A brief history of SARS-CoV-2 sequencing in Denmark

Mads Albertsen

Professor MSO

Center for Microbial Communities | Aalborg University

covid19genomics.dk/statistics

Aalborg University

Two small stories

How we started sequencing SARS-CoV-2

The Danish pandemic seen through genomics

Albertsen lab

"First movers in applying and developing new methods within DNA sequencing and microbial ecology"

Mads (PI)
Thomas (PhD)
Emil (PhD)

Vibeke (PD)
Thomas (PhD)
Mantas (PhD)
Simon (RA)

Andre (PD, co)
Morten (MSc)
Mette (MSc)
Søren (MSc)

Sebastian (MSc)
Amalie (MSc)
Erika (MSc)
Frederik (RA)

nature biotechnology

Genome sequences of rare, uncultured bacteria obtained by differential coverage binning of multiple metagenomes

Mads Albertsen[1], Philip Hugenholtz[2,3], Adam Skarshewski[2], Kåre L Nielsen[1], Gene W Tyson[2,4] & Per H Nielsen[1]

Science AAAS

Growth of nitrite-oxidizing bacteria by aerobic hydrogen oxidation

Hanna Koch,[1] Alexander Galushko,[1] Mads Albertsen,[2] Arno Schintlmeister,[1,3] Christiane Gruber-Dorninger,[1] Sebastian Lücker,[1+] Eric Pelletier,[4,5,6] Denis Le Paslier,[4,5,6] Eva Spieck,[7] Andreas Richter,[3] Per H. Nielsen,[2] Michael Wagner,[1] Holger Daims[1]†

nature

Complete nitrification by *Nitrospira* bacteria

Holger Daims[1], Elena V. Lebedeva[2], Petra Pjevac[1], Ping Han[1], Craig Herbold[1], Mads Albertsen[3], Nico Jehmlich[4], Marton Palatinszky[1], Julia Vierheilig[1], Alexandr Bulaev[5], Rasmus H. Kirkegaard[3], Martin von Bergen[4,5], Thomas Rattei[6], Bernd Bendinger[7], Per H. Nielsen[3] & Michael Wagner[1]

nature

Complete nitrification by a single microorganism

Maartje A. H. J. van Kessel[1], Daan R. Speth[1], Mads Albertsen[2], Per H. Nielsen[2], Huub J. M. Op den Camp[1], Boran Kartal[1], Mike S. M. Jetten[1,4] & Sebastian Lücker[1]

nature biotechnology

Retrieval of a million high-quality, full-length microbial 16S and 18S rRNA gene sequences without primer bias

Søren M Karst[1,2], Morten S Dueholm[1,2], Simon J McIlroy[1], Rasmus H Kirkegaard[1], Per H Nielsen[1] & Mads Albertsen[1]

nature

Kinetic analysis of a complete nitrifier reveals an oligotrophic lifestyle

K. Dimitri Kits[1], Christopher J. Sedlacek[1], Elena V. Lebedeva[2], Ping Han[1], Alexandr Bulaev[2], Petra Pjevac[1], Anne Daebeler[1], Stefano Romano[1], Mads Albertsen[3], Lisa Y. Stein[4], Holger Daims[1] & Michael Wagner[1]

nature methods — ARTICLES
https://doi.org/10.1038/s41592-020-01041-y

High-accuracy long-read amplicon sequences using unique molecular identifiers with Nanopore or PacBio sequencing

Søren M. Karst[1,7], Ryan M. Ziels[2,7], Rasmus H. Kirkegaard[1], Emil A. Sørensen[1], Daniel McDonald[3], Qiyun Zhu[3], Rob Knight[3,4,5,6] and Mads Albertsen[1]

High-throughput amplicon sequencing of large genomic regions remains challenging for short-read technologies. Here, we report a high-throughput amplicon sequencing approach combining unique molecular identifiers (UMIs) with Oxford Nanopore Technologies (ONT) or Pacific Biosciences circular consensus sequencing, yielding high-accuracy single-molecule consensus sequences of large genomic regions. We applied our approach to sequence ribosomal RNA operon amplicons (~4,500 bp) and genomic sequences (>10,000 bp) of reference microbial communities in which we observed a chimera rate <0.02%. To reach a mean UMI consensus error rate <0.01%, a UMI read coverage of 15× (ONT R10.3), 25× (ONT R9.4.1) and 3× (Pacific Biosciences circular consensus sequencing) is needed, which provides a mean error rate of 0.0042%, 0.0041% and 0.0007%, respectively.

High-throughput amplicon sequencing is a ubiquitous method for studying genetics with low-abundance variants or high heterogeneity, including cancer driver genes[1-3], viral populations[4-6] and microbial communities[7]. Short-read Illumina sequencing has dominated amplicon-related research due to its unprecedented throughput and low native error rate of ~0.1%, but its maximum amplicon size of ~500 bp[8] limits important long-range information and assay resolution[9]. UMIs have been applied to enable sequencing of longer amplicons with short-reads via assembly of synthetic long reads[10]. Each template molecule in a sample is tagged with a UMI sequence consisting of 10–20 random bases, which can subsequently be used to sort and analyze reads based on their original template molecule. UMIs can enable sequencing of synthetic long reads up to ~11,000 bp, but this approach cannot resolve amplicons with repeats longer than the short-read length[11], which limits its application. The high native error rates of ONT (5–25%[12]) and Pacific Biosciences (PacBio) (~13%[13]) have until now, made it difficult to confidently identify true UMI tag sequences that are necessary to accurately assign raw reads to their template molecules. Furthermore, the combination of UMIs with long-read sequencing is relatively unexplored and only recently has this combination been applied with PacBio circular consensus sequencing (CCS)[14-16], but without using dual UMIs for chimera filtering[17] and profiling the error of the generated consensus sequences.

Here, we present a simple workflow that combines UMIs with sequencing of long amplicons on the ONT and PacBio platforms to produce highly accurate single-molecule consensus sequences with a low chimera rate. To improve recognition of UMI-tagged error-prone reads, we designed UMIs to contain recognizable internal patterns (Fig. 1a and Supplementary Table 1) that avoid error-prone homopolymer stretches[18] and, combined with filtering
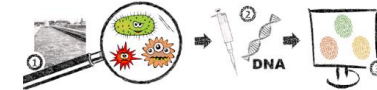
based on UMI length and pattern, allow for robust determination of true UMI sequences in raw error-prone ONT and PacBio data.

Results

Applying dual-UMI tagging for long-read amplicon sequencing. The DNA template is initially diluted to a target number of output sequences, which is estimated based on the desired single-molecule coverage and expected sequencing yield. This initial dilution step must be optimized for the genomic material of a given study to ensure that the target number of amplifiable target molecules can be achieved, either by trial sequencing or using methods such as semi-quantitative PCR and a suitable amplicon product standard. The genetic region of interest is then targeted using two cycles of PCR with a customized set of tailed primers (Supplementary Table 1), which includes a target-specific primer, a UMI sequence and a synthetic priming site used for downstream amplification (Fig. 1b, step 1). For PCR-free approaches, such as whole-genome or metagenomic DNA sequencing, adaptors containing UMIs can be ligated to template DNA molecules. The product from the initial PCR is subsequently amplified by PCR targeting the synthetic primer sites (Fig. 1b, step 2) and prepared for long-read sequencing with ONT or PacBio CCS (Fig. 1b, step 3). After sequencing, reads are binned based on the concatenation of the two terminal UMIs (UMI pair) (Fig. 1c, steps 1 and 2). High-quality UMI sequences are detected on the basis of the presence of the designated pattern, as well as the expected UMI length of 18 bp (Fig. 1a). Chimeric sequences are filtered de novo by removing UMI pairs in which either terminal UMI is observed in a more abundant UMI pair[17] (Fig. 1c, step 2). The filtered, high-quality

