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# How openness is changing the impact of research

Deborah Kahn, Executive Vice President, BioMed  
Central

# What I will cover

- Openness in its many flavours and how it has extended impact
  - Open collaboration and crowdsourcing
  - Open research projects
  - Patient and public involvement in research
  - Open and collaborative peer review

1. On May 2, 2011 German doctors reported the first case of an E.coli infection, that was accompanied by hemolytic-uremic syndrome
2. On May 21, 2011 the first death occurred from this bacteria (denoted E.coli O104:H4)
3. On June 3, 2014, BGI completed a draft sequence of E.coli O104:H4 from a sample provided by doctors at the University Medical Centre Hamburg-Eppendorf
4. At this point- the question arose “If the data were released immediately, would it affect the researchers’ ability to publish later?”
5. The researchers decided public health was more important than obtaining a publication and released the data immediately.



# E. Coli #crowdsourcing: the first tweenome?

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What's happening?

Timeline @Mentions Retweets Searches Lists

**BGI\_Events** BGI Shenzhen  
We've uploaded the sequence of the new #EHEC strain to NCBI (SRA037315.1) & here: <ftp://ftp.genomics.org.cn> /pub/Ecoli\_TY-2482 #Ecoli  
2 Jun

**pathogenomenick** Nick Loman  
I've done a first pass assembly of the BGI Ion Torrent E. coli data with MIRA. N50 = 3675. <http://bit.ly/lXO60t>  
2 Jun

**marina\_manrique** Marina Manrique  
Era7 Bioinformatics annotates the E. coli strain of EU outbreak <http://bit.ly/k0lMjd> seq from @BGI\_Events assembly by @pathogenomenick #EHEC  
3 Jun

**NCBI** NCBI Staff  
NCBI's SRA database contains genome sequence reads of the strain suspected of causing the European E. coli outbreak: <http://1.usa.gov/kldix4>  
3 Jun

**BGI\_Events** BGI Shenzhen  
Crowdsourced #EHEC genome data is getting organised with @marina\_manrique Github repository <http://ow.ly/5af5p> & wiki <http://ow.ly/5af5j>  
5 Jun

Your Tweets 952  
10 hours ago: @phylogenomics (\*^.^\*)

Following 509 Followers 609

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**IrishCentral** IrishCentral Follow Promoted

**MPPjournal** Molecular Plant Path Follow Followed by @KamounLab and others.

**maroscarvalho** Marcos de Carvalho Follow Followed by @EdwardWinstead and others.

Trends · Worldwide · change

#hpveer Promoted  
#whenihadamspace  
#thanksjustin  
#dontlookatmeif  
LuanSnozzoNamorado  
Lemonade Mouth  
Last Friday Night



# E. Coli #crowdsourcing: the first tweenome?

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## E.coli O104:H4 Genome Analysis Crowdsourcing

New Page Edit Page Page History

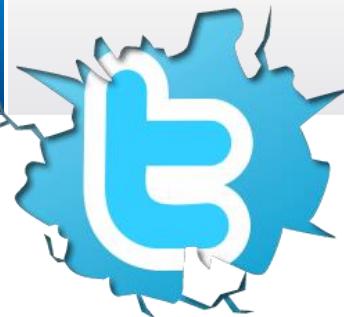
In this wiki we aim to gather all the results of the analysis of the *E. coli* O104:H4 strain responsible for the current outbreak in Germany and Europe.

NINE isolates from the outbreak have been sequenced so far:

- TY2482 (BGI in collaboration with University Medical Centre Hamburg-Eppendorf)
- LB226692 (Life Tech in-house in collaboration with University of Muenster)
- 5 isolates: H112180280 (released earlier with 454 scaffold) plus 4 additional isolates (Health Protection Agency, Colindale, UK)
- 2 isolates, unnamed (Göttingen Genomics Lab, Germany)

A historical O104:H4 ST678 isolate from 2001 has also been sequenced by Univ. Hospital Muenster and Life Tech but data not available.

