



# What are the applications of DSI?

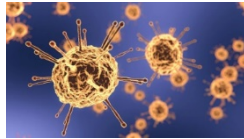
**DSI 101 webinar**  
**December 1, 2020**



Dr. Amber Hartman Scholz, Deputy to the Director



# DSI enables a LOT of public good



Epidemiology



Wildlife conservation



Thicklip grey mullet

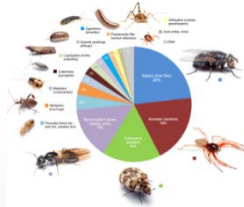
Pollutant effects in fish



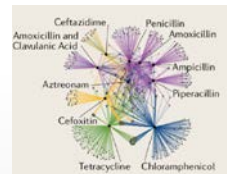
Reducing waste in pig feed



PANGAEA: Data Publisher for Earth & Environmental Science



Insect taxonomy & Loss of pollinators



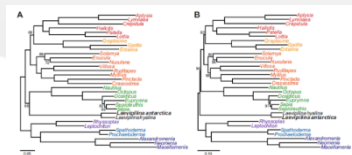
Antimicrobial resistance



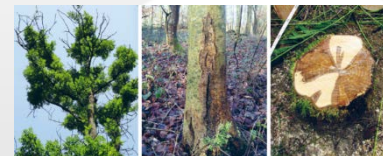
Tropical ecosystem research & climate change adaptation



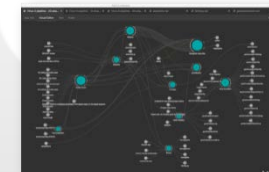
Poaching & Wildlife trade



Mollusk barcoding



Fungal diversity & nutrient cycling



Viral metagenomics & bioprospecting



Freshwater Biodiversity and Evolution

# 3 GOALS OF THE CBD → 3 EXAMPLES

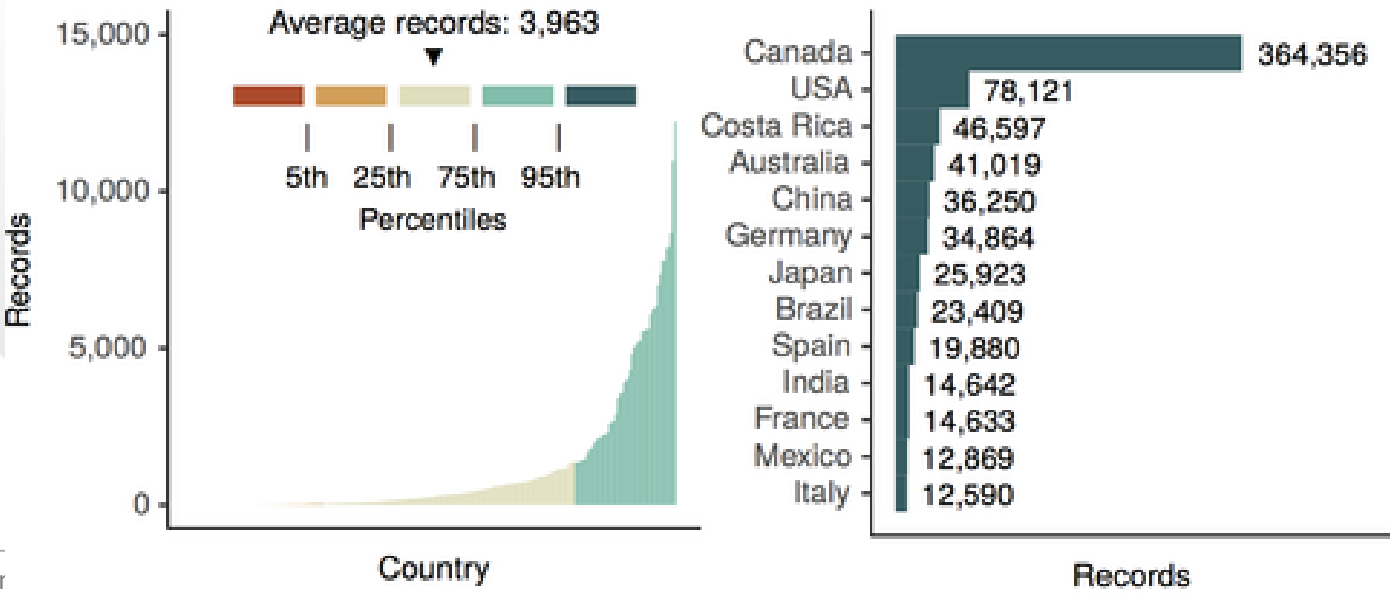
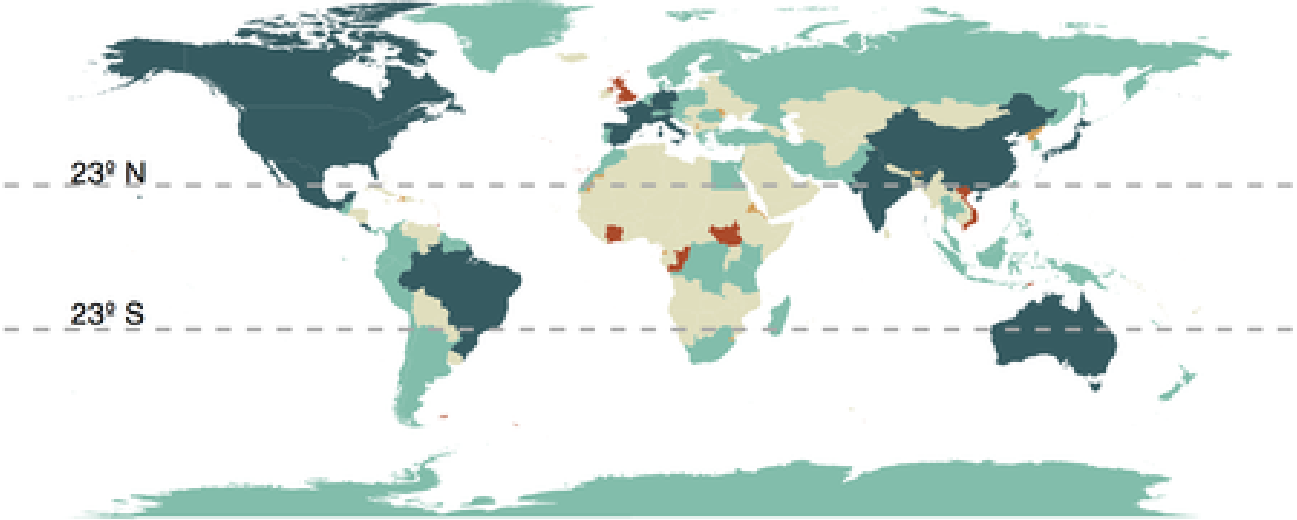
FOR EACH EXAMPLE:  
WHAT IS DSI USED FOR?