"Danish research result of the year 2015"

DE BANSKE FORSKNINGSRESULTAT
2015
præsenteres af
Videnskab.dk

DNAsense — *more than just the sequence*

RAMBØLL
TEKNOLOGISK INSTITUT
GRUNDFOS
novozymes — Rethink Tomorrow
2A PHARMA
novo nordisk
UNIVERSITY OF COPENHAGEN

CENTER FOR MICROBIAL COMMUNITIES | AALBORG UNIVERSITY

We play with new technology…

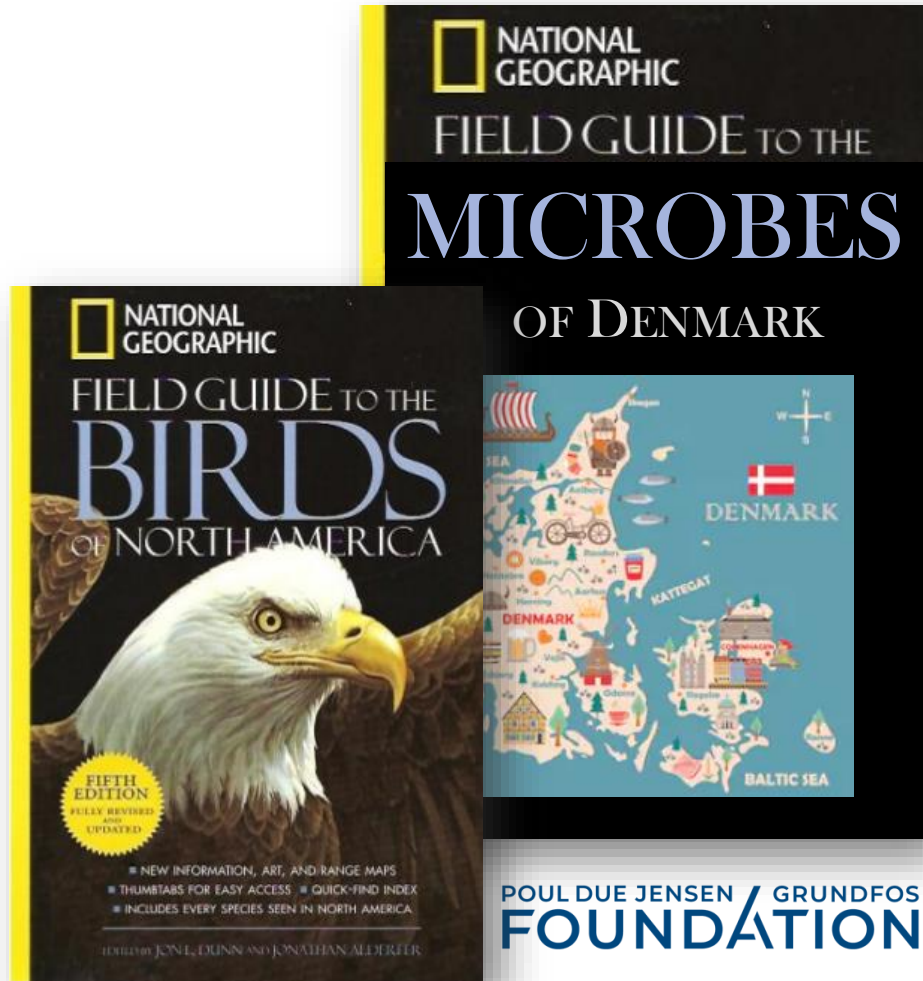[Early access users since 2014]

[Early access users since 2017]

Microflora Danica: The microbiome of Denmark
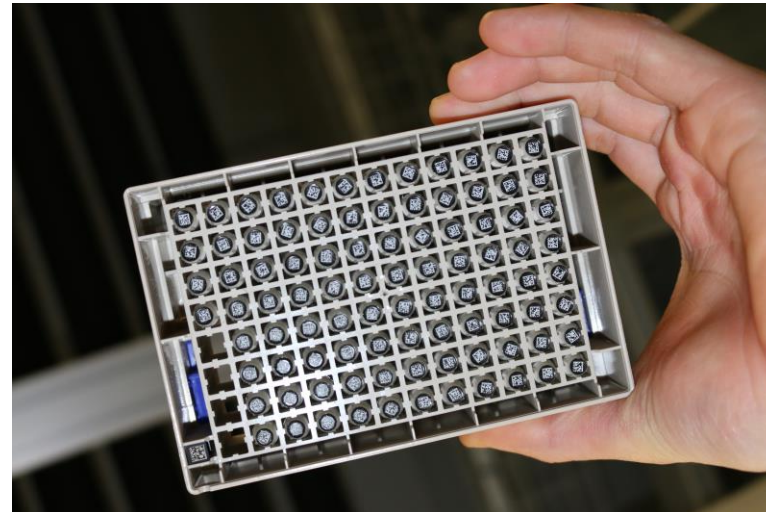
Per H. Nielsen

*"Sounds awesome, here is 30 mill. DKK.
Go do great science."*

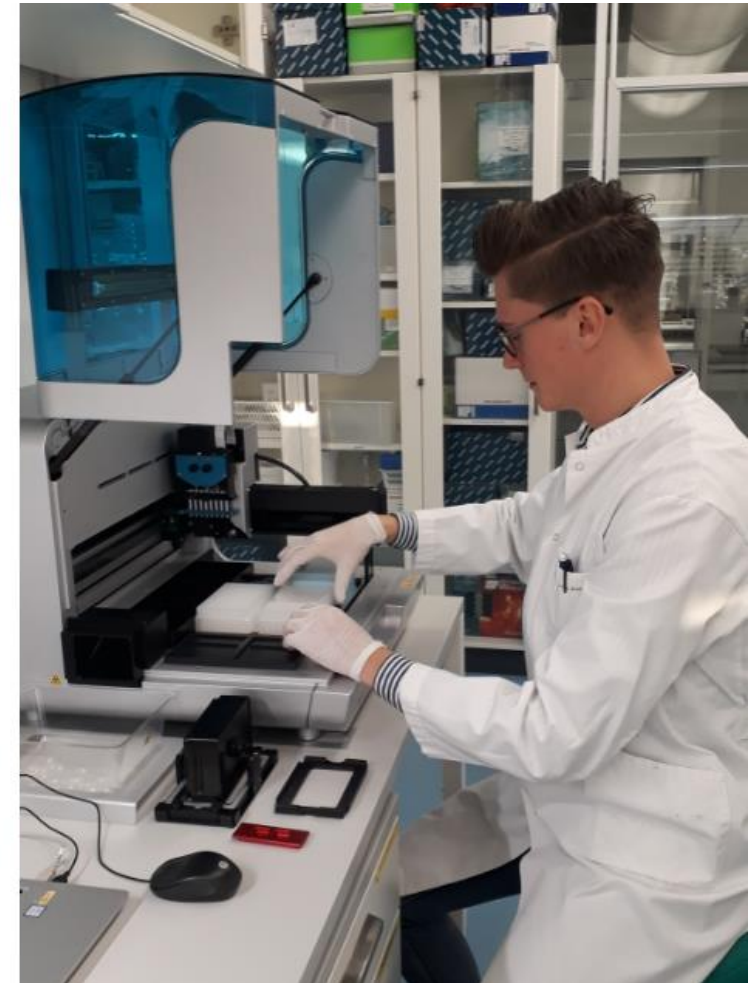# A high-throughput system for analysis of 10.000 samples

Sample and plate barcoding system

Scanning system
(collected samples & 96 sample format)

Automated extraction platform
(96 sample format, 2 hours turnaround)

Thomas BN Jensen

Ny coronavirus fra Wuhan

SUNDHEDSSTYRELSEN

Siden december 2019 er der i den kinesiske storby Wuhan fundet flere tilfælde af svær lungebetændelse og dødsfald, som er forårsaget af en ny coronavirus. Der er også fundet tilfælde i andre asiatiske lande hos personer, der har opholdt sig i Wuhan. Sundhedsstyrelsen vurderer, at der er meget lille sandsynlighed for, at sygdommen kommer til Danmark, men følger situationen nøje. Sundhedsstyrelsen anbefaler ikke screeningstiltag i fx lufthavne i forbindelse med indrejse i Danmark. Hvis der mod forventning skulle komme personer til Danmark med mistanke om sygdommen, så er de danske sundhedsmyndigheder og sundhedsvæsenet klar til at håndtere dette.

