (2012)	Retainally, Punishment and Public Boods: Strategic Shifts Towards Cooperation as a Matter of Dispositional Honesty-Humility	0.303	0.15 Study ENG01135_1	http://dx.doi.org/20.1002/per.850
ENG01139_1.9.1.0 [d] [r]	Hilbig, Zettler & Heydasch (2012)	Personality, Punishment and Public Goods: Strategic Shifts Towards Cooperation as a Matter of Dispositional Honesty-Humility	0.699	0.33 Study ENG01139_1	http://dx.doi.org/10.1002/per.RS0
ENG01139_2.10.1.0 [d] [r]	Hilbig, Zettler & Heydasch (2012)	Personality, Punishment and Public Goods: Strategic Shifts Towards Cooperation as a Matter of Dispositional Honesty-Humility	0.02	0.04 Study ENG01139_2	http://dx.doi.org/10.1002/per.230
ENG01139_2.9.1.0 [d] [r]	Hilbig, Zettler & Heydasch (2012)	Personality, Punishment and Public Goods: Strategic Shifts Towards Cooperation as a Matter of Dispositional Honesty-Humility	0.516	0.25 Study ENG01139_2	http://dx.doi.org/10.1002/per.930
ENG01334_1.6.1.0 [d] [r]	Kieslich & Hilbig (2014)	Cognitive conflict in social dilemmas: An analysis of response dynamics	0.327	0.19 Study ENG01334_1	NA
ENG01707_3.5.1.0 [d] [r]	Mischkowski & Glöckner (2016)	Spontaneous cooperation for prosocials, but not for proselfs: Social value orientation moderates spontaneous cooperation behavior	0.277	0.137 Study ENG01707_3	http://dx.doi.org/10.1038/srep21555
ENG01296_1.9.1.0 [d] [r]	Perugini, Tan, & Zizzo (2010)	Which is the More Predictable Gender? Public Good Contribution and Personality	0.122	0.061 Study ENG01896_1	http://dx.doi.org/10.2139/sam.676808
ENG02424_1.5.1.0 [d] [r]	Urbig, Terjesen, Procher, Muehlfeld, & Van Witteloostuijn (2016)	Come on and take a free ride: Contributing to public goods in native and foreign language settings	0.232	0.115 Study ENG02424_1	NA
ENG02641_1.4.1.0 [d] [r]	Zettler, Hilbig & Heydasch (2013)	Two sides of one coin: Honesty-humility and situational factors mutually shape social dilemma decision making	0.62	0.296 Study ENG02641_1	http://dx.doi.org/10.1016/j.jrp.2013.01.012
ENG02641_1.5.1.0 [d] [r]	Zettler, Hilbig & Heydesch (2013)	Two sides of one coin: Honesty-humility and situational factors mutually shape social dilemma decision making	0.44	0.215 Study ENG02641_1	http://dx.doi.org/10.1016/j.jrp.2013.01.012