HOW WAS IT USED?

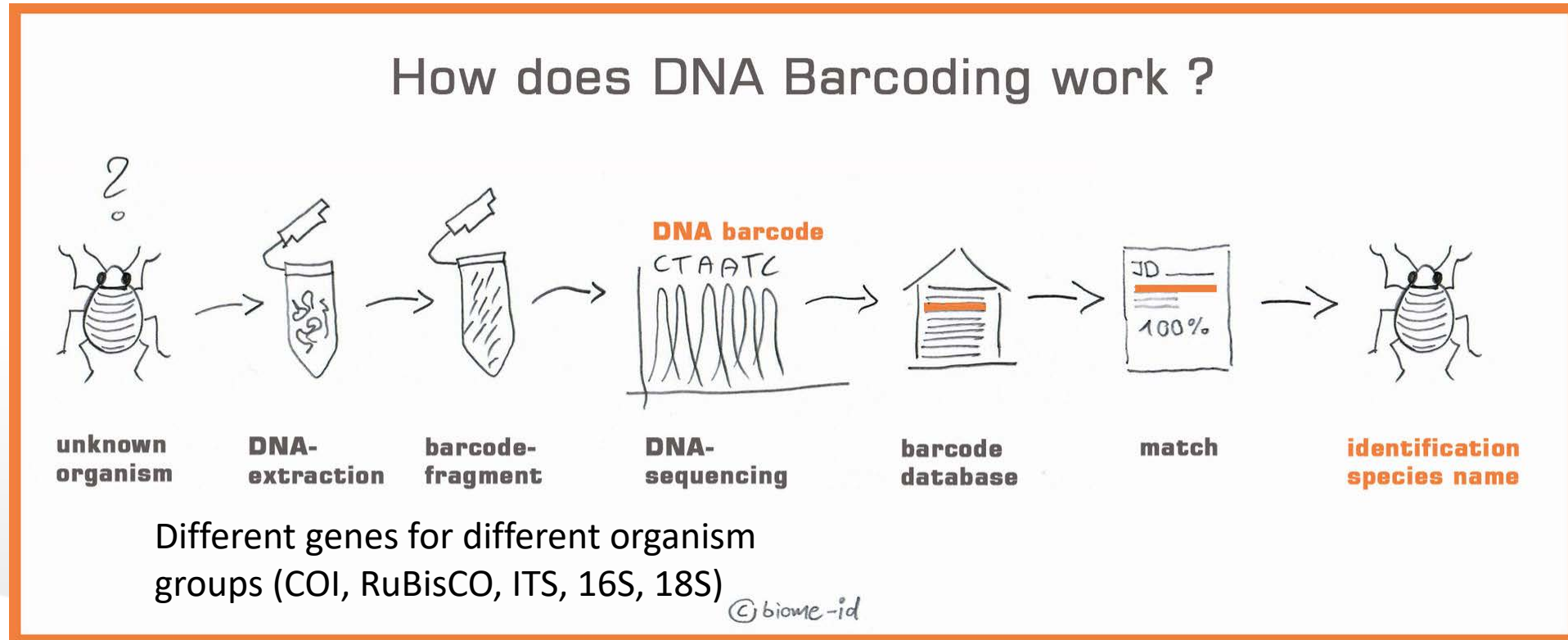
# CBD GOAL 1. DSI FOR BIODIVERSITY CONSERVATION

