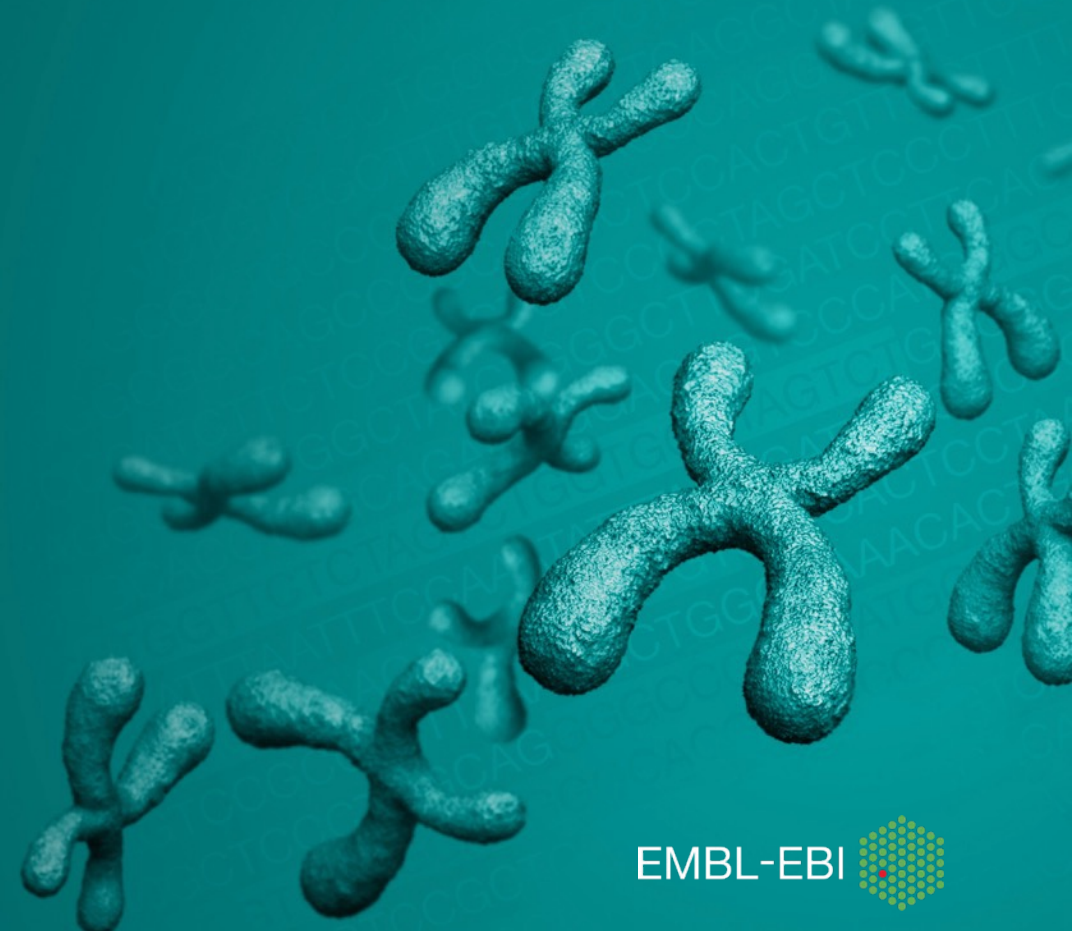


Management of digital sequence information

Guy Cochrane



CCTAACCAAGTACTACTTAAAATCAGTAAACTGCCACTCCCTCCCCACTACCCTATATGA
AAATAATTAAAAAGCTCCTACGCTTCTTTTTTTGACCGCCCTCTACCTCTTTTCACAAA
GGCTATCAACTCGAATTTTCTATTGCTTTATTTTATCAAAAAAACATAAAAATTTTGT
ATCAAAAAATATCATTCAAGAGGGGGGGATTTTCACCCCACCGCCGGCACCAAAGCCAA
AATTCTTGGAATCAAACCTACCTCTTGTCCTGGTTTTCTAATGTACGAGTAACGTGGCAA
CATATTATGCCTATCGTGCATCCAACCTATCTGCCACACGACTATTTTTTAGTACTCTTCG
GAGTGTAAGCCGAACACTTAGGGCGAGAAACCACCAACCCGCTCCTGACGATACGATGAC
CAGATCTGAGGACTTTTATTGTAGAGTGCCTTACTTCCCTTGAGGCGCCACTGGTTAAAA
TCTATGGACACGACTCGAAGATTCATTCATCAATTGGATCGAACGGGTACCTGGCGGCTG
CTTGATAACTAATCAGCCCATGATCCCTCAGCCTCCTCTAAGCACATCTGGTAATTTTTT
ATTTTTCTGTGTGGTCAACCAACATTACGGTAATATGTCTGGTACTACACGATCTAAAGC
TGAACATAACATGCAATTGTTTTATTTGGACCAAATAGAATGAGTAAATTATATGAATGA
TTAT