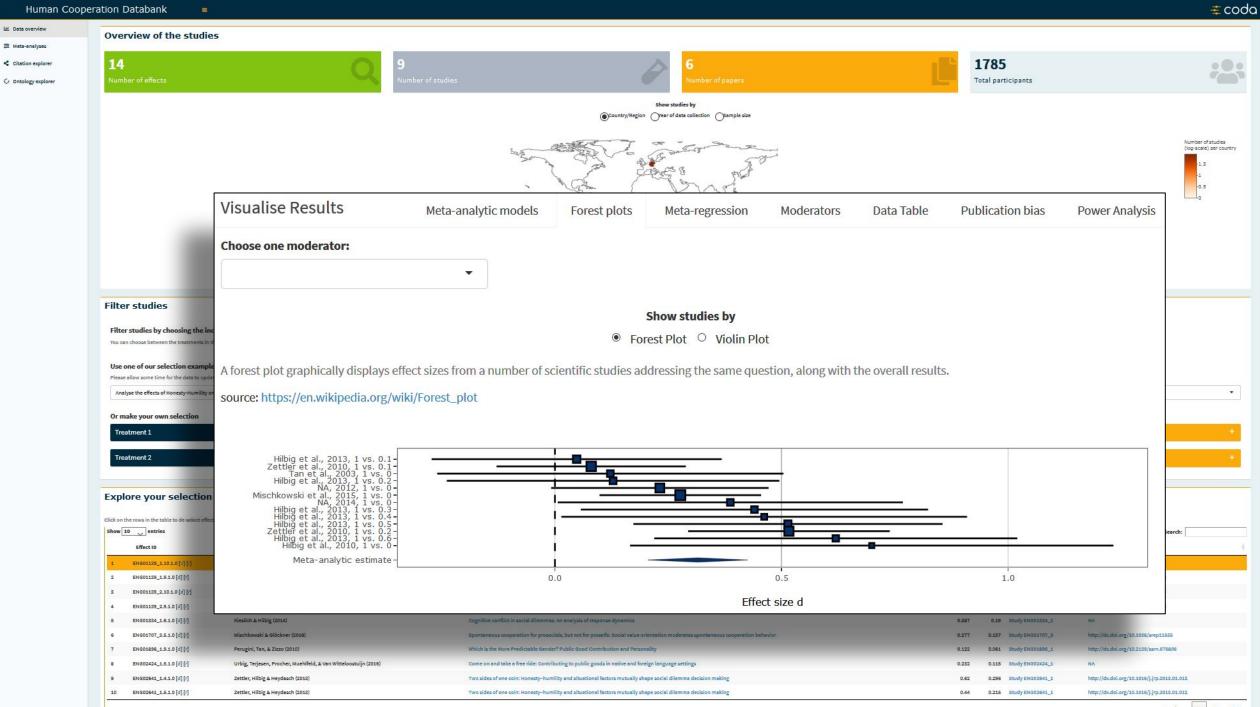
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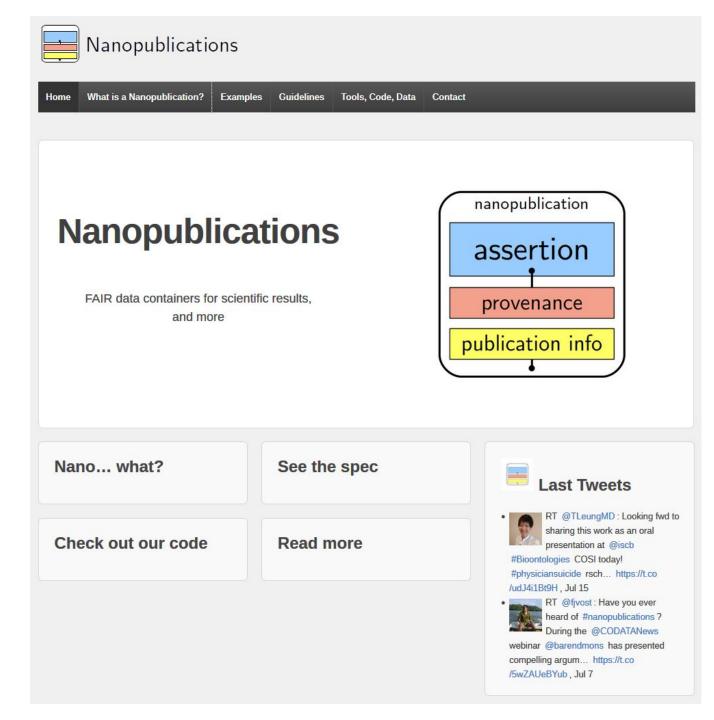
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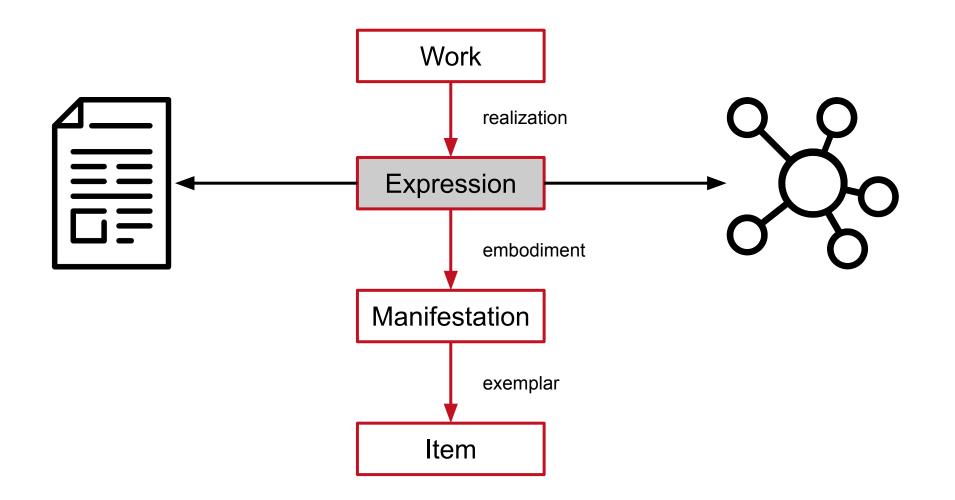
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# With Crowdsourcing and Text Mining