IDENTIFY SPECIES → BARCODING  
UNKOWN SEQUENCES → BLAST

# You want to conserve biodiversity? You can only protect what you know you have. How? Barcoding.



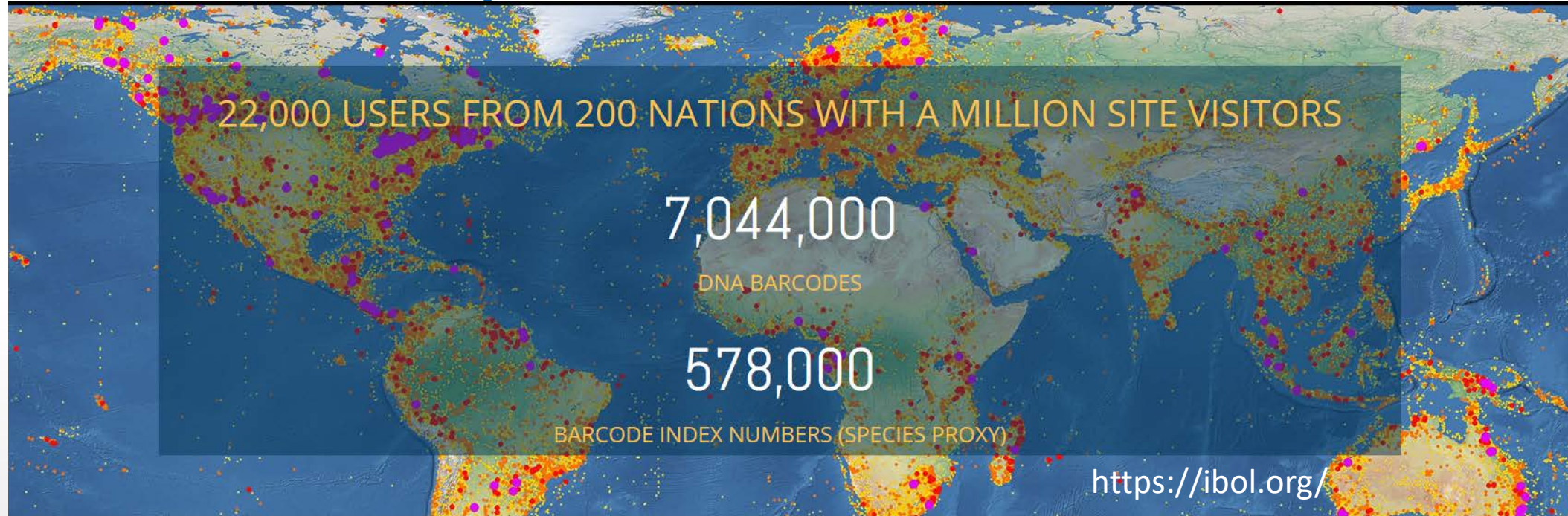
# Step 1. Identifying biodiversity through barcoding



Barcoding is not looking at the *function* of the genes but rather variations in the letters to give a “name tag”