A sequence in isolation...

```
CCTAACCAAGTACTACTTAAAATCAGTAAACTGCCACTCCCTCCCCACTACCCTATATGA
AAATAATTAAAAAAGCTCCTACGCTTCTTTTTTTGACCGCCCTCTACCTCTTTTCACAAA
GGCTATCAACTCGAATTTTCTATTGCTTTATTTTATCAAAAAAACATAAAAATTTTGT
ATCAAAAAATATCATTCAAGAGGGGGGGATTTTCACCCCCACCGCCGGCACCAAAGCCAA
AATTCTTGGAATCAAACCTACCTCTTGTCCTGGTTTTTCCTAATGTACGAGTAACGTGGCAA
CATATTATGCCTATCGTGCATCCAACCTATCTGCCACACGACTATTTTTTAGTACTCTTCG
GAGTGTAAGCCGAACACTTAGGGCGAGAAACCACCAACCCGCTCCTGACGATACGATGAC
CAGATCTGAGGACTTTTATTGTAGAGTGCCTTACTTCCCTTGAGGCGCCACTGGTTAAAA
TCTATGGACACGACTCGAAGATTCATTCATCAATTGGATCGAACGGGTACCTGGCGGCTG
CTTGATAACTAATCAGCCCATGATCCCTCAGCCTCCTCTAAGCACATCTGGTAATTTTTT
ATTTTTCTGTGTGGTCAACCAACATTACGGTAATATGTCTGGTACTACACGATCTAAAGC
TGAACATAACATGCAATTGTTTTATTTGGACCAAATAGAATGAGTAAATTATATGAATGA
TTAT
```

.. cannot be interpreted

.. is unlikely to be informative

<https://www.ebi.ac.uk/ena/browser/view/HM544578.1>

A collection of sequences..

260 million sequences



.. can be interpreted

.. drives discovery

International Nucleotide Sequence Database Collaboration (INSDC)



Values

- open access for all
- globally comprehensive
- spanning life science domains
- permanent database of record
- public forum for the scientific process



<http://www.insdc.org/>

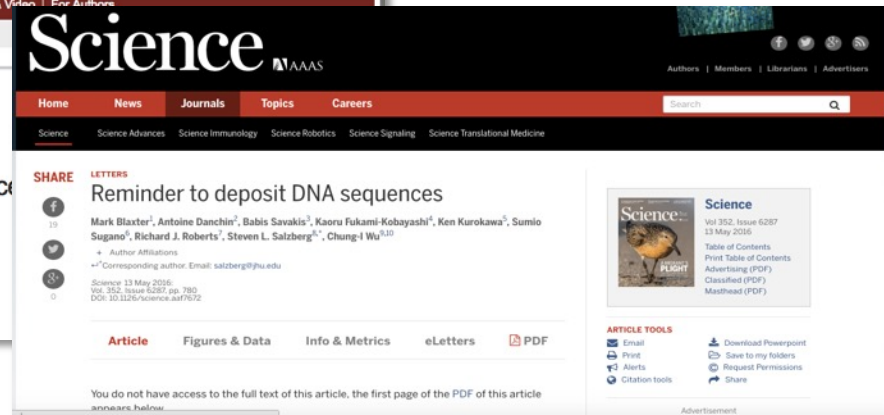
Organisation

- established early 1980s
- major ongoing investment
- structure and governance
- model for scientific collaboration



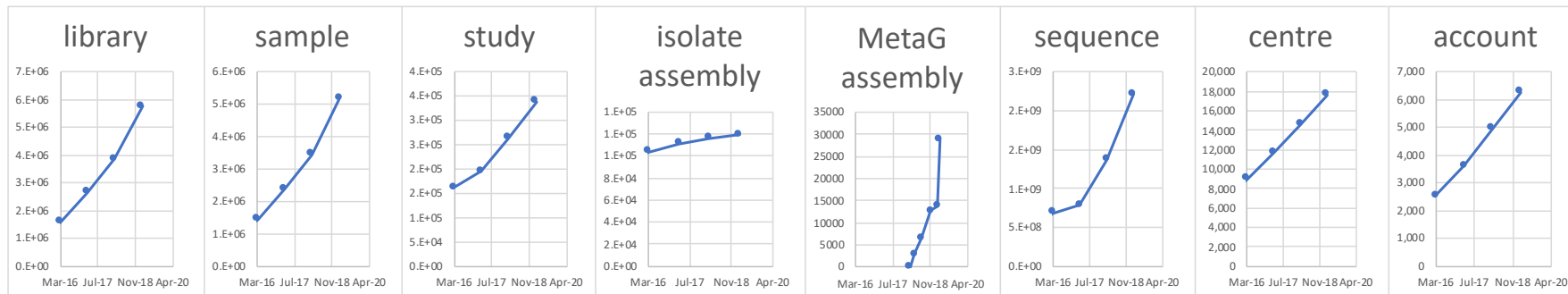
Instruments

- regular data exchange
- accession scheme
- data standards
- mandatory submission agreement
- services and software (node-level)