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Aims Iron deficiency (ID) is associated with adverse outcomes in heart failure (HF) mechanisms are incompletely understood. Intracellular iron availability is secured to regulatory proteins (IRPs), IRP1 and IRP2. We generated mice with a cardiomyocyt and Irp2 to explore the functional implications of ID in the heart independent of s Methods and results Iron content in cardiomyocytes was reduced in Irp-targeted anaemic and did not show a phenotype under baseline conditions. Irp-targeted m to increase left ventricular (LV) systolic function in response to an acute dobutam myocardial infarction, Irp-targeted mice developed more severe LV dysfunction w Mechanistically, the activity of the iron-sulphur cluster-containing complex I of th transport chain was reduced in left ventricles from Irp-targeted mice. As demonst analysis in vitro, mitochondrial respiration was preserved at baseline but failed to i dobutamine in Irp-targeted cardiomyocytes. As shown by 31P-magnetic resonan phosphocreatine/ATP ratio declined during dobutamine stress in Irp-targeted mice control mice. Intravenous injection of ferric carboxymaltose replenished cardiac irc mitochondrial respiratory capacity and inotropic reserve, and attenuated adverse i myocardial infarction in Irp-targeted mice but not in control mice. As shown by e assays, IRP activity was significantly reduced in LV tissue samples from pat reduced LV tissue iron content. Conclusions ID in cardiomyocytes imp mitocho adaptation to acute and chronic increases in workload. Iron supplementation and function in iron-deficient hearts

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Material 12

Method 1

#### Commentary | Open Access | Published: 07 June 2005 Which gene did you mean?

#### Barend Mons

 BMC Bioinformatics
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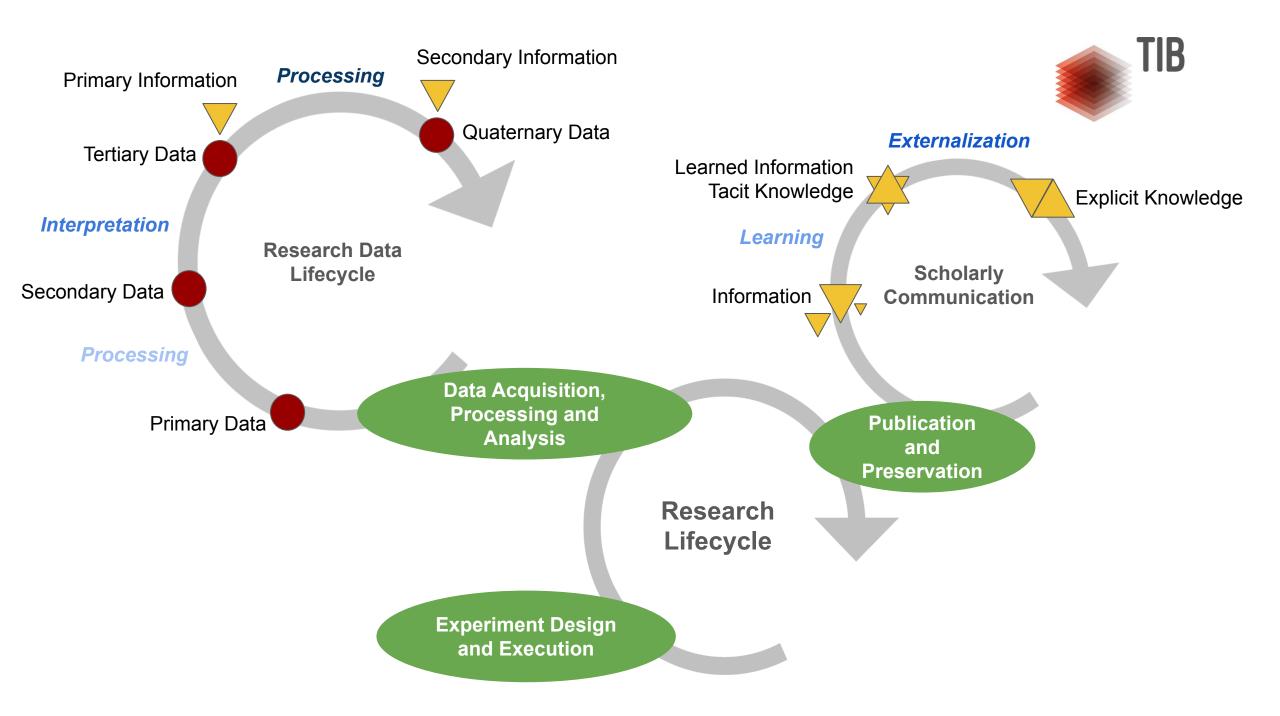
#### Abstract