### Sequence reads



# *E. Coli* #crowdsourcing: the first **tweenome**?



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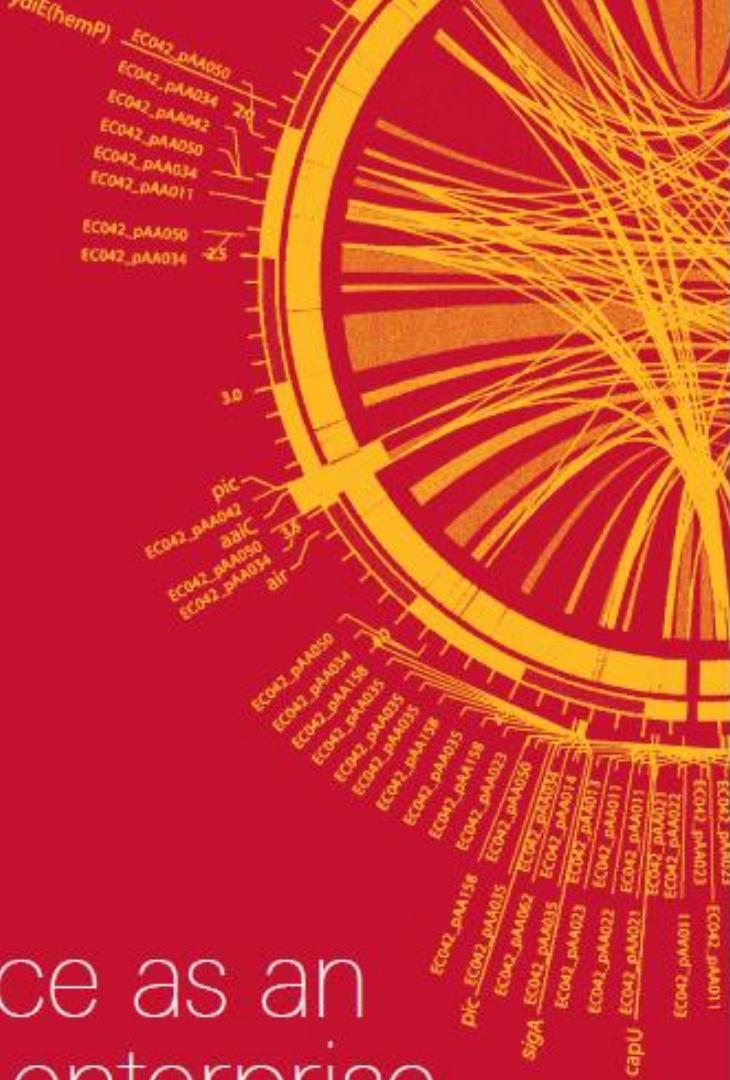
## Open-Source Genomic Analysis of Shiga-Toxin–Producing *E. coli* O104:H4

Holger Rohde, M.D., Junjie Qin, Ph.D., Yujun Cui, Ph.D., Dongfang Li, M.E., Nicholas J. Loman, M.B., B.S., Moritz Hentschke, M.D., Wentong Chen, B.S., Fei Pu, B.S., Yangqing Peng, B.S., Junhua Li, B.E., Feng Xi, B.E., Shenghui Li, B.S., Yin Li, B.S., Zhaoxi Zhang, B.S., Xianwei Yang, B.S., Meiru Zhao, M.S., Peng Wang, B.M., Yuanlin Guan, B.E., Zhong Cen, M.E., Xiangna Zhao, B.S., Martin Christner, M.D., Robin Kobbe, M.D., Sebastian Loos, M.D., Jun Oh, M.D., Liang Yang, Ph.D., Antoine Danchin, Ph.D., George F. Gao, Ph.D., Yajun Song, Ph.D., Yingrui Li, B.S., Huanming Yang, Ph.D., Jian Wang, Ph.D., Jianguo Xu, M.D., Ph.D., Mark J. Pallen, M.D., Ph.D., Jun Wang, Ph.D., Martin Aepfelbacher, M.D., Ruifu Yang, M.D., Ph.D., and the *E. coli* O104:H4 Genome Analysis Crowd-Sourcing Consortium

July 27, 2011 (10.1056/NEJMoa1107643)