# Large barcoding databases

## iBOL Example



**Other than identifying new species, barcoding can also be used to identify:**

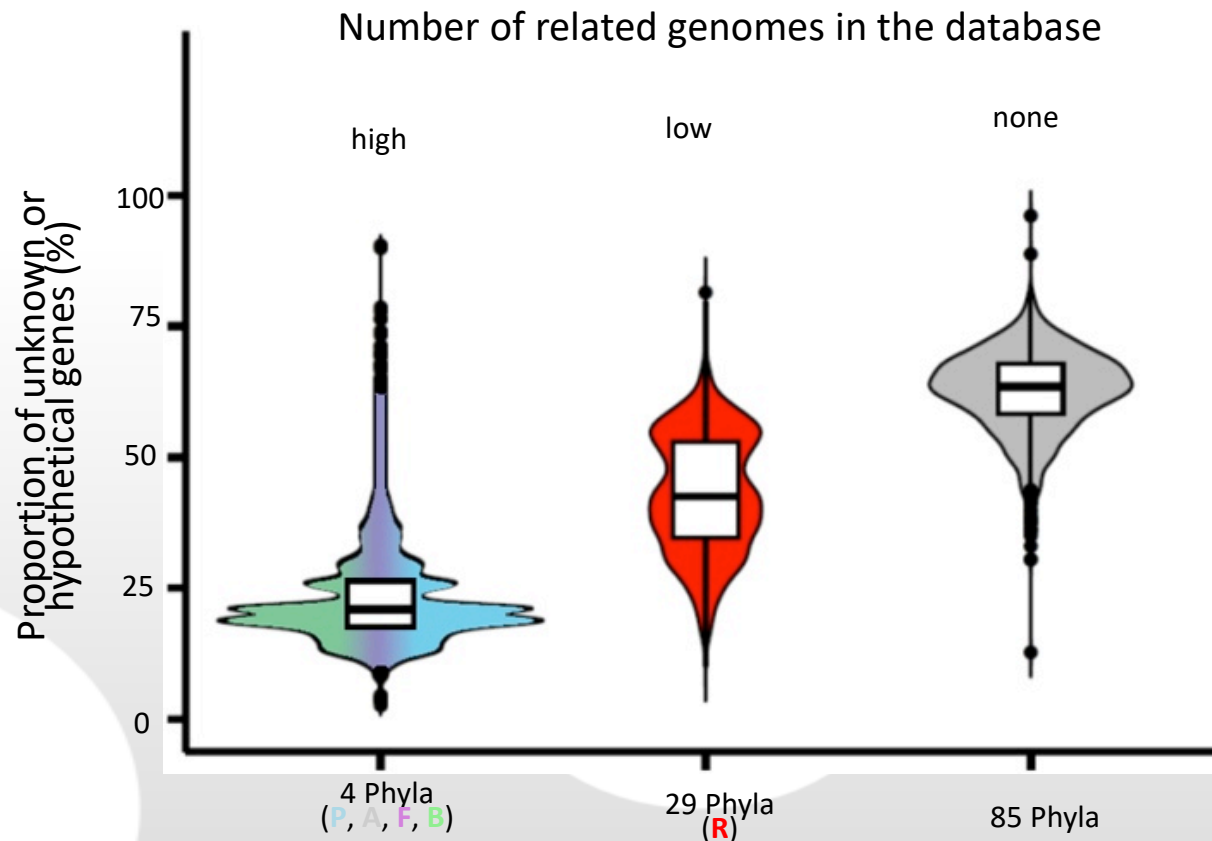
- Invasive species
- Pests & pathogens
- Contaminants

# Step 2. Understanding new, unknown biodiversity by BLASTing it against all DSI in INSDC

## Pop quiz:

What does this mean?

AACCGTCTACGGCCCGATCTCCCTGCACCCTGGCCCCACCCTTCCAAATGCGGCATATCCAGT



Unknown genes = unusable DNA baby babble.

The bigger and more complete the DSI dataset is, the better the chance we will understand novel biodiversity.

**This means science needs one big, central database!**



# **CBD GOAL 2. SUSTAINABLE USE OF BIOLOGICAL DIVERSITY**

## **COMPARING DSI TO REDUCE POLLUTION**

**THANKS TO MARKUS WYSS, DSM**



# Goal: improve water quality, decrease phosphorous pollution



[https://www.usgs.gov/special-topic/water-science-school/science/phosphorus-and-water?qt-science\\_center\\_objects=0#qt-science\\_center\\_objects](https://www.usgs.gov/special-topic/water-science-school/science/phosphorus-and-water?qt-science_center_objects=0#qt-science_center_objects)

# Phytases break down when heated



# Many sequences contributed a little bit to a more heat stable phytase

Protein Engineering vol.13 no.1 pp.49–57, 2000

## 1 From DNA sequence to improved functionality: using protein sequence comparisons to rapidly design a thermostable consensus phytase

Martin Lehmann<sup>1</sup>, Dirk Kostrewa, Markus Wyss, Roland Brugger, Allan D'Arcy, Luis Pasamontes and Adolphus P.G.M. van Loon

F.Hoffmann-La Roche Ltd, Grenzacherstrasse 124, CH-4070 Basel, Switzerland

<sup>1</sup>To whom correspondence should be addressed; email: Martin.Lehmann@Roche.com

Naturally-occurring phytases having the required level of thermostability for application in animal feeding have not been found in nature thus far. We decided to *de novo* construct consensus phytases using primary protein sequence comparisons. A consensus enzyme based on 13 fungal phytase sequences had normal catalytic properties, but showed an unexpected 15–22°C increase in unfolding temperature compared with each of its parents. As a first step towards understanding the molecular basis of

and 63°C (see below), we were interested in developing a rapid procedure to increase the unfolding temperature and thus the thermostability of phytases.