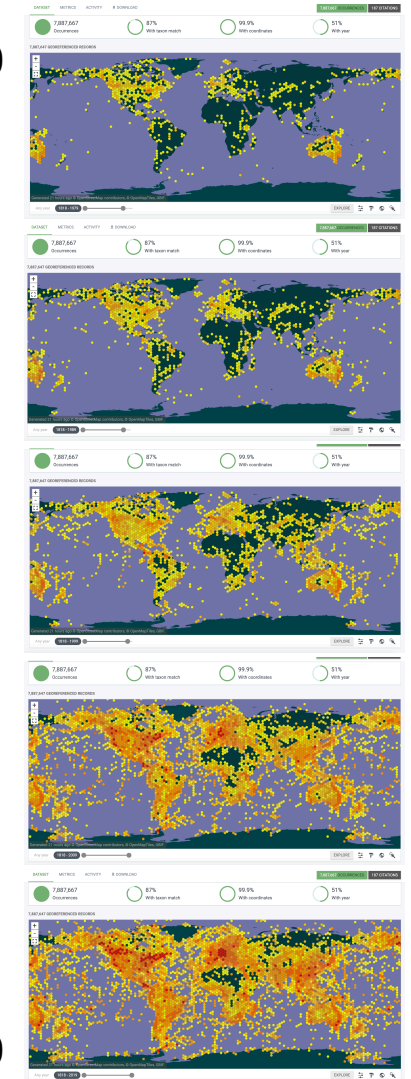
Scale

- **Rate:** 1 new dataset every 6 minutes
- **Data:** 2×10^9 sequences and 1×10^{16} base pairs of read data across 2×10^6 taxa
- **Usage:** 2,000 submitters; 10x thousands monthly consumers; 10x millions of monthly hits, many times this globally
- **Support:** 46 tickets per day and in-person training delivered to more than 350 users per annum
- **Infrastructure:** includes 100s of petabytes of storage, ~\$50 USD mil./year
- **Growth:**



- **E.G. biodiversity data**
 - 7.2 million records point to natural history museums, culture collections and biobanks
 - 7.9 million sequences with geographical coordinates
 - 2.1 million sequences have place name annotation
 - 1 million raw sequencing data sets have coordinates

1980

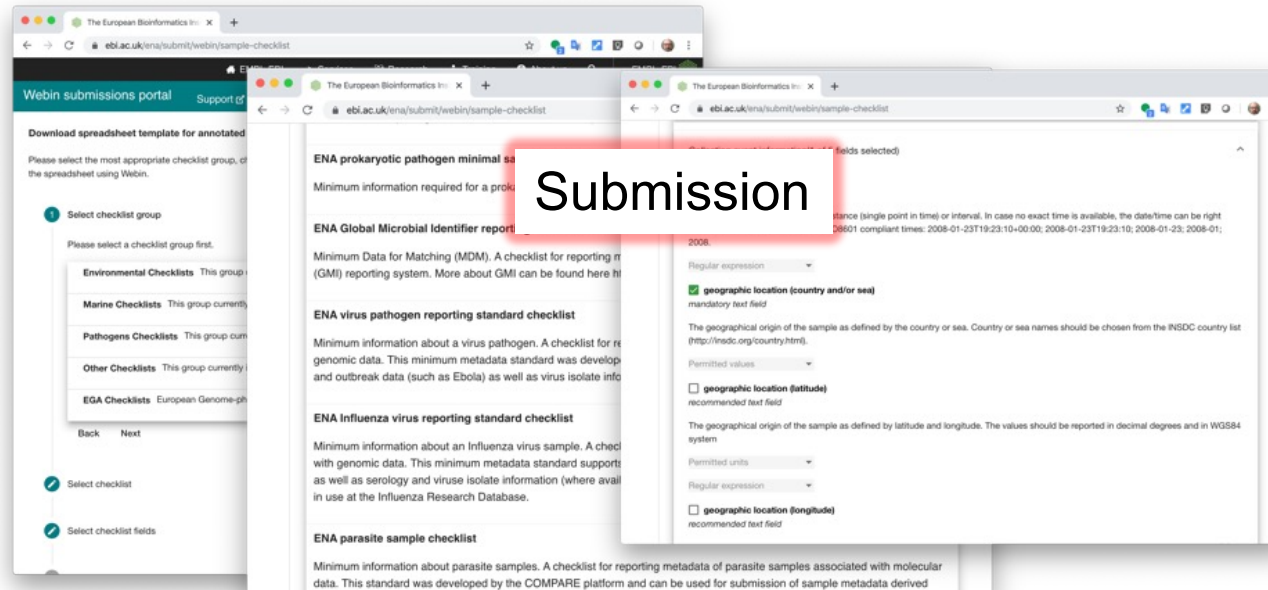
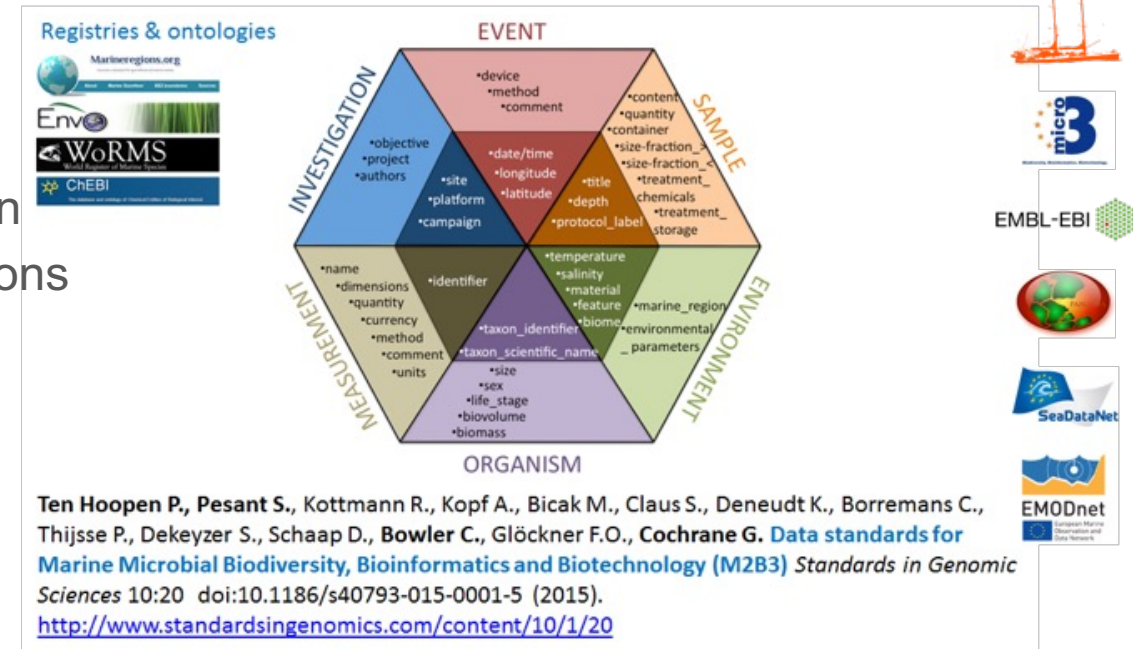