22 JAN 2020

sst.dk/da/nyheder/2020/ny-coronavirus-fra-wuhan

31. december 2019 - Kina advarer WHO om udbrud af, hvad der forventes at være lungebetændelse i Wuhan.

3. januar - Øjenlægen Li Wenliang arresteres i Wuhan, da de kinesiske myndigheder mener, at han har spredt falske rygter om coronavirussen. Han dør 6. februar af coronavirus.

11. januar - Kina registrerer det første dødsfald som følge af coronavirus i Wuhan.

22. januar - WHO: Uenighed om at erklære Covid-19 for en international sundhedskrise.

23. januar - Kina: Wuhan lukkes ned.

24. januar - Frankrig registrerer første tilfælde af Covid-19 i Europa.

nature

Article

A pneumonia outbreak associated with a new coronavirus of probable bat origin

Peng Zhou[1,5], Xing-Lou Yang[1,5], Xian-Guang Wang[2,5], Ben Hu[1], Lei Zhang[1], Wei Zhang[1], Hao-Rui Si[1,3], Yan Zhu[1], Bei Li[1], Chao-Lin Huang[2], Hui-Dong Chen[2], Jing Chen[1,3], Yun Luo[1,3], Hua Guo[1,3], Ren-Di Jiang[1,3], Mei-Qin Liu[1,3], Ying Che ̄[.3]..., Y..., Yi ̄...[13] Xiao-Shuang Zheng[1,3], Kai Zhao[1,3], Quan-Jiao Chen..., Fa-Xian Zhan[4], Yan-Yi Wang[1], Geng-Fu Xiao[1] & Zhen...

Since the outbreak of severe acute respiratory ...
number of SARS-related coronaviruses (SARS... natural reservoir host, bats[1-4]. Previous studie... have the potential to infect humans[5-7]. Here we... characterization of a new coronavirus (2019-n... acute respiratory syndrome in humans in Wuh... on 12 December 2019, had caused 2,794 labora... deaths by 26 January 2020. Full-length genom... patients at an early stage of the outbreak. The s... share 79.6% sequence identity to SARS-CoV. Fu... 96% identical at the whole-genome level to a b... sequence analysis of seven conserved non-stru... virus belongs to the species of *SARSr-CoV*. In a... the bronchoalveolar lavage fluid of a critically... from several patients. Notably, we confirmed t... receptor—angiotensin converting enzyme II (A...

ORIGINAL ARTICLE   BRIEF REPORT

A Novel Coronavirus from Patients with Pneumonia in China, 2019

Na Zhu, Ph.D., Dingyu Zhang, M.D., Wenling Wang, Ph.D., Xingwang Li, M.D., Bo Yang, M.S., Jingdong Song, Ph.D., Xiang Zhao, Ph.D., Baoying Huang, Ph.D., Weifeng Shi, Ph.D., Roujian Lu, M.D., Peihua Niu, Ph.D., Faxian Zhan, Ph.D., et al., for the China Novel Coronavirus Investigating and Research Team

Article   Figures/Media   Metrics

17 References   9817 Citing Articles

Summary

Related Articles

In December 2019, a cluster of patients with pneumonia of unknown cause was linked to a seafood wholesale market in Wuhan, China. A previously unknown betacoronavirus was discovered through the use of unbiased sequencing in samples from patients with pneumonia. Human airway epithelial cells were used to isolate a novel coronavirus, named 2019-nCoV, which formed a clade within the subgenus sarbecovirus, Orthocoronavirinae subfamily. Different from both MERS-CoV and

EDITORIAL   FEB 20, 2020

Another Decade, Another Coronavirus

S. Perlman

ADVERTISEMENT

Using sequencing to understand virus outbreaks

Using sequencing to understand virus outbreaks
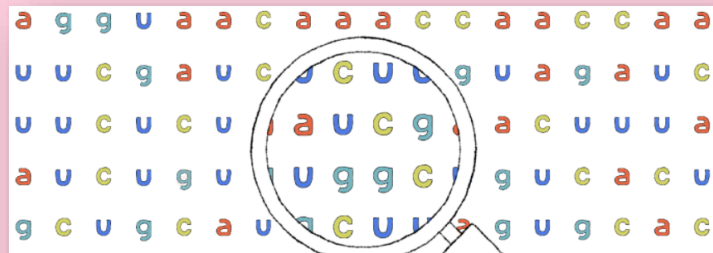
CENTER FOR MICROBIAL COMMUNITIES | AALBORG UNIVERSITY

Da lyden af død begyndte i Bergamo, var Italien for længst blevet Europas patient 0

På blot en måned har coronaepidemien bragt Italien ud i landets værste krisen siden Anden Verdenskrig. Overhørte advarsler og skødesløshed har givet virussen mulighed for at løbe løbsk. Dermed har Italien vist andre europæiske nationer, hvad man skal og ikke skal gøre, hvis man vil undgå den skarpt opadgående dødelige kurve

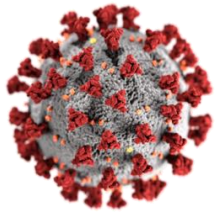En overfyldt hospitalsgang i Bergamo, Italien, hvor patienter, der er formodet smittet med COVID-19, er indlagt.

Tidslinje: Corona i Italien

- **20. februar:** En 38-årig mand bliver registreret som den første, der er smittet med COVID-19 i Italien.

- **23. februar:** Ti mindre byer med i alt 50.000 indbyggere i Norditalien bliver sat i karantæne. Skoler lukker i Norditalien.

- **4. marts:** Skoler og universiteter lukker i hele landet.

- **8. marts:** 16 mio. italienere i Lombardiet, Veneto og Emilia-Romagna bliver sat i karantæne.

- **10. marts:** Alle Italiens 60 mio. indbyggere bliver sat i karantæne.

- **19. marts:** For første gang er der samlet flere coronadøde i Italien (3.405) end i Kina (3.245).

- **22. marts:** Alle fabrikker og al produktion, der ikke er absolut nødvendig, lukkes ned.