# Science as an open enterprise

June 2012



## 1.3 The power of intelligently open data

The benefits of intelligently open data were powerfully illustrated by events following an outbreak of a severe gastro-intestinal infection in Hamburg in Germany in May 2011. This spread through several European countries and the US, affecting about 4000 people and resulting in over 50 deaths. All tested positive for an unusual and little-known Shiga-toxin-producing E. coli bacterium. The strain was initially analysed by scientists at BGI-Shenzhen in China, working together with those in Hamburg, and three days later a draft genome was released under an open data licence. This generated interest from bioinformaticians on four continents. 24 hours after the release of the genome it had been assembled. Within a week two dozen reports had been filed on an open-source site dedicated to the analysis of the strain. These analyses provided crucial information about the strain's virulence and resistance genes – how it spreads and which antibiotics are effective against it. They produced results in time to help contain the outbreak. By July 2011, scientists published papers based on this work. **By opening up their early sequencing results to international collaboration, researchers in Hamburg produced results that were quickly tested by a wide range of experts, used to produce new knowledge and ultimately to control a public health emergency.**

document should be submitted to

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T +44 20 7451 2500  
E science.policy@royalsociety.org  
W royalsociety.org

Cover image: *The Spanish Cucumber E. Coli*. In May 2011, there was an outbreak of a unusual Shiga-Toxin producing strain of *E. coli*, beginning in Hamburg in Germany. This has been dubbed the 'Spanish cucumber' outbreak because the bacteria were initially thought to have come from cucumbers produced in Spain. This figure compares the genome of the outbreak *E. coli* strain C227-11 (left side) and the genome of a similar *E. coli* strain 55989 (right semi-circle). The 55989 reference strain and other similar *E. coli* have had a few sporadic human cases but never large scale outbreak. The ribbons inside the track represent homologous mappings between the two genomes, indicating a high degree of similarity between these genomes. The lines show the chromosomal positioning of repeat elements such as insertion sequences and other mobile elements, which reveal some heterogeneity between the genomes. Section 1.3 explains how this genome was analysed within weeks because of a global and open effort; data about the strain's genome sequence were released over the internet as soon as they were produced. This figure is from Rohde H et al (2011). Open-Source Genomic Analysis of Shiga Producing *E. coli* O104:H4. New England Journal of Medicine, 365, 718-724. © New England Journal of Medicine.

# OpenAshDieBack

A hub for crowdsourcing information and genomic resources for Ash Dieback

[Ash dieback](#)[Crowdsourcing](#)[How to Help](#)[Analyses](#)[FAQ and Contact Us](#)

**A hub for finding and sharing genomics data on Ash and Ash Dieback**

# The problem

- Chalara dieback of ash is caused by an aggressive fungal pathogen which causes a range of symptoms and can be fatal for young saplings, secondarily infect mature trees ultimately killing or severely inhibiting their growth. In Denmark the infection of up to 90 % of the ash tree population has been attributed to ash dieback.
- The disease was first reported in Britain in 2012, and up to 90 % of the 80+ million ash trees in the UK are under threat.
- There is no known treatment, so in December 2012, the research group rapidly generated and released genomic sequence data through the website, <http://oadb.tsl.ac.uk>

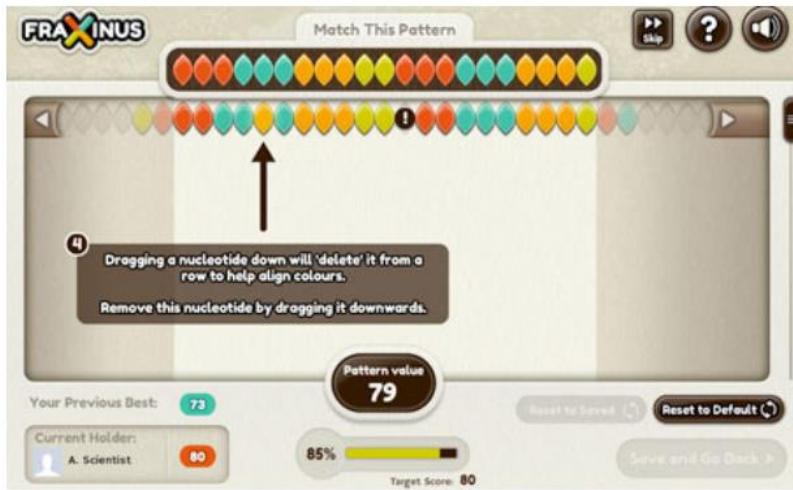
## Two sites were established

- OpenAshDieBack - a news and report hub
  - a friendly and intuitive website through which announcements of new datasets could be made and through which analyses could be presented.
- ash-dieback-crowdsource - an open access GitHub repository database
  - A public repository on the GitHub website set up to share data and make contributions clearly attributable to the provider