2020

<https://doi.org/10.15468/cndomy>,
courtesy of GBIF

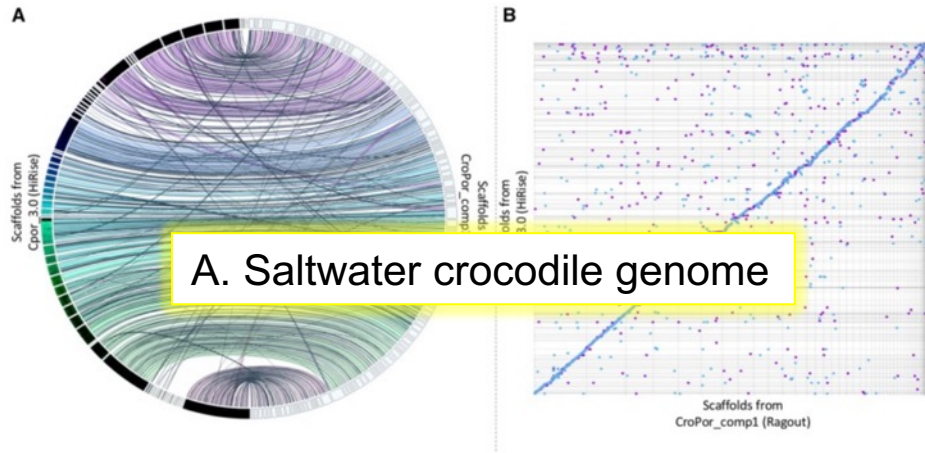
The INSDC data cycle

- Data provider
 - Validation, organization, adding structure and curation
 - Compliance with standards and established conventions
 - Links to external data (e.g. academic publications)
- Database
 - Curation and integration with the overall corpus
 - Indexing for discovery and reuse
 - Open services, freely available to the world

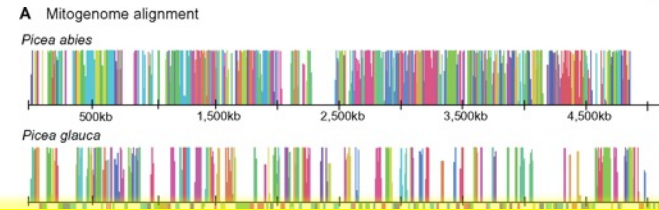


Direct use

- 1,600 publications citing sequence accessions per month in 2020

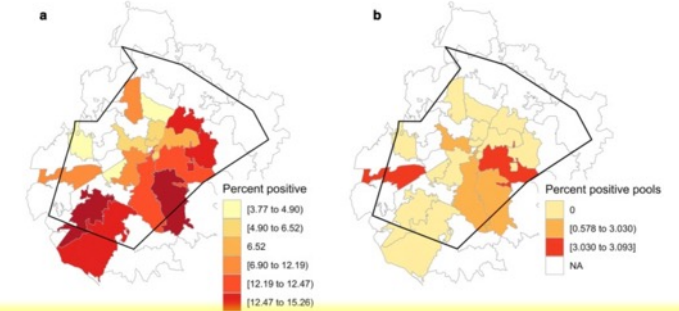
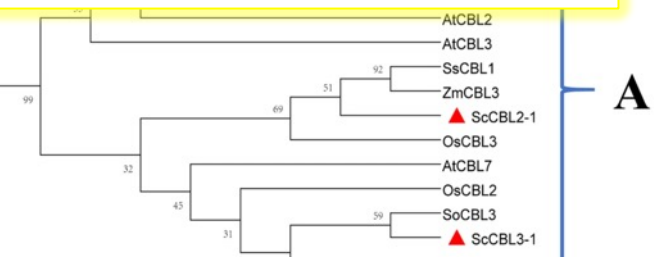