- **27. marts:** I alt 86.498 tilfælde af coronavirus er registreret i Italien. Af dem er 10.950 meldt raske og 9.134 er døde.
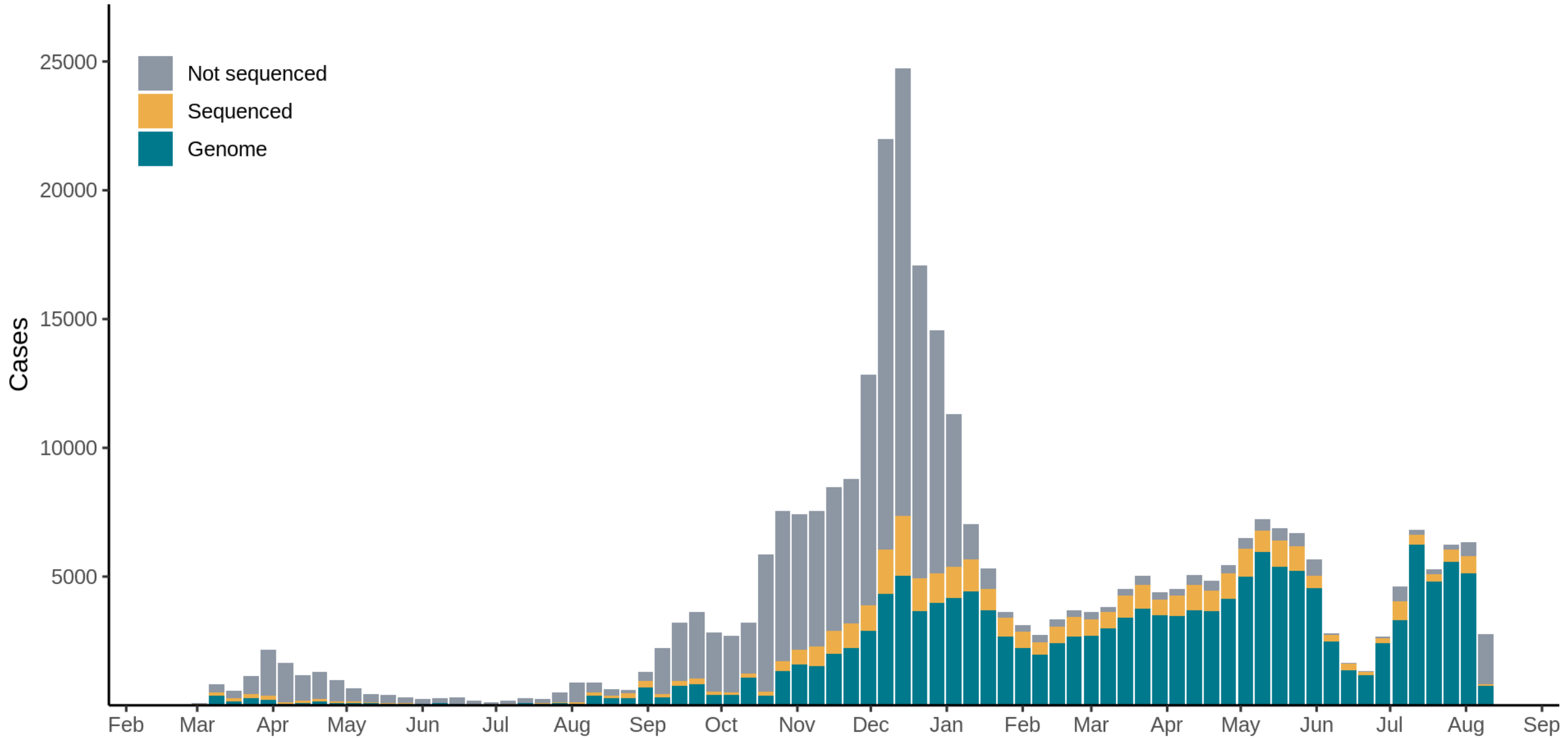
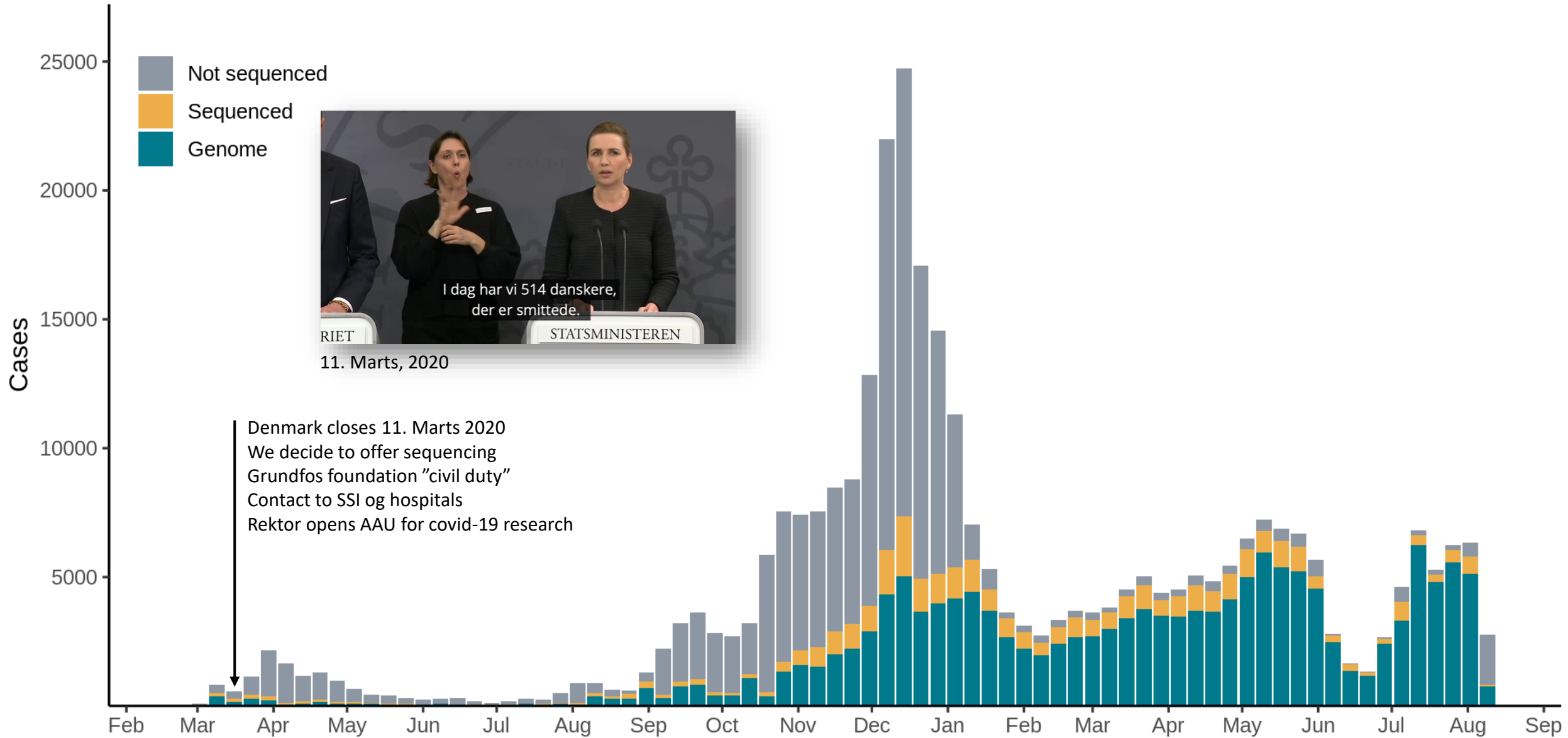# Two small stories