Increasing the thermostability of an enzyme usually requires combining multiple amino acid exchanges, each of which slightly increases the unfolding temperature of the protein. The main problem, however, is the identification of the relevant amino acid residues. In general terms mutations that increase thermostability may, for example, result in formation of hydrogen bonds, salt or disulphide bridges, increase the hydrophobic packing or the  $\alpha$ -helix or  $\beta$ -sheet stability or stabilize  $\beta$ -turns or flexible termini or loops (for review see Jaenicke *et al.*, 1996). Despite extensive knowledge of the general mechanisms governing protein stability (Dill *et al.*, 1989; Dill, 1990; Fersht and Serrano, 1993; Matthews, 1993; Cordes *et al.*, 1996) no rapid and reliable procedures are available for increasing the thermostability of a given protein. For successful thermostabil-

# **CBD GOAL 3. FAIR & EQUITABLE BENEFIT SHARING**

## **USING SYNTHETIC BIOLOGY TO FIGHT A PANDEMIC FAST**



# Goal: respond to a pandemic by developing a diagnostic kit.

Neuartiges Coronavirus in China

## Zahl der Patienten steigt sprunghaft an - auf 201

In China  
Fälle hat  
drei Tod



**EVAg**  
European Virus Archive Global

European Virus Archive - GLOBAL

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20.01.202



Wuhan  
coronavirus  
outbreak ...

New  
Diagnostic  
reagents

AVAILABLE

Click  
Here

The best way to get viral material within the *Scientific Community*.  
Browse our viruses and derived products from the EVAg Portal.

Visit our Portal!

or learn more.

# 1. Chinese researchers upload SARS-CoV-2 DSI to INSDC on January 10, 2020

GenBank ▾

Send to: ▾

## Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, complete genome

NCBI Reference Sequence: NC\_045512.2

[FASTA](#) [Graphics](#)

Go to:

LOCUS NC\_045512 29903 bp ss-RNA linear VRL 18-JUL-2020  
DEFINITION Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, complete genome.  
ACCESSION NC\_045512  
VERSION NC\_045512.2  
DBLINK BioProject: [PRJNA485481](#)  
KEYWORDS RefSeq.  
SOURCE Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)  
ORGANISM [Severe acute respiratory syndrome coronavirus 2](#)  
Viruses; Riboviria; Orthornavirae; Pisuviricota; Pisoniviricetes; Nidovirales; Cornidovirineae; Coronaviridae; Orthocoronavirinae; Betacoronavirus; Sarbecovirus.  
REFERENCE 1 (bases 1 to 29903)  
AUTHORS Wu, F., Zhao, S., Yu, B., Chen, Y.M., Wang, W., Song, Z.G., Hu, Y., Tao, Z.W., Tian, J.H., Pei, Y.Y., Yuan, M.L., Zhang, Y.L., Dai, F.H., Liu, Y., Wang, Q.M., Zheng, J.J., Xu, L., Holmes, E.C. and Zhang, Y.Z.  
TITLE A new coronavirus associated with human respiratory disease in China  
JOURNAL Nature 579 (7798), 265-269 (2020)  
PUBMED [32015508](#)  
REMARK Erratum: [Nature. 2020 Apr;580(7803):E7. PMID: 32296181]  
REFERENCE 2 (bases 13476 to 13503)  
AUTHORS Baranov, P.V., Henderson, C.M., Anderson, C.B., Gesteland, R.F., Atkins, J.F. and Howard, M.T.  
TITLE Programmed ribosomal frameshifting in decoding the SARS-CoV genome  
JOURNAL Virology 332 (2), 498-510 (2005)  
PUBMED [15680415](#)  
REFERENCE 3 (bases 29728 to 29768)  
AUTHORS Robertson, M.P., Igel, H., Baertsch, R., Haussler, D., Ares, M. Jr. and Scott, W.G.  
TITLE The structure of a rigorously conserved RNA element within the SARS virus genome  
JOURNAL PLoS Biol 3 (1), e5 (2005)  
PUBMED [15630477](#)  
REFERENCE 4 (bases 29609 to 29657)  
AUTHORS Williams, G.D., Chang, R.Y. and Brian, D.A.  
TITLE A phylogenetically conserved hairpin-type 3' untranslated region pseudoknot functions in coronavirus RNA replication  
JOURNAL J Virol 73 (10), 8349-8355 (1999)  
PUBMED [10482585](#)  
REFERENCE 5 (bases 1 to 29903)  
CONSRM NCBI Genome Project  
TITLE Direct Submission