A. Saltwater crocodile genome



B. Norway spruce evolutionary biology

C. Stress response in sugarcane



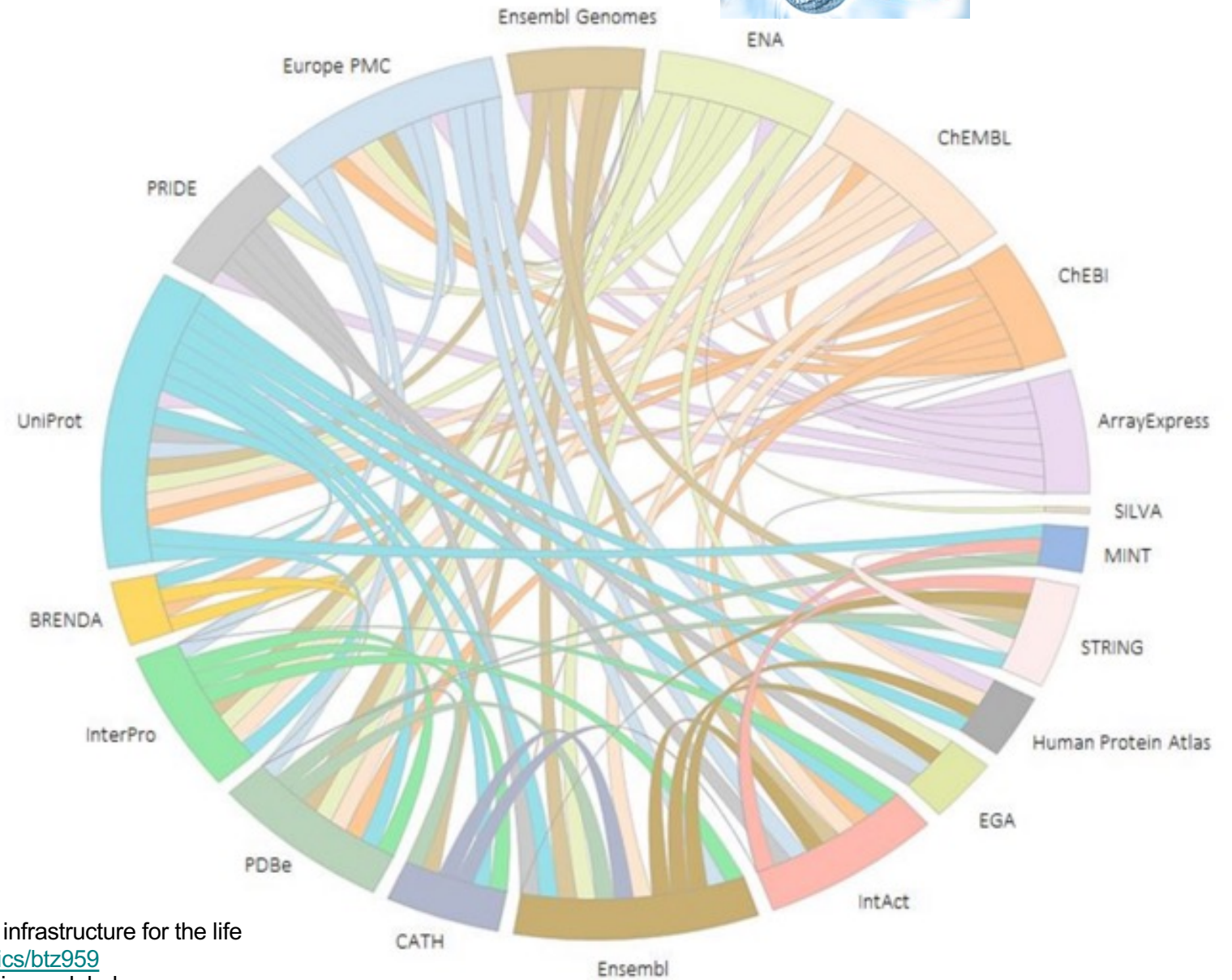
E. Mosquito-borne heartworm in dogs

- A. Ghosh A et al., Genome Biol Evol. 2020 Jan;12(1) 3635-3646. doi:10.1093/gbe/evz269. PMID: 31821505; © The Author(s) 2020; <http://creativecommons.org/licenses/by/4.0/>
- B. Sullivan AR et al., Genome Biol Evol. 2020 Jan;12(1) 3586-3598. doi:10.1093/gbe/evz263. PMID: 31774499; © The Author(s) 2020; <http://creativecommons.org/licenses/by-nc/4.0/>
- C. Su W et al., Sci Rep. 2020 Jan;10(1) 167. doi:10.1038/s41598-019-57058-7. PMID: 31932662; <http://creativecommons.org/licenses/by/4.0/>
- D. Saeed AM et al., Curr Microbiol. 2020 Jan. doi:10.1007/s00284-020-01874-y. PMID: 31925514.
- E. Spence Beaulieu MR et al., Parasit Vectors. 2020 Jan;13(1) 12. doi:10.1186/s13071-019-3874-0. PMID: 31924253; PMCID: PMC6953185. <http://creativecommons.org/licenses/by/4.0/>; <http://creativecommons.org/publicdomain/zero/1.0/>