# And a Citizen Science project

## Facebook game Fraxinus targeted at beating ash dieback

Players who match on-screen patterns will be speeding the process of breeding trees resistant to the disease



In the Fraxinus app, players match sequences of coloured leaves, which represent strings of genetic information. Photograph: John Innes Centre/PA guardian.co.uk

Saving the ash forests of Britain from the devastation of an emerging fungal menace could actually be fun - if a computer game devised by botanists is a success.

Facebook enthusiasts will be able to log on from Tuesday and take part in one of the biggest experiments to harness computing and brain power to discover genetic variants that could help to counter ash dieback disease, caused by the fungus *Chalara fraxinea*. If thousands of people play the game, which involves



# Crowdsourced analysis of ash and ash dieback through the Open Ash Dieback project: A year 1 report on datasets and analyses contributed by a self-organising community.

Diane Saunders<sup>1</sup>, Kentaro Yoshida<sup>1</sup>, Christine Sambles<sup>2</sup>, Rachel Glover<sup>3</sup>, Bernardo Clavijo<sup>4</sup>, Manuel Corpas<sup>4</sup>, Daniel Bunting<sup>1</sup>, Suomeng Dong<sup>1</sup>, Ghanasyam Rallapalli<sup>1</sup>, Matthew D Clark<sup>4</sup>, David Swarbreck<sup>4</sup>, Sarah Ayling<sup>4</sup>, Matthew Bashton<sup>5</sup>, Steve Collin<sup>6</sup>, Tsuyoshi Hosoya<sup>7</sup>, Anne Edwards<sup>8</sup>, Lisa Crossman<sup>9</sup>, Graham Etherington<sup>1</sup>, Joe Win<sup>1</sup>, Liliana Cano<sup>1</sup>, David J Studholme<sup>2</sup>, J Allan Downie<sup>8</sup>, Mario Caccamo<sup>4</sup>, Sophien Kamoun<sup>1</sup>, and Dan MacLean<sup>1\*</sup>

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<sup>5</sup>Newcastle University, Newcastle upon Tyne, UK, NE1 7RU

<sup>6</sup>Norfolk Wildlife Trust, Foxley Wood, Norfolk, UK, NR20 4QR.

<sup>7</sup>National Museum of Nature and Science, Amakubo 4-1-1, Tsukuba, Ibaraki 305-0005, Japan

<sup>8</sup>The John Innes Centre, Norwich Research Park, Norwich, UK, NR4 7UH

<sup>9</sup>SequenceAnalysis.co.uk, Norwich Research Park, Norwich, UK, NR4 7UH

\*To whom correspondence should be sent

August 4, 2014

## Abstract

Ash dieback is a fungal disease of ash trees caused by *Hymenoscyphus pseudoalbidus* that has swept across Europe in the last two decades and is a significant threat to the ash population. This emergent pathogen has been relatively poorly studied and little is known about its genetic make-up. In response to the arrival of this dangerous pathogen in the UK we took the unusual step of providing an open access database and initial sequence datasets to the scientific community for analysis prior to performing an analysis of our own. Our goal was to crowdsource genomic and other analyses and create a community analysing this pathogen. In this report on the evolution of the community and data and analysis obtained in the first year of this activity, we describe the nature and the volume of the contributions and reveal some preliminary insights into the genome and biology of *H. pseudoalbidus* that emerged. In particular our nascent community generated a first-pass genome assembly containing abundant collapsed AT-rich repeats indicating a typically complex genome structure. Our open science and crowdsourcing effort has brought a wealth of new knowledge about this emergent pathogen within a short time-frame. Our community endeavour highlights the positive impact that open, collaborative approaches can have on fast, responsive modern science.

“Our open science and crowdsourcing effort has brought a wealth of new knowledge about this emergent pathogen within a short time-frame. Our community endeavour highlights the positive impact that open, collaborative approaches can have on fast, responsive modern science.”