Leibniz-Institut • DSMZ

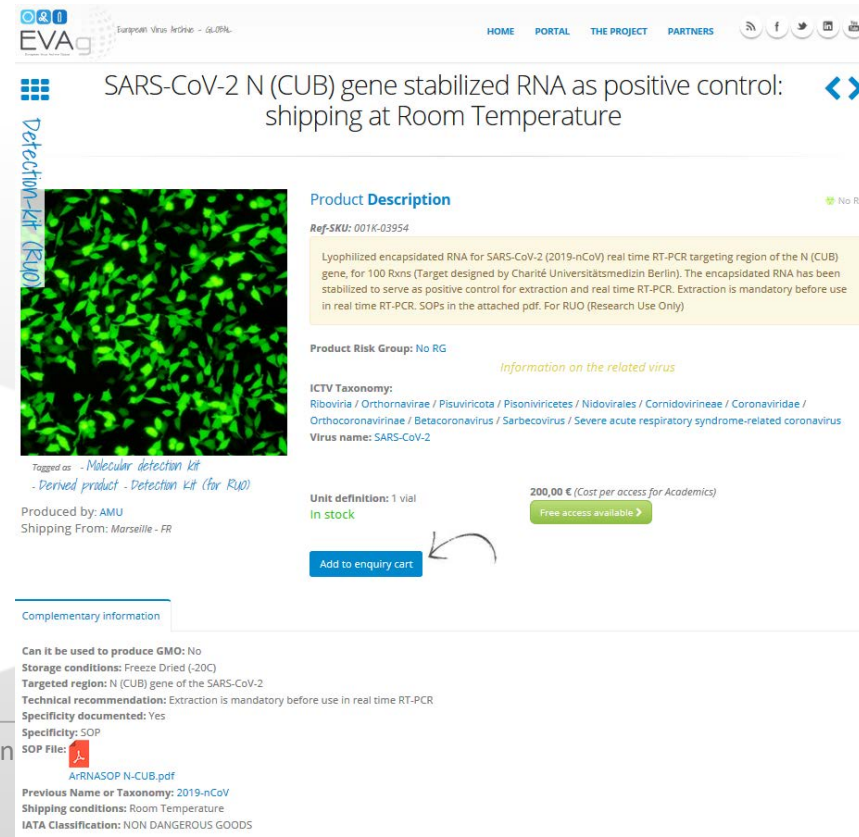
<https://www.ncbi.nlm.nih.gov/nuccore/NC045512>

# 2. German researchers synthesize SARS-CoV-2

“A virus is a piece of bad news wrapped in protein”

Dorothy H. Crawford

Direct synthesis is only possible for viruses!



**EVA** European Virus Archive - GERMANY

HOME PORTAL THE PROJECT PARTNERS

## SARS-CoV-2 N (CUB) gene stabilized RNA as positive control: shipping at Room Temperature

**Product Description** No RG

Ref-SKU: 001K-03954

Lyophilized encapsidated RNA for SARS-CoV-2 (2019-nCoV) real time RT-PCR targeting region of the N (CUB) gene, for 100 Rxns (Target designed by Charité Universitätsmedizin Berlin). The encapsidated RNA has been stabilized to serve as positive control for extraction and real time RT-PCR. Extraction is mandatory before use in real time RT-PCR. SOPs in the attached pdf. For RUO (Research Use Only)

Product Risk Group: No RG

**Information on the related virus**

ICTV Taxonomy:  
Riboviria / Orthornavirae / Pisuviricota / Pisoniviricetes / Nidovirales / Coronavirineae / Coronaviridae / Orthocoronavirinae / Betacoronavirus / Sarbecovirus / Severe acute respiratory syndrome-related coronavirus  
Virus name: SARS-CoV-2

Unit definition: 1 vial  
In stock  
200,00 € (Cost per access for Academics)  
Free access available

[Add to enquiry cart](#)

**Complementary information**

Can it be used to produce GMO: No  
Storage conditions: Freeze Dried (-20C)  
Targeted region: N (CUB) gene of the SARS-CoV-2  
Technical recommendation: Extraction is mandatory before use in real time RT-PCR  
Specificity documented: Yes  
Specificity: SOP  
SOP File: [ArRNASOP N-CUB.pdf](#)

Previous Name or Taxonomy: 2019-nCoV  
Shipping conditions: Room Temperature  
IATA Classification: NON DANGEROUS GOODS

Driouich et al. 2018





# 3. Identify a stable but unique gene for diagnosis

- **Unique**: only possible by comparing to other viruses.
- **Stable**: only possible by comparing to multiple patient samples of same virus. (Large dataset or prior knowledge needed)

# 4. Diagnostic kits shipped Feb.9

## Commercial test kits available 1-2 months later.



Primers, Probe and encapsidated RNA pos. control - SARS-CoV-2 N (CUB) gene, small packaging



Tagged as - Derived product - Bundle  
- Molecular detection kit  
- Detection Kit (for RUO)

Produced by: AMU  
Shipping From: Marseille - FR

### Product Description

No RG

Ref-SKU: 001B-03965

Lyophilized encapsidated RNA for SARS-CoV-2 real time RT-PCR targeting region of the N(CUB) gene (for 100 Rxns) AND Lyophilized ready-to-use primers and probe (Lyoph-P&P) for real time RT-PCR (96 rxns in the form of 4x24 rxns). Target, primers and probe designed by Charité (CUB) Berlin. SOPs in the attached pdf.