Data reach



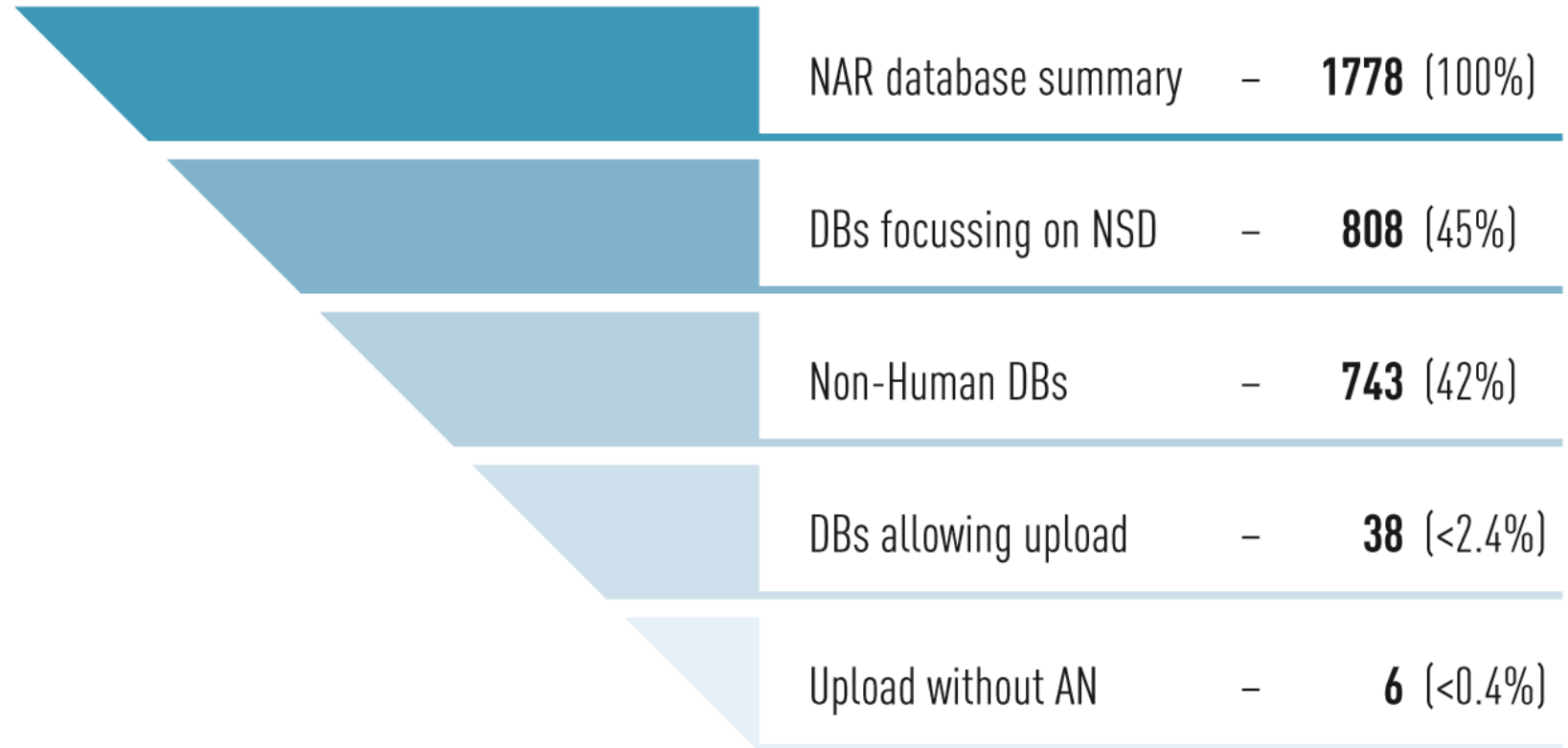
Drysdale *et al.* (2020) The ELIXIR Core Data Resources: fundamental infrastructure for the life sciences. *Bioinformatics*, 2020, 1–7; <http://doi.org/10.1093/bioinformatics/btz959>
Cook *et al.* (2020) The European Bioinformatics Institute in 2020: building a global infrastructure of interconnected data resources for the life sciences. *Nucleic Acids Research* 48:D17-D23; <http://doi.org/10.1093/nar/gkz1033>