How we started sequencing SARS-CoV-2

The Danish pandemic seen through genomics

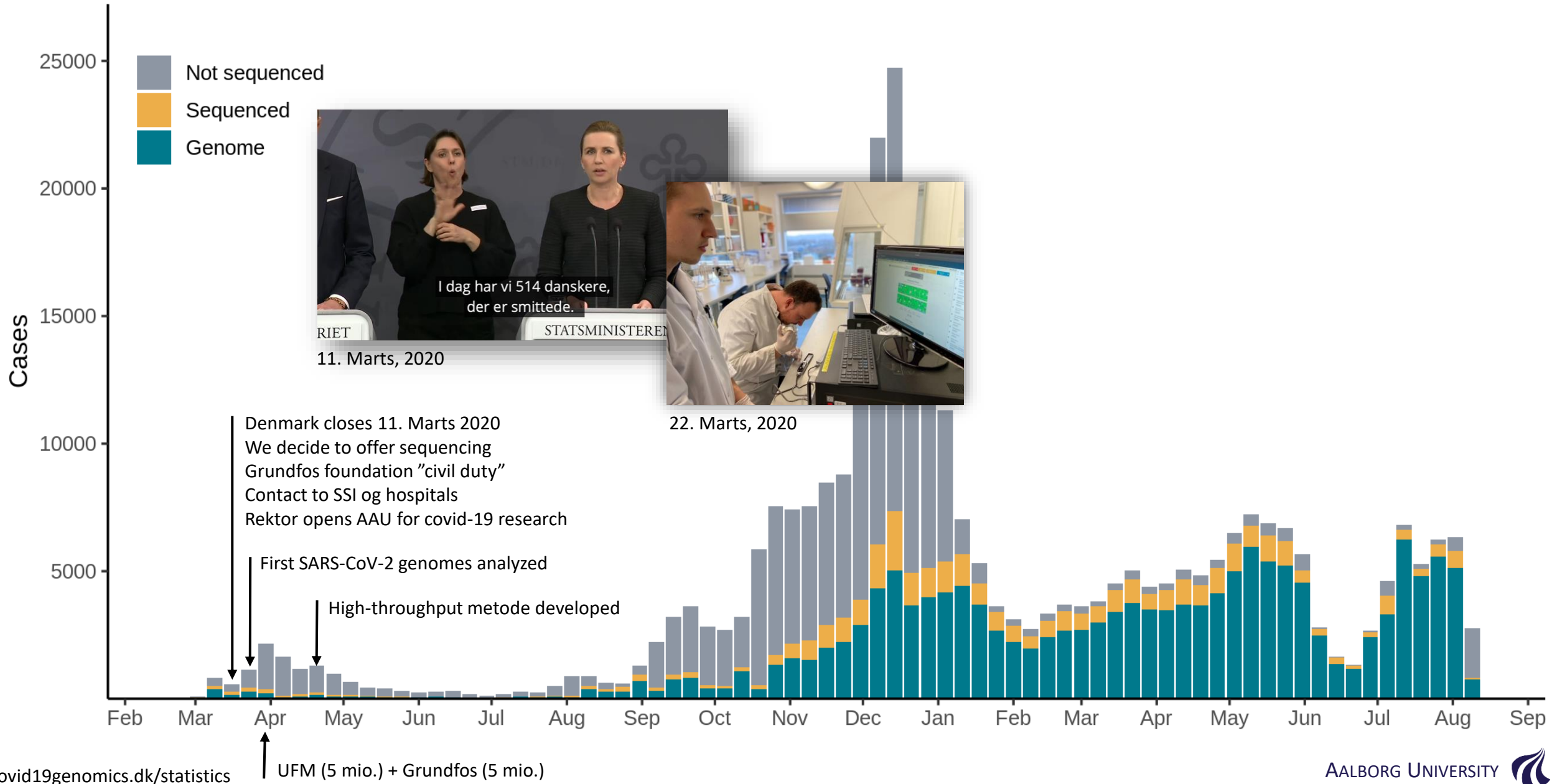# A brief history of SARS-CoV-2 sequencing in Denmark

covid19genomics.dk/statistics

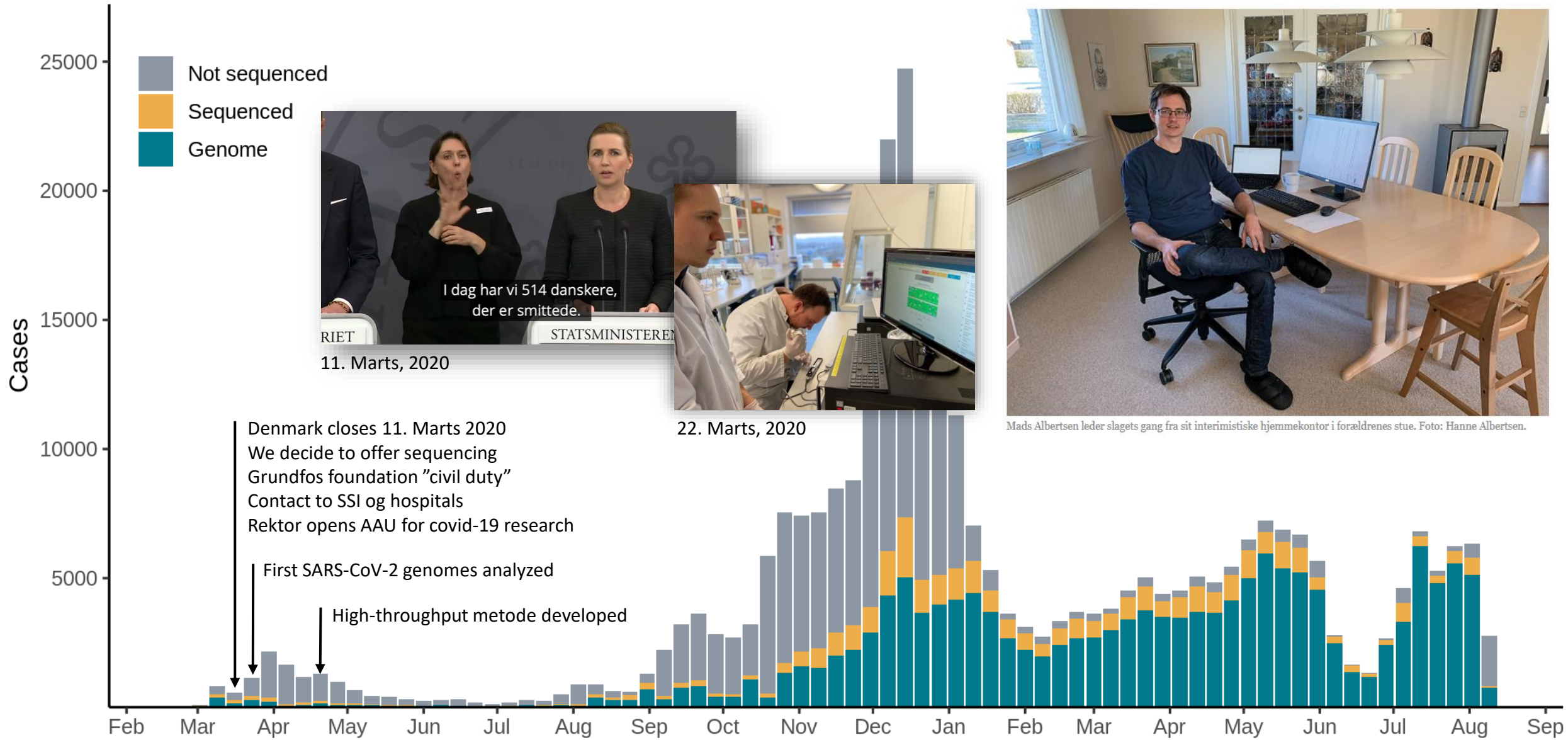# A brief history of SARS-CoV-2 sequencing in Denmark

11. Marts, 2020

Denmark closes 11. Marts 2020
We decide to offer sequencing
Grundfos foundation "civil duty"
Contact to SSI og hospitals
Rektor opens AAU for covid-19 research

Legend:
- Not sequenced (grey)
- Sequenced (orange)
- Genome (teal)

Cases

covid19genomics.dk/statistics

A brief history of SARS-CoV-2 sequencing in Denmark

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22. Marts, 2020

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First SARS-CoV-2 genomes analyzed

High-throughput metode developed

UFM (5 mio.) + Grundfos (5 mio.)

covid19genomics.dk/statistics

A brief history of SARS-CoV-2 sequencing in Denmark

Cases

25000

20000

15000

10000

5000

Not sequenced
Sequenced
Genome

11. Marts, 2020

I dag har vi 514 danskere, der er smittede.

22. Marts, 2020

Mads Albertsen leder slagets gang fra sit interimistiske hjemmekontor i forældrenes stue. Foto: Hanne Albertsen.