Disclaimer:

### LIST OF

Ref-SKU

001K-03964

001K-03954

Product Risk

ICTV Taxonomy

Riboviria / Ort

Orthocoronav

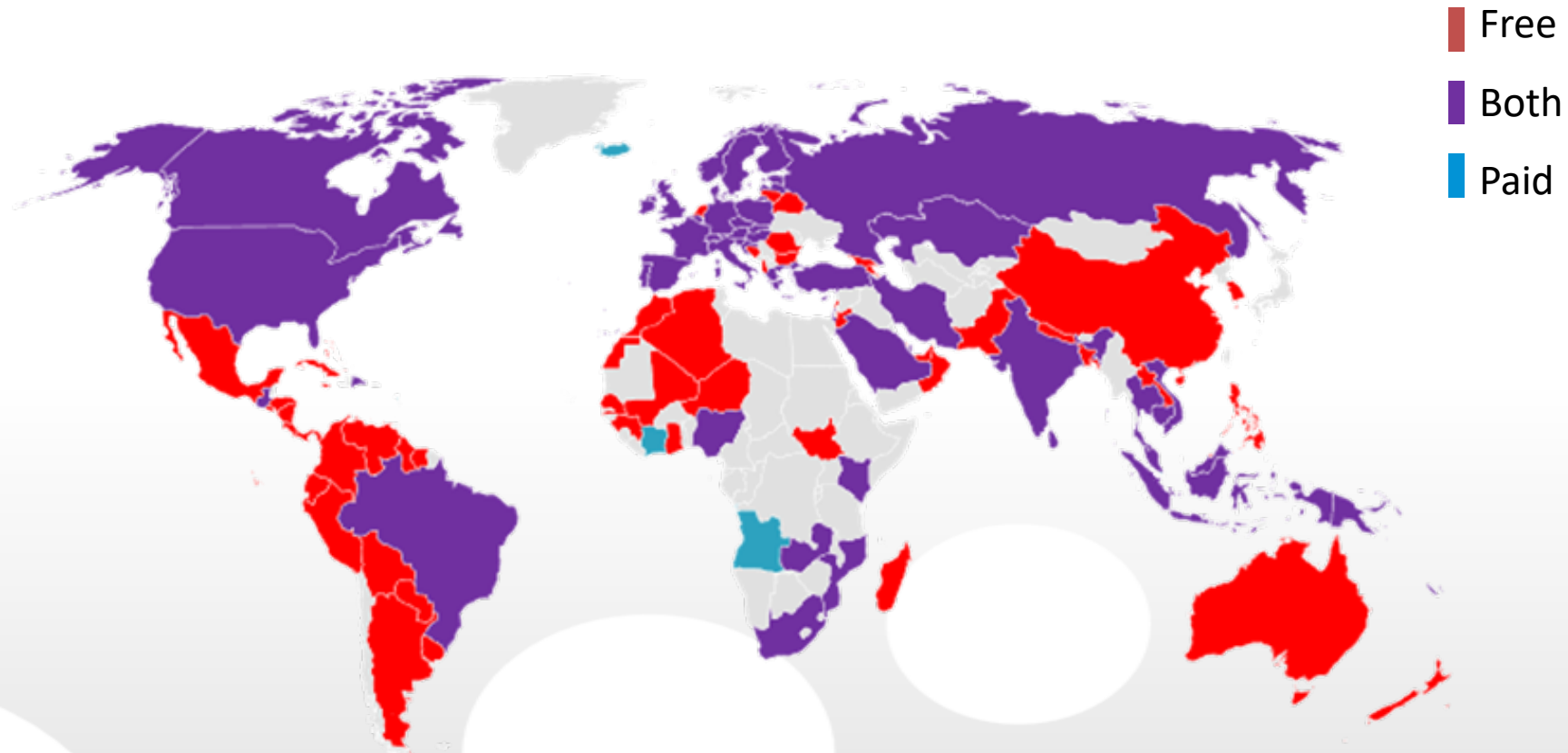
Virus name: S



<https://www.youtube.com/watch?v=tgyzdgf66eM>



## 5. Send it around the world for FREE. (Non-)monetary benefit-sharing?



- All customers had the free option available but some declined.
- African and Oceania not as severely affected by covid19 pandemic
- Funded by the EU Commission = €### million.
- 114 countries have received diagnostic kits to-date.