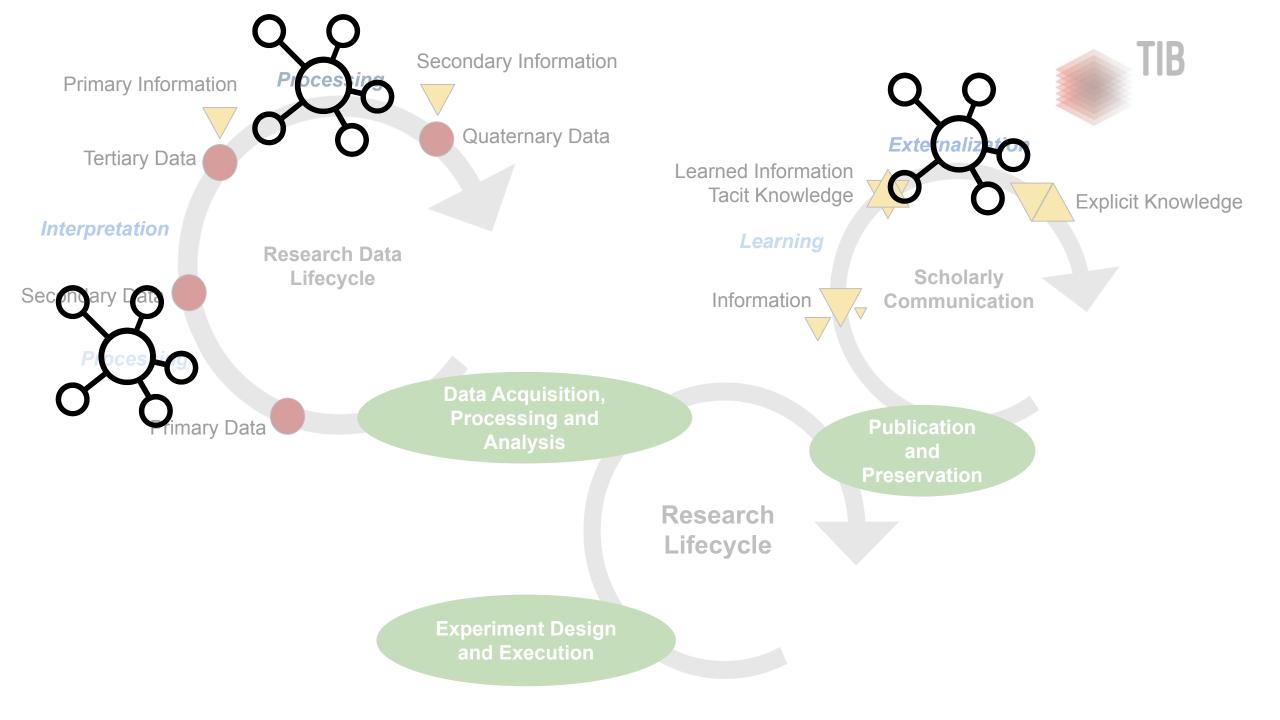
Computational Biology needs computer-readable information records. Increasingly, metaanalysed and pre-digested information is being used in the follow up of high throughput experiments and other investigations that yield massive data sets. Semantic enrichment of plain text is crucial for computer aided analysis. In general people will think about semantic tagging as just another form of text mining, and that term has quite a negative connotation in the minds of some biologists who have been disappointed by classical approaches of text mining. Efforts so far have tried to develop tools and technologies that retrospectively extract the correct information from text, which is usually full of ambiguities. Although remarkable results have been obtained in experimental circumstances, the wide spread use of information mining tools is lagging behind earlier expectations. This commentary proposes to make semantic tagein