Further reach



Public database inventory



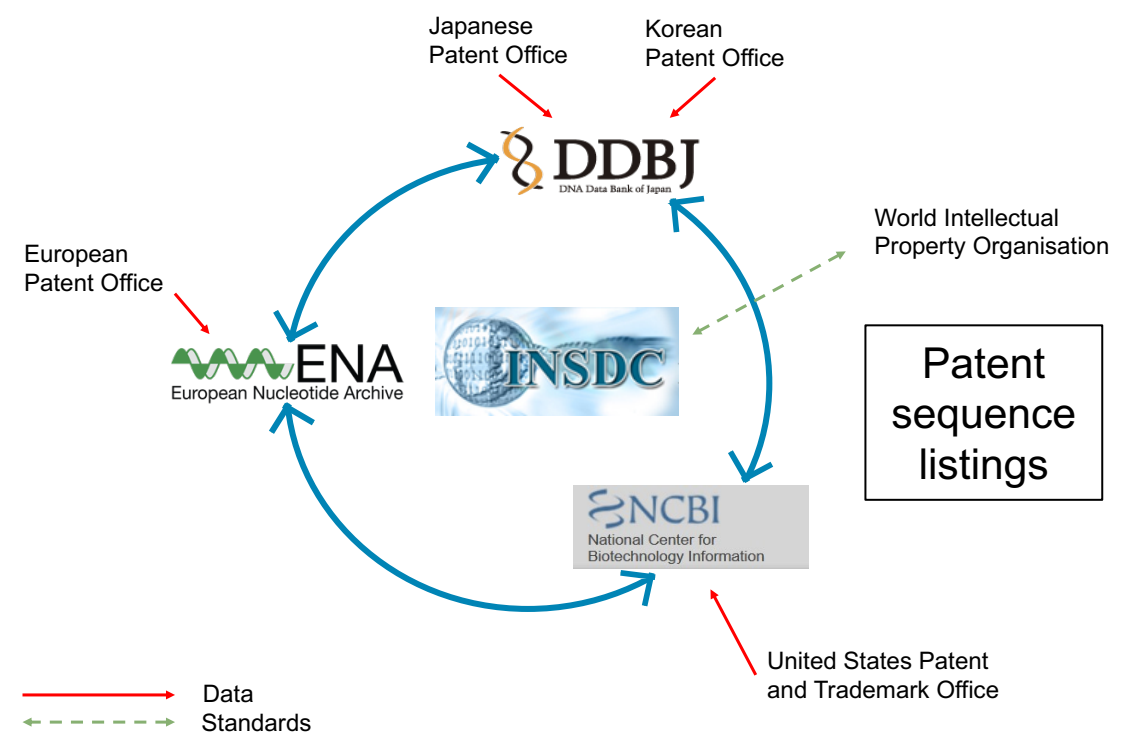
Rohden F, Huang S, Dröge G, Hartman Scholz A, and contributing authors (2019). Combined study in DSI in public and private databases and DSI traceability. <https://www.cbd.int/abs/DSI-peer/Study-Traceability-databases.pdf>

Terms of use

Data Services

1. The online data services and databases of EMBL-EBI are generated in part from data contributed by the community who remain the data owners.
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<https://www.ebi.ac.uk/about/terms-of-use>



Project type	Prepublication data release recommended	Prepublication data release optional
Genome sequencing	Whole-genome or mRNA sequence(s) of a reference organism or tissue	Sequences from a few loci for cross-species comparisons in a limited number of samples
Polymorphism discovery	Catalogue of variants from genomic and/or transcriptomic samples in one or more populations	Variants in a gene, a gene family or a genomic region in selected pedigrees or populations
Genetic association studies	Genomewide association analysis of thousands of samples	Genotyping of selected gene candidates
Somatic mutation discovery	Catalogue of somatic mutations in exomes or genomes of tumour and non-tumour samples	Somatic mutations of a specific locus or limited set of genomic regions
Microbiome studies	Whole-genome sequence of microbial	Sequencing of target locus in a limited number of samples
RNA profiling	Large-scale screen of a cell line or organism analysed for standard phenotypes	Expression profiles of a specific gene or set of genes
Proteomic studies	Mass spectrometry data sets from large panels of normal and disease tissues	Mass spectrometry data sets from a well-defined and limited set of tissues
Metabolomic studies	Catalogue of metabolites in one or more tissues of an organism	Analyses of metabolites induced in a perturbed biological system(s)
RNAi or chemical library screen	Large-scale screen of a cell line or organism analysed for standard phenotypes	Focused screens used to validate a hypothetical gene network
3D-structure elucidation	Large-scale cataloguing of 3D structures of proteins or compounds	3D structure of a synthetic protein or compound elucidated in the context of a focused project

Toronto Principles

ABS-related obligations in existing agreements

Nature volume 461, pages168–170(2009)

COVID-19 open data

Viral Sequences Host Sequences Expression Proteins Biochemistry Literature

All (262,317)

Sequences (27,649)

Raw reads (125,159)

Sequenced samples
(96,632)

Studies (163)

Genes (22)

Browser (1)

Variants (12,691)

All (1,046)

Human studies

(controlled access) (4)

Human reads (consented
for full access) (784)

Other species reads
(250)

Association studies (8)

All (82)

Gene expression (4)

Gene expression

experiments (23)

Single cell expression (4)

Single cell expression
experiments (19)

Protein expression

experiments (32)

All (712)

Protein sequences (57)

Protein families (126)