# Implications for DSI policymakers

1. **DSI is essential for different types of public good and all 3 CBD goals.**
2. **Modern-day biodiversity research depends on DSI**
  - Species identification (barcoding)
  - Learning about unknown biology
3. **DSI can be commercially utilized but it is a complex, iterative process based on huge datasets.**
4. **Determining benefit-sharing “credit” is very hard. (Lots of things contribute. Some more, some less.)**

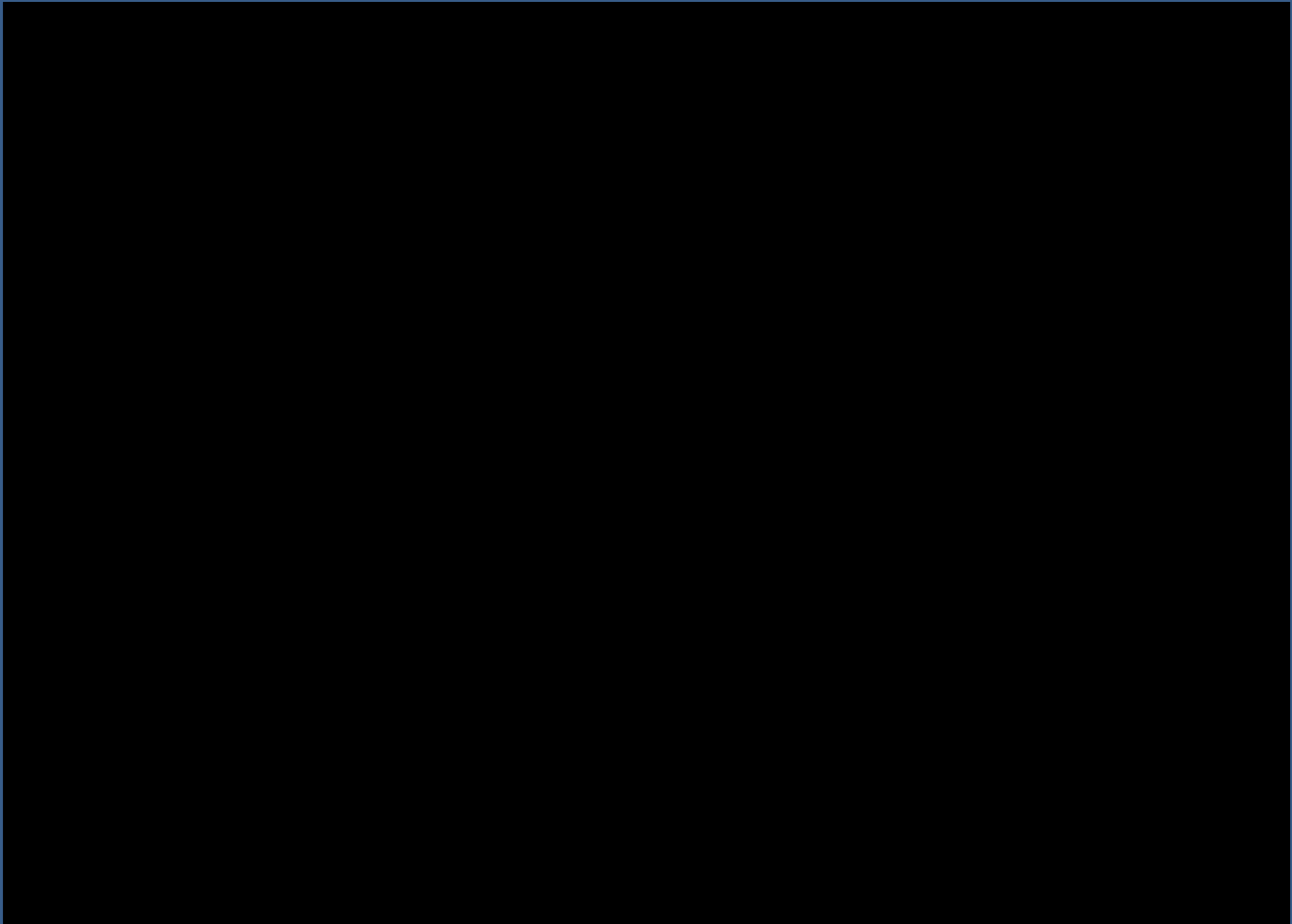
# Thank you!

[amber.h.scholz@dsmz.de](mailto:amber.h.scholz@dsmz.de)



<https://www.dsmz.de/collection/nagoya-protocol/digital-sequence-information>





DSI

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