#### Text mining? ......Why bury it first and then mine it again?

suitable for proncering

databases and information systems used by drug researchers are already in, or are ready to be transformed to, machine-readable formats' [1].







# "Crowdsourced"



# Yet, we publish PDFs





## Open Research Knowledge Graph



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- API Documentation: https://www.orkg.org/orkg/doc/api/
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- Skype: https://join.skype.com/giNqo7JBpvtw
- Mailing list: https://groups.google.com/forum/#!forum/orkg



# Example COVID-19 basic reproduction number

#### arXiv.org > <u>q-bio</u> > arXiv:2003.09320

#### Quantitative Biology > Populations and Evolution

#### COVID-19 e-print

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#### [Submitted on 20 Mar 2020]

#### The early phase of the COVID-19 outbreak in Lombardy, Italy

Cereda D, Tirani M, Rovida F, Demicheli V, Ajelli M, Poletti P, Trentini F, Guzzetta G, Marziano V, Barone A, Magoni M, Deandrea S, Diurno G, Lombardo M, Faccini M, Pan A, Bruno R, Pariani E, Grasselli G, Piatti A, Gramegna M, Baldanti F, Melegaro A, Merler S

In the night of February 20, 2020, the first case of novel coronavirus disease (COVID-19) was confirmed in the Lombardy Region, Italy. In the week that followed, Lombardy experienced a very rapid increase in the number of cases. We analyzed the first 5,830 laboratory-confirmed cases to provide the first epidemiological characterization of a COVID-19 outbreak in a Western Country. Epidemiological data were collected through standardized interviews of confirmed cases and their close contacts. We collected demographic backgrounds, dates of symptom onset, clinical features, respiratory tract specimen results, hospitalization, contact tracing. We provide estimates of the reproduction number and serial interval. The epidemic in Italy started much earlier than February 20, 2020. At the time of detection of the first COVID-19 case, the epidemic had already spread in most municipalities of Southern-Lombardy. The median age for of cases is 69 years (range, 1 month to 101 years). 47% of positive subjects were hospitalized. Among these, 18% required intensive care. The mean serial interval is estimated to be 6.6 days (95% Cl, 0.7 to 19). We estimate the basic reproduction number at 3.1 (95% Cl, 2.9 to 3.2). We estimated a decreasing trend in the net reproduction number starting around February 20, 2020. We did not observe significantly different viral loads in nasal swabs between symptomatic. The transmission potential of COVID-19 is very high and the number of critical cases may become largely unsustainable for the healthcare system in a very short-time horizon. We observed a slight decrease of the reproduction number, possibly connected with an increased population awareness and early effect of interventions. Aggressive containment strategies are required to control COVID-19 spread and catastrophic outcomes for the healthcare system.

Subjects: Populations and Evolution (q-bio.PE)

Cite as: arXiv:2003.09320 [q-bio.PE] (or arXiv:2003.09320v1 [q-bio.PE] for this version)

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Search... All fields V Search Help | Advanced Search Download: PDF only (license) Current browse context: q-bio.PE next > < prev new | recent | 2003 Change to browse by: q-bio **References & Citations**  NASA ADS Google Scholar Semantic Scholar Export citation Bookmark 💥 💀 👾 Science WISE

We gratefully acknowledge support from

the Simons Foundation and member institutions

## Results

The epidemic in Italy started much earlier than February 20, 2020. At the time of detection of the first COVID-19 case, the epidemic had already spread in most municipalities of Southern-Lombardy. The median age for of cases is 69 years (range, 1 month to 101 years). 47% of positive subjects were hospitalized. Among these, 18% required intensive care. The mean serial interval is estimated to be 6.6 days (95% CI, 0.7 to 19). We estimate the basic reproduction number at 3.1 (95% CI, 2.9 to 3.2). We estimated a decreasing trend in the net reproduction number starting around February 20, 2020. We did not observe significantly different viral loads in nasal swabs between symptomatic and asymptomatic.