Protein structures -

Knowledge Base (7)

Protein structures (260)

Electron microscopy

density maps (250)

Electron microscopy

public image archive (12)

All (2,255)

Pathways (16)

Interactions (1,812)

Complexes (29)

Compound document (8)

Drug targets (390)

All (212,276)

Coronaviruses (109,172)

Diseases (96,222)

Related viruses and

diseases (2,109)

Genes, receptors and
antibodies (4,773)

PF-0702048 (BNT162 RNA-Based COVID-19 Vaccines)
Protocol C4591001



A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND,
DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY,
IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE
CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS

Study Sponsor: BioNTech
Study Conducted By: Pfizer
Study Intervention Number: PF-0702048
Study Intervention Name: RNA-Based COVID-19 Vaccines
US IND Number: 19736

<https://www.covid19dataportal.org/>

2.2. Background

In December 2019, a pneumonia outbreak of unknown cause occurred in Wuhan, China. In January 2020, it became clear that a novel coronavirus (2019-nCoV) was the underlying cause. Later in January, the genetic sequence of the 2019-nCoV became available to the World Health Organization (WHO) and public ([MN908947.3](https://www.gISAAC.org/entry/MN908947.3)), and the virus was categorized in the *Betacoronavirus* subfamily. By sequence analysis, the phylogenetic tree revealed a closer relationship to severe acute respiratory syndrome (SARS) virus isolates than to another coronavirus infecting humans, the Middle East respiratory syndrome (MERS) virus.

https://pfe-pfizercom-d8-prod.s3.amazonaws.com/2020-11/C4591001_Clinical_Protocol_Nov2020.pdf

SARS-CoV-2
Genome submitted



Launch of COVID-19
Data platform

ENA
EMDB
EPMC
Expression Atlas
InterPro
PDB
PRIDE
UniProt

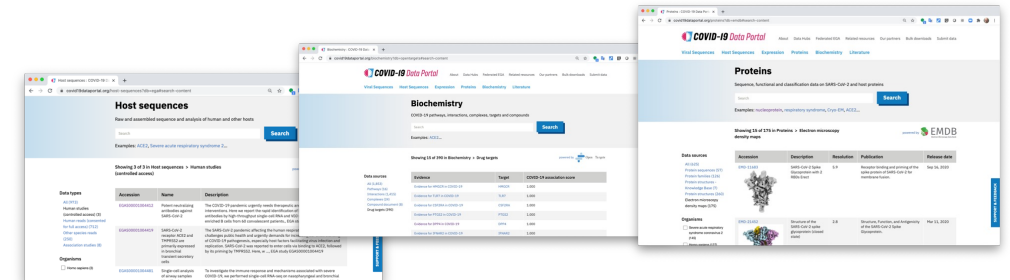
Reactome
Complex Portal
Ensembl

ChEMBL

6 month
anniversary

Data submissions/growth
by EMBL-EBI services,

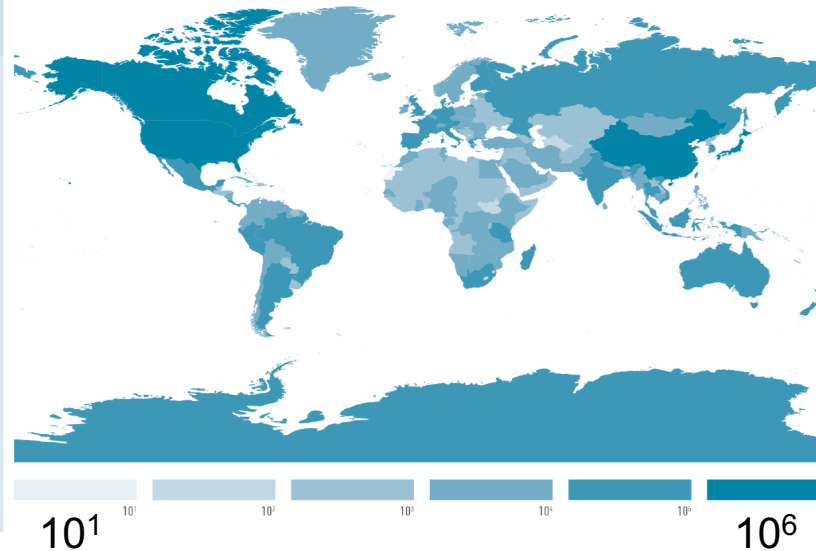
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov



Direction of flow of non-monetary benefit

What is the country of origin for non-human NSD?

1. China	18.23 %
2. United States	17.39 %
3. Canada	9.10 %
4. Japan	7.24 %
5. India	3.46 %
6. Australia	2.66 %
7. Mexico	2.54 %
8. Brazil	2.30 %
9. Germany	1.83 %
10. Spain	1.58 %



Countries of DSI origin

DSI user countries

1. United States	22.69 %
2. China	15.42 %
3. India	6.16 %
4. Japan	3.97 %
5. Germany	3.67 %
6. United Kingdom	3.45 %
7. France	2.84 %
8. Brazil	2.83 %
9. Spain	2.31 %
10. Russian Federation	2.25 %