# Open source research

SEE ACTIVITY JOIN THE TEAM MEET THE TEAM

**OPEN SOURCE MALARIA**  
Looking for New Medicines

The Open Source Malaria project is trying a different approach to curing malaria. Guided by open source principles, everything is open and anyone can contribute. [About](#)

**Project Activity**

See More

15 Nov 2014 at 23:31 | Next Open Meeting - November 24th - Assemble Agendas  
Next open meeting time: November 24th, 8:30 a.m. UK time. Corresponding times elsewhere:  
[Meeting location: <http://webconf.ucc.usyd.edu/uosm24thNov14/> Agendas will be assembled in outline below. Detailed version will go on ELN here: \[http://malaria.oxfuses.org/ossdmalaria\\\_meeting\\\_1120s\]\(http://malaria.oxfuses.org/ossdmalaria\_meeting\_1120s\). Either edit this entry or add comment below for other things you'd like to discuss. 1. Previous Action Items a\) Chemistry b\) Biology 2. New Developments a\) Chemistry b\) Biology c\) New sources of project inputs. \(3. What else?\) 3 comments](http://www.timeanddate.com/worldclock/meetingdetails.html?year=2014&month=11&day=24&hour=8&min=30&sec=0&label=1244&pct=179&str=1233&pct=487&pst=16&dst=240&n=1800)

18 Nov 2014 at 07:21 | Characterisation of Compounds  
Mackenzie Shaw recently asked about characterisation of the 950 compounds on Twitter. I was wondering if we could do some characterisation of some of the compounds. [@all\\_seee](https://twitter.com/all_seee) @willat343  
[@O\\_S\\_M](https://twitter.com/O_S_M)  
[@JasonCham](https://twitter.com/JasonCham)  
[@onzy73](https://twitter.com/onzy73)  
[@EvanHockings](https://twitter.com/EvanHockings) — Mackenzie Shaw (@mact\_is\_back\_7)  
[https://twitter.com/mact\\_is\\_back\\_7/status/531123938360889344](https://twitter.com/mact_is_back_7/status/531123938360889344) November 14, 2014

It has taken me a couple of days to speak everyone but I have some great news. If you guys would like to help me with this project I would be more than happy to have you come over and show you how to use the NMR. If we can fit this in then you guys could come over otherwise I'll run your samples for you and make a video to show you how everything works. We also need to run IR and MS samples and that will also be grand. Just need to work out timing with Dr. Walls and Dr. Sheridan. 2 comments

See More

Twitter Activity

@BioRadLifeSci  
@BNTD\_Press Please add 'Take part in an open source project' to Q3...  
27 Nov 2014 at 21:17

@TrentWalls:  
@ChemistryBinn @O\_S\_M  
Malaria Box (last remaining hydrazine)  
#RealTimeChem  
<http://it.co/DLPRhnyDV>  
26 Nov 2014 at 08:00

@cdsouthern Definitely...  
Detailed list of stuff coming in next few days. Thanks, Chris.  
24 Nov 2014 at 11:38

RT @MattTodo: Any chemists have similar snafu with Chem3Dwrs CLogP prediction?  
<http://colinkin2Nebo> immune open alternative?  
<http://it...>  
24 Nov 2014 at 11:09

@cdsouthern Boo! Will share recording and you see what's what. Good meeting, and well be having them more often.  
24 Nov 2014 at 09:44

Many thanks to our friends and supporters



**Sage** BIONETWORKS

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## About us

We are redefining biomedical research through open systems, incentives, and norms.

At Sage Bionetworks, we work to redefine how complex biological data is gathered, shared and used. We

Catalysing neglected disease drug discovery

# THE PATHOGEN BOX

## The Pathogen Box project

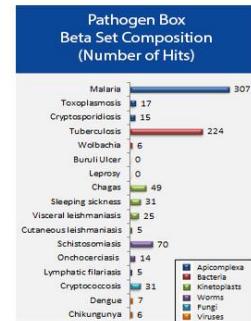
Modeled after the Malaria Box, the Pathogen Box will contain ~400 diverse, drug-like molecules active against neglected diseases of interest and will be available free of charge at the end of 2015. Upon request, researchers around the world will receive a Pathogen Box of molecules to help catalyse neglected disease drug discovery. In return, researchers are asked to share any data generated in the public domain within 2 years, creating an open and collaborative forum for neglected diseases drug research.