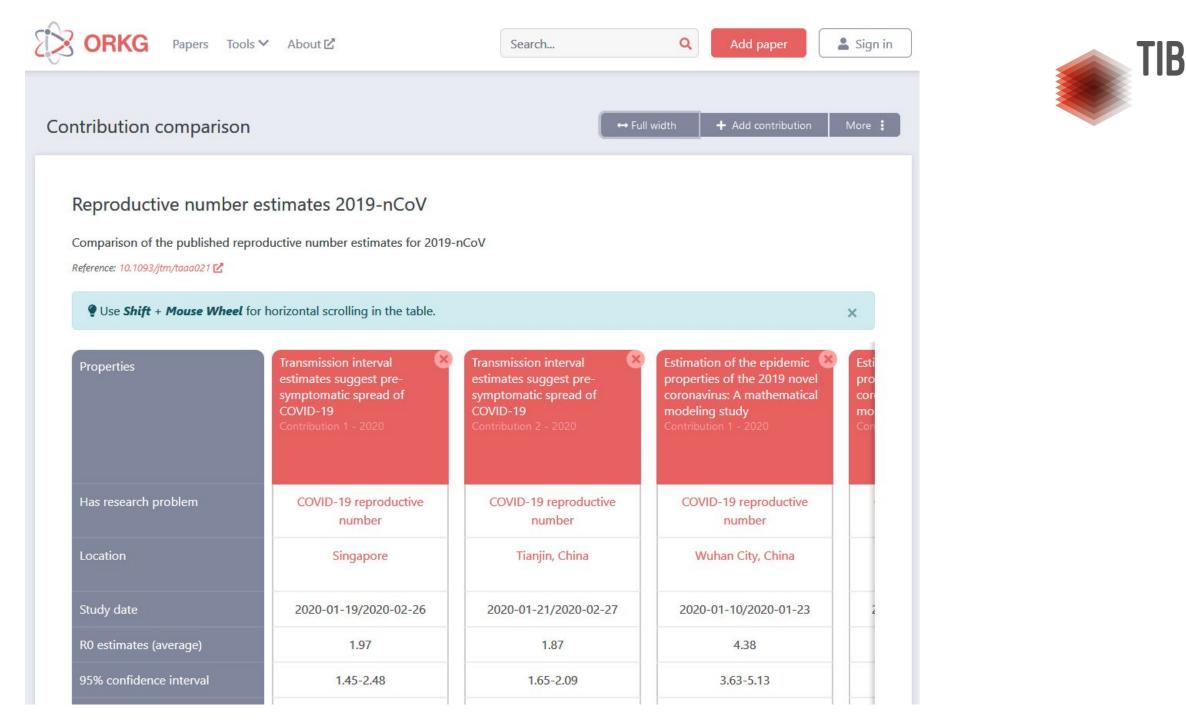
Here we provide an analysis of the first 5,830 laboratory-confirmed cases reported in Lombardy, with date of symptoms onset over the period from January 14 to March 8, 2020. Epidemiological analyses of the confirmed cases and their background demographic and exposure characteristics are presented here as well as the transmission dynamics of the infection within the Region. Also, the virological analysis on a subsample of the reported cases is included to provide preliminary assessment of the level of the viral load among symptomatic and asymptomatic cases.