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Feb   Mar   Apr   May   Jun   Jul   Aug   Sep   Oct   Nov   Dec   Jan   Feb   Mar   Apr   May   Jun   Jul   Aug   Sep

UFM (5 mio.) + Grundfos (5 mio.)

covid19genomics.dk/statistics

aktuelnaturvidenskab.dk/find-artikel/nyeste-numre/2-2020/corona-forskning/

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A brief history of SARS-CoV-2 sequencing in Denmark

11. Marts, 2020

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22. Marts, 2020

Foto: Hanne Albertsen.

Legend:
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First SARS-CoV-2 genomes analyzed

High-throughput metode developed

Legal "databehandleraftale"

GDPR secure environment established
- 64-core AMD CPU og 1 TB RAM
- 200 TB CEPH storage
- Strictly controlled personal access
- 2 factor authentication
- Server and data access logging
- VPN access for selected SSI employees

UFM (5 mio.) + Grundfos (5 mio.)

A brief history of SARS-CoV-2 sequencing in Denmark

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A brief history of SARS-CoV-2 sequencing in Denmark

Ny genforskning afslører: Sådan endte Midt- og Vestjylland med at blive hotspot for corona

Herning og Holstebro blev kaldt lille-Bergamo, og området flød med rygter om årsag til udbredt corona-smitte.

TV AVISEN 21:00: Nyt våben mod corona
28. MAJ 2020 21:00 | 26M

HERNING HOLSTEBRO

ANDERS FOMSGAARD

Det er bare en **virus**

Vilde beretninger om virus og kampen mod dem

A brief history of SARS-CoV-2 sequencing in Denmark

A brief history of SARS-CoV-2 sequencing in Denmark

covid19genomics.dk/statistics

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A brief history of SARS-CoV-2 sequencing in Denmark

Blitz-scaling

Mads Albertsen
@MadsAlbertsen85

Testing our new brute-force high-throughput setup for SARS-CoV-2 sequencing. Emilio and the lab-team just started 14 @nanopore flowcells. 5 on GridION and 9 MinIONs with raw data streamed to our Tesla V100 GPU node. Also asked for 300 TB extra storage: IT - sure, mounting it now!

8:05 PM · Nov 12, 2020 · Twitter Web App

View Tweet activity

52 Retweets   8 Quote Tweets   320 Likes

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Blitz-scaling

Mads Albertsen
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8:05 PM · Nov 12, 2020 · Twitter Web App

 View Tweet activity

52 Retweets   8 Quote Tweets   320 Likes

50% of a NVIDIA DGX-2 server (KVM VM):
- **8 NVIDIA Tesla V100 GPU's**
- 750 GB RAM
- Intel Xeon CPU 24 cores
- 15 TB intern NVMe file-storage

750 TB CEPH storage
2 servers:
- 64-core AMD CPU og 1 TB RAM (main)
- 36-core Intel CPU og 768 GB RAM (test)

≈ 200 GB signal-level data pr. hour

1000 samples pr. day (max 2304)
Overnight data turnaround
Live signal processing
Workflow triggers
Direct metadata from SSI
Direct metadata from Test Center Denmark

Daily data-release before 12.00
- SSI, Modelling, Contact-tracing

A brief history of SARS-CoV-2 sequencing in Denmark

covid19genomics.dk/statistics

UFM (5 mio.) + Grundfos (5 mio.)

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A brief history of SARS-CoV-2 sequencing in Denmark

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A brief history of SARS-CoV-2 sequencing in Denmark

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A brief history of SARS-CoV-2 sequencing in Denmark

Mink-case
5000 samples pr. week

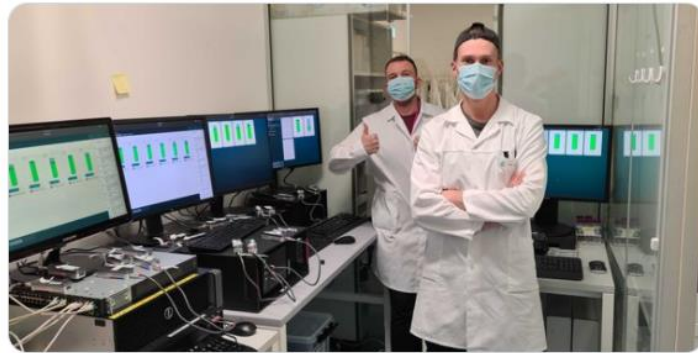"Alpha" notifikation from UK

Mads Albertsen @MadsAlbertsen85

The @aauengineering SARS-CoV-2 lab-team ends the year strong with 24 @nanopore flowcells running 2304 samples! Cheers to @SSI_dk and DK hospitals for feeding us with samples throughout 2020. Hats off to the bioinformatic, admin, and legal teams that work behind the scenes.
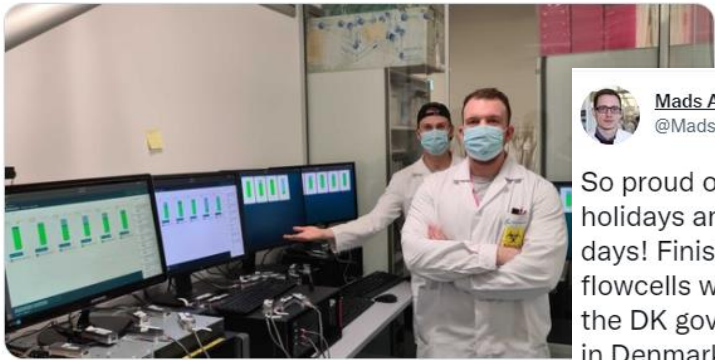
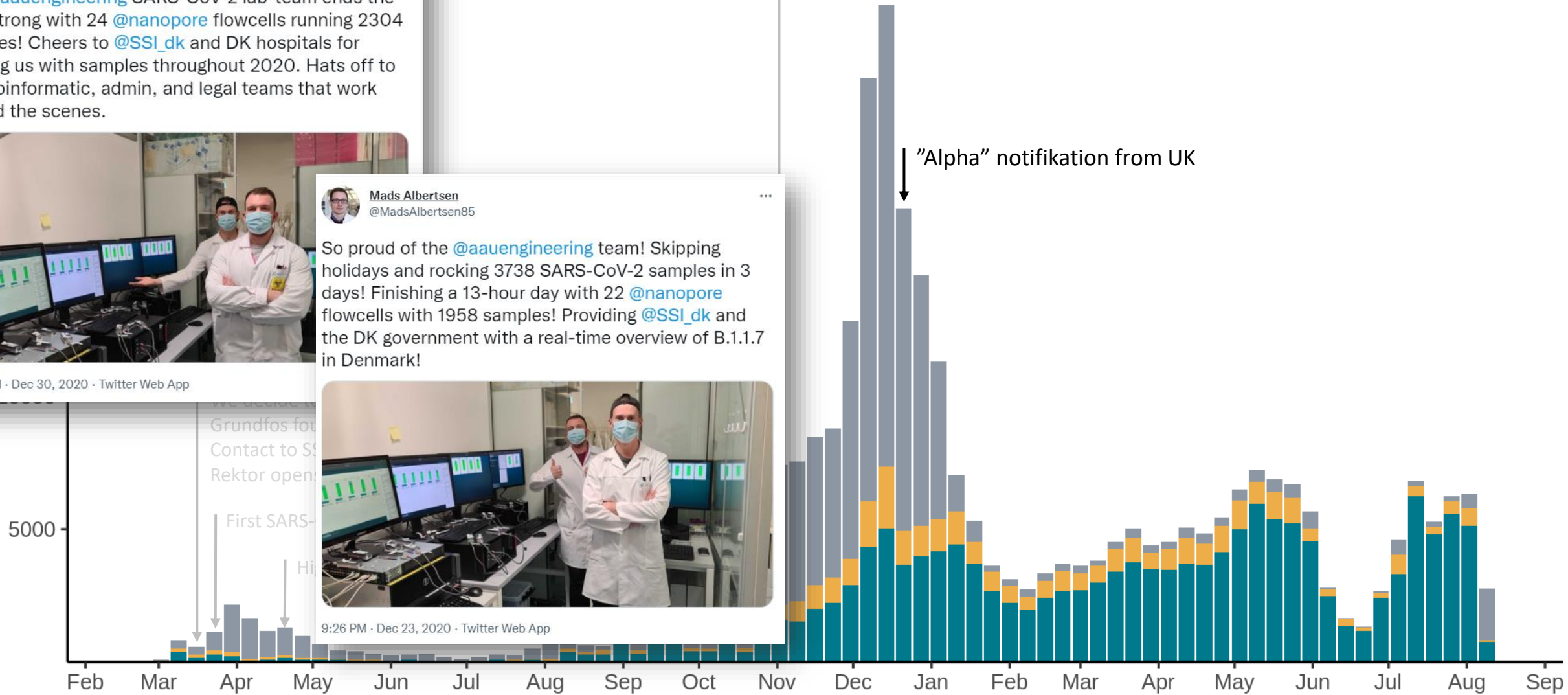10:30 PM · Dec 30, 2020 · Twitter Web App