## What's happening with the Pathogen Box

The European Bioinformatics Institute's open access database, (ChEMBL17) was analyzed and triaged to identify active chemotypes against the diseases of interest. In parallel partners from many disease areas were approached to share their expertise and contribute quality hit molecules or screening platforms. This effort has led to an initial list of 819 diverse chemotypes.

In June 2014, a Scientific Selection Committee (see below) composed of leading figures in medicinal chemistry reviewed the initial set of compounds to select 635 chemotypes termed as the "beta-set".

These compounds are now being procured or synthesized for confirmatory screening.



# Patient and public involvement in research

- Research '**by**' and '**with**', rather than research '**about**', '**to**' or '**for**' patients, carers and the public:
- Working with patients and the public to make sure that what is being done is relevant to their needs, appropriate and effective.
- Making sure the research is asking the right questions and using the right processes.
- This concept is now embedded in the work of key organisations:



# RESEARCH INVOLVEMENT AND ENGAGEMENT

- Research Involvement and Engagement is an international, interdisciplinary, health and social care journal focussing on patient and wider involvement and engagement in research, at all stages. **The journal is co-produced by all key stakeholders, including patients, academics, policy makers and service users.**

# The aims of the journal

- Develop our understanding of the concept, theory and methods of involvement and engagement in research.
- Highlight good examples and benchmark standards.
- Encourage innovation and allow for comparisons between different methods.
- Establish a strong evidence base for the benefits of public involvement.
- Harness an active and involved community, to drive and encourage co-production of knowledge.
- Improve and expand patient and public involvement, including greater collaboration across all health and social care.

# Co-produced by all key stakeholders

- RIE co-produces the journal, involving academics, policy-makers, patients and service users, with a unique governance structure:
- Co-Editors-in-Chief – one academic (Sophie) and one patient (Richard)
- The Editorial Board who control the direction and strategy of the journal is representative of all key groups
- Unlike a traditional journal, all articles will be reviewed by at least one academic referee and one patient/public referee, with the reviews given equal weight in deciding eventual publication.



# THE ASSEMBLATHON

About



## Feedback and analysis of the Assemblathon 2 pre-print and published paper

There has already been some discussion of the [pre-print](#) of the Assemblathon 2 manuscript. Although a pre-print is not the same thing as a peer-reviewed, accepted paper — I don't want us to get too ahead of ourselves! — I thought it useful to start collecting together some of the online commentaries:

- [Homolog.us blog post 1](#): highlights a few conclusions from the paper
- [Homolog.us blog post 2](#): delves into the results, and attempts to estimate some of the costs of genome assembly. Assemblathon co-author Sébastien Boisvert adds some useful comments.
- [Haldane's Steve post](#): an invited blog post by lead author Keith Bradnam, that summarizes what the Assemblathons are all about by way of a pizza-themed analogy
- [Reevaluating Assembly Evaluations with Feature Response Curves: GAGE and Assemblathons](#): this is not a blog post, but a recently published paper that evaluates some of the Assemblathon 2 data
- [Thoughts on the Assemblathon 2 paper](#): by C. Titus Brown (a reviewer of the manuscript)
- [Homolog.us blog post 3](#): reactions to the previous post by C. Titus Brown
- [Assemblathon 2 review, round 1, parts thereof](#): a concise version of C. Titus Brown's formal manuscript review (minus the specific suggestions)
- [On assembly uncertainty \(Inspired by the Assemblathon 2 debate\)](#): blog post by Lex Nederbragt in response to post by C. Titus Brown

Since the paper was [officially published](#) (22nd July, 2013) there has been several commentaries about the paper and about the open nature of the writing and peer review process:

- [Genome assembly contest prompts soul-searching](#): commentary on the official publication of the paper on Nature's News blog
- [Homolog.us blog post 4](#): Two Important Papers Published – Assemblathon and First Genome using Molecule
- [Genome assembly in the spotlight](#): press release by BioMed Central
- [Unusual 'meta' peer review](#): A video of GigaScience Editor-in-chief, Laurie Goodman, discussing the open nature of the peer-review process.
- [Ultra-Open Peer Review](#): A blog post by Laurie Goodman writing about the issues discussed in the video of the previous link.
- [Genome assembly in the spotlight](#): a blog post that expands on the press release (mentioned above).
- [Writing the Assemblathon 2 paper, an experiment in openness](#): another post from this blog about the whole experience of writing, and reviewing, the paper.
- [Mining Altmetric Data To Discover What Types Of Research Article Get The Most Social Media Engagement](#): a personal blog post by me (Keith Bradnam) about the impact of both Assemblathon papers as assessed by chatter on social media sites.
- [Assemblathon 2 Results Highlight Emphases, Challenges of De Novo Genome Assembly Algorithms](#): a long piece by Uduak Grace Thomas at GenomeWeb that discusses the paper and interviews me (Keith Bradnam) and one of the reviewers (Mick Watson). A (free) account is needed with GenomeWeb to view this article.
- [Exploring Genome Characteristics and Sequence Quality Without a Reference](#): a new pre-print in *arXiv.org* by Jared Simpson. The Acknowledgements include the following: *The project was motivated in part by online discussion of the Assemblathon 2 paper centered on a blog post by Titus Brown*.

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## Research

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### Assemblathon 2: evaluating *de novo* methods of genome assembly in three vertebrate species

Keith R Bradnam<sup>\*†</sup>, Joseph N Fass<sup>†</sup>, Anton Alexandrov, Paul Baranay, Michael Bechner, Inanç Birol, Sébastien Boisvert, Jarrod A Chapman, Guillaume Chapuis, Rayan Chikhi, Hamidreza Chitsaz, Wen-Chi Chou, Jacques Corbeil, Cristian Del Fabbro, T Roderick Docking, Richard Durbin, Dent Earl, Scott Emrich, Pavel Fedotov, Nuno A Fonseca, Ganeshkumar Ganapathy, Richard A Gibbs, Sante Gnerre, Élénie Godzardis, Steve Goldstein, Matthias Haimel, Giles Hall, David Haussler, Joseph B Hiatt, Isaac Y Ho, Jason Howard, Martin Hunt, Shaun D Jackman, David B Jaffe, Erich D Jarvis, Huaiyang Jiang, Sergey Kazakov, Paul J Kersey, Jacob O Kitzman, James R Knight, Sergey Koren, Tak-Wah Lam, Dominique Lavenier, François Laviolette, Yingrui Li, Zhenyu Li, Binghang Liu, Yue Liu, Ruibang Luo, Iain MacCallum, Matthew D MacManes, Nicolas Maillet, Sergey Melnikov, Delphine Naquin, Zemin Ning, Thomas D Otto, Benedict Paten, Octávio S Paulo, Adam M Phillippy, Francisco Pina-Martins, Michael Place, Dariusz Przybyski, Xiang Qin, Carson Qu, Filipe J Ribeiro, Stephen Richards, Daniel S Rokhsar, J Graham Ruby, Simone Scalabrin, Michael C Schatz, David C Schwartz, Alexey Sergushichev, Ted Sharpe, Timothy I Shaw, Jay Shendure, Yujian Shi, Jared T Simpson, Henry Song, Fedor Tsarev, Francesco Vezzi, Riccardo Vicedomini, Bruno M Vieira, Jun Wang, Kim C Worley, Shuangye Yin, Siu-Ming Yiu, Jianying Yuan, Guojie Zhang, Hao Zhang, Shiguo Zhou and Ian F Korf<sup>\*</sup>

\* Corresponding authors: Keith R Bradnam krbradnam@ucdavis.edu - Ian F Korf ifkorf@ucdavis.edu

† Equal contributors

GigaScience 2013, 2:10 doi:10.1186/2047-217X-2-10

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Last 365 days: 24584 accesses

All time: 34022 accesses

These numbers are accesses on BioMed Central websites only, and an underestimate of total usage. More information

## Cited by

# Conclusions

Openness is changing the way research is done. It is speeding up the process, it is allowing new collaborations and allowing people to get involved who previously would not have had the chance. This is all showing real benefits in public health and many other important areas.