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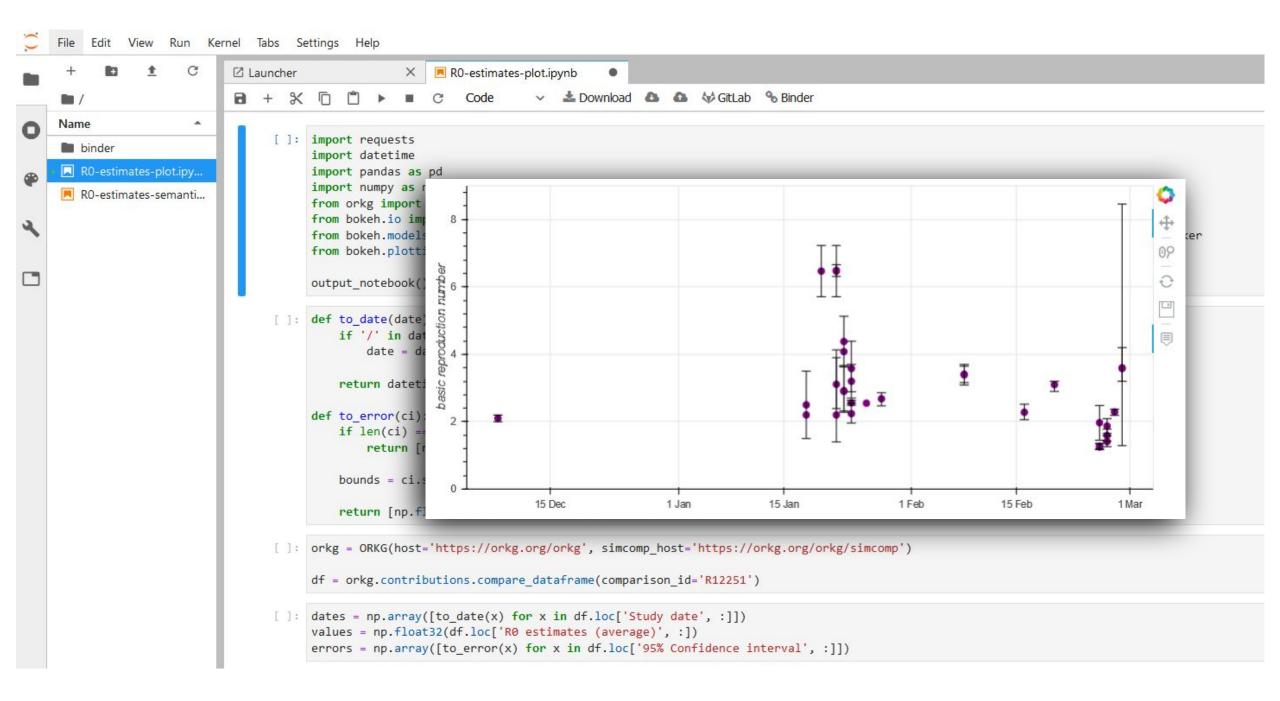
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🛔 Marziano 🔹 Barone A 🔒 M	agoni M 🔒 Deandrea S	💄 Diurno G	💄 Lombardo M	💄 Faccini M	🌲 Pan A	Bruno R		
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## Repeat for other papers, then ...



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Name 🔺	
binder	[]: import requests
R0-estimates-plot.ipy	import datetime import pandas as pd
R0-estimates-semanti	import numpy as np
Ko-estimates-semantian	from orkg import ORKG
	<pre>from bokeh.io import export_png from bokeh.models import ColumnDataSource, HoverTool, WheelZoomTool, ResetTool, SaveTool, PanTool, DatetimeTickFormatter, Whisker</pre>
	from bokeh.plotting import figure, show, output_notebook
	output_notebook()
	[]: def to_date(date):
	if '/' in date:
	<pre>date = date.split('/')[1]</pre>
	return datetime.date.fromisoformat(date)
	<pre>def to_error(ci):</pre>
	<pre>if len(ci) == 0:     return [on non non]</pre>
	return [np.nan, np.nan]
	<pre>bounds = ci.split('-')</pre>
	<pre>return [np.float32(bounds[0]), np.float32(bounds[1])]</pre>
	[]: orkg = ORKG(host='https://orkg.org/orkg', simcomp_host='https://orkg.org/orkg/simcomp')
	<pre>df = orkg.contributions.compare_dataframe(comparison_id='R12251')</pre>
	<pre>[]: dates = np.array([to_date(x) for x in df.loc['Study date', :]])</pre>
1	values = np.float32(df.loc['R0 estimates (average)', :])



## Take aways



- Scholarly work can be realized as expressions other than an article
- Content can also be realized so that it is more machine actionable
- Thus easier to reuse, for machines and people
- Turning the vision and prototypes into reality at scale is very challenging
- Advance scholarly communication from digitization to digitalization
- In addition to PDF publish essential scholarly knowledge also in structured form
- Requires a significant rethinking and rewiring of the current approaches and infrastructure