Mads Albertsen @MadsAlbertsen85

So proud of the @aauengineering team! Skipping holidays and rocking 3738 SARS-CoV-2 samples in 3 days! Finishing a 13-hour day with 22 @nanopore flowcells with 1958 samples! Providing @SSI_dk and the DK government with a real-time overview of B.1.1.7 in Denmark!
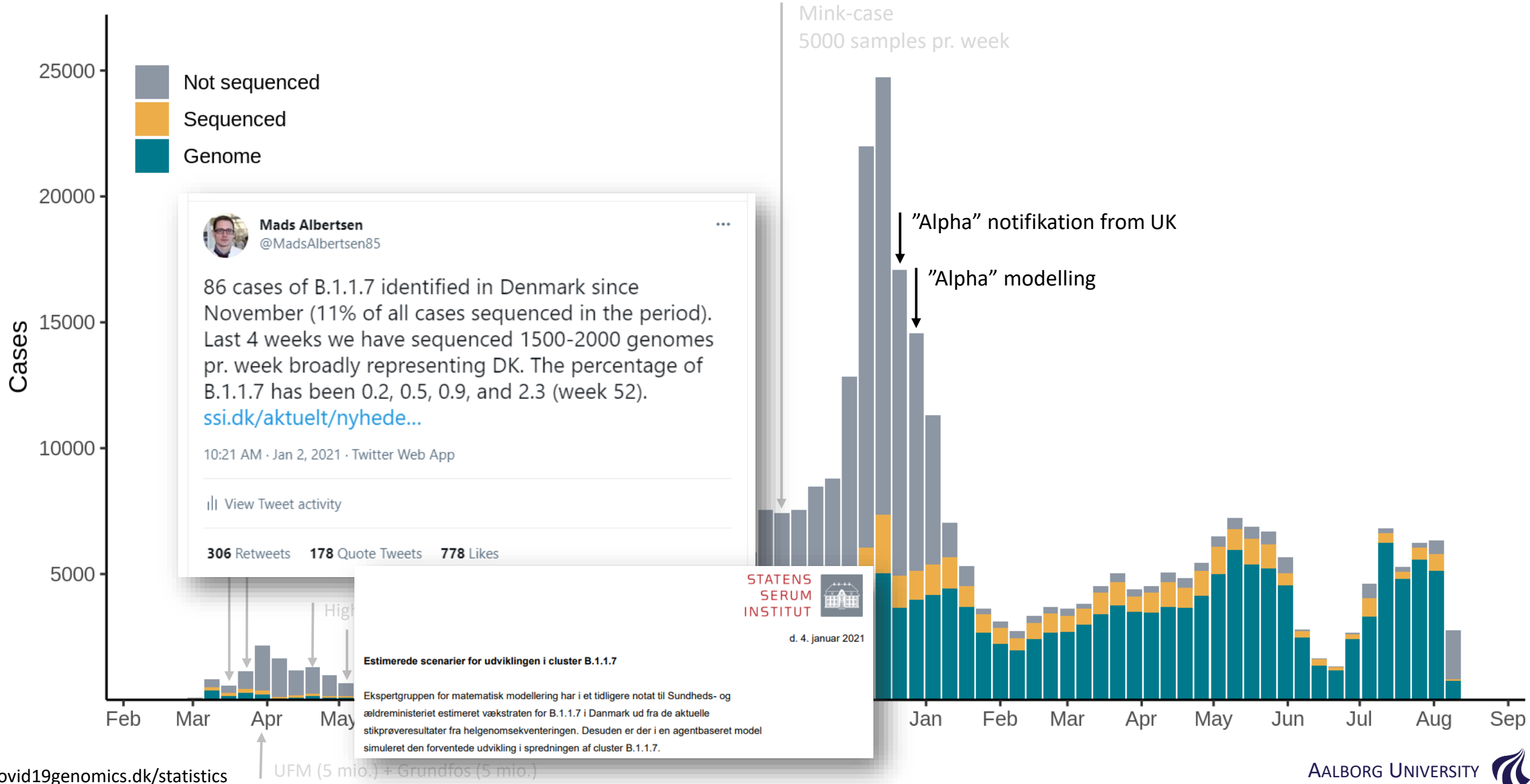
9:26 PM · Dec 23, 2020 · Twitter Web App

We decide t
Grundfos fo
Contact to S
Rektor open

First SARS-

Hj

5000

UFM (5 mio.) + Grundfos (5 mio.)

Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep

covid19genomics.dk/statistics

A brief history of SARS-CoV-2 sequencing in Denmark

Not sequenced
Sequenced
Genome

Mink-case
5000 samples pr. week

"Alpha" notifikation from UK

"Alpha" modelling

Mads Albertsen
@MadsAlbertsen85

86 cases of B.1.1.7 identified in Denmark since November (11% of all cases sequenced in the period). Last 4 weeks we have sequenced 1500-2000 genomes pr. week broadly representing DK. The percentage of B.1.1.7 has been 0.2, 0.5, 0.9, and 2.3 (week 52).
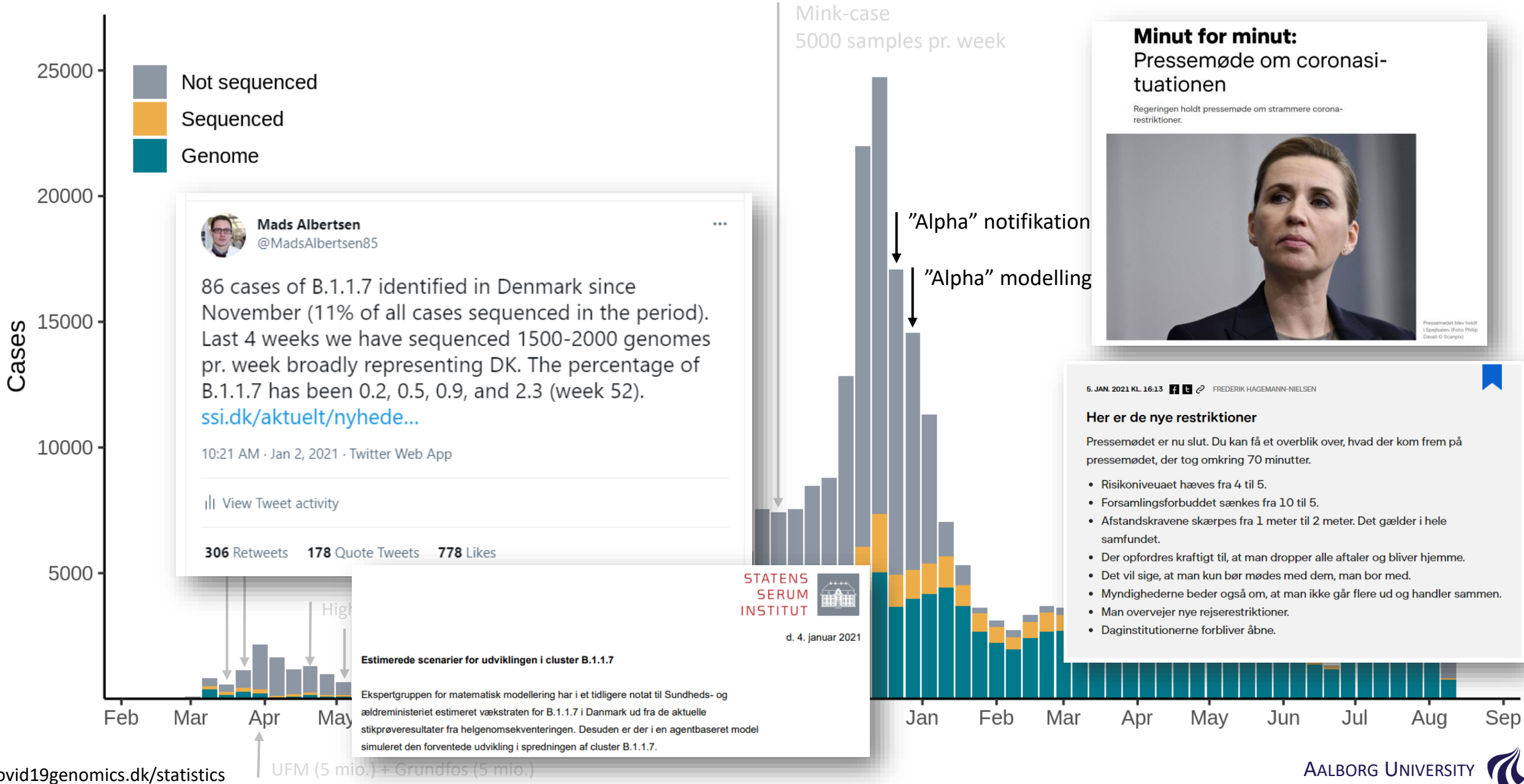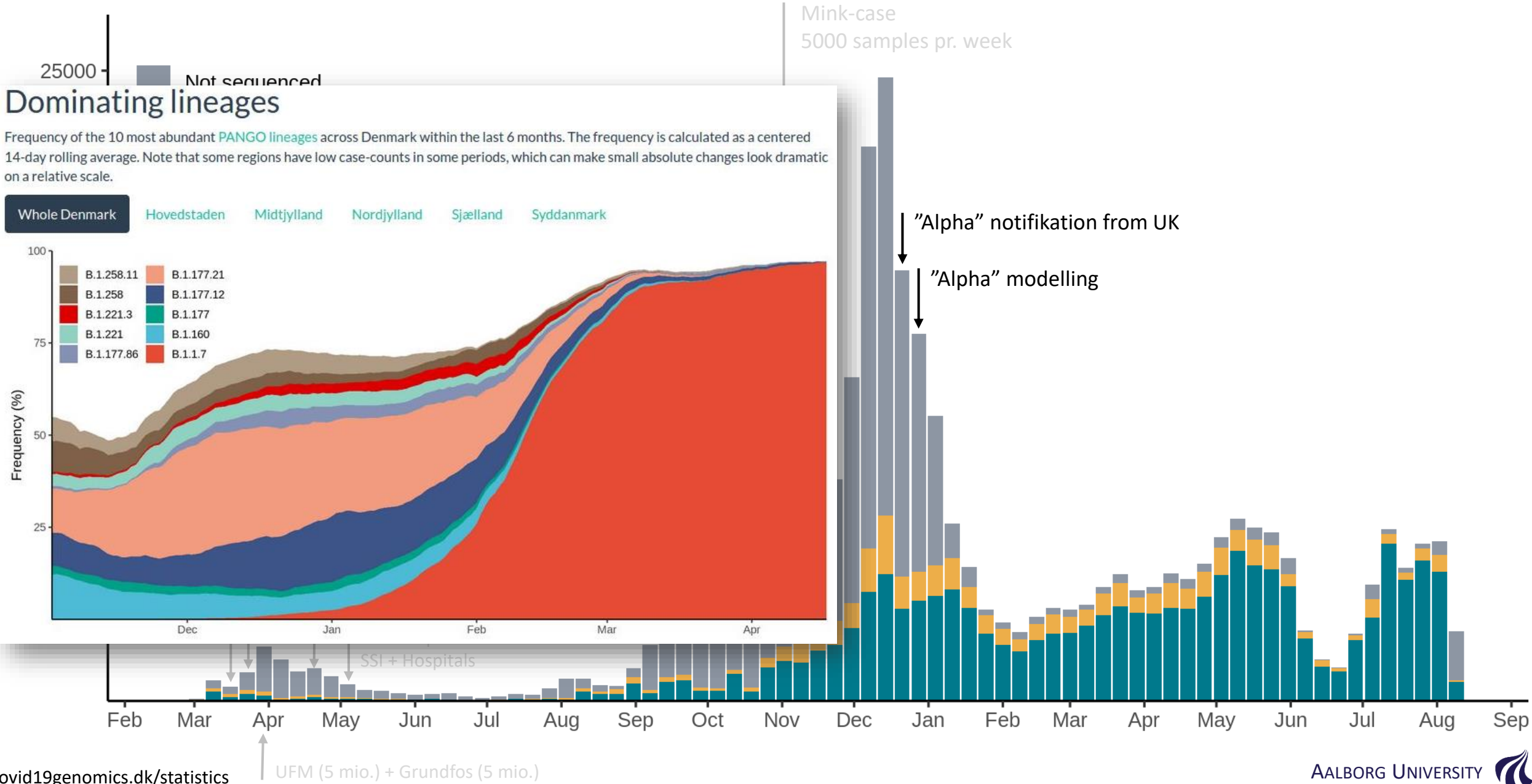ssi.dk/aktuelt/nyhede...

10:21 AM · Jan 2, 2021 · Twitter Web App

306 Retweets   **178** Quote Tweets   **778** Likes

STATENS SERUM INSTITUT

d. 4. januar 2021

Estimerede scenarier for udviklingen i cluster B.1.1.7

Ekspertgruppen for matematisk modellering har i et tidligere notat til Sundheds- og ældreministeriet estimeret vækstraten for B.1.1.7 i Danmark ud fra de aktuelle stikprøveresultater fra helgenomsekventeringen. Desuden er der i en agentbaseret model simuleret den forventede udvikling i spredningen af cluster B.1.1.7.

High

UFM (5 mio.) + Grundfos (5 mio.)

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A brief history of SARS-CoV-2 sequencing in Denmark

Mink-case
5000 samples pr. week

"Alpha" notifikation from UK

"Alpha" modelling

Dominating lineages

Frequency of the 10 most abundant PANGO lineages across Denmark within the last 6 months. The frequency is calculated as a centered 14-day rolling average. Note that some regions have low case-counts in some periods, which can make small absolute changes look dramatic on a relative scale.

Whole Denmark   Hovedstaden   Midtjylland   Nordjylland   Sjælland   Syddanmark

- B.1.258.11
- B.1.258
- B.1.221.3
- B.1.221
- B.1.177.86
- B.1.177.21
- B.1.177.12
- B.1.177
- B.1.160
- B.1.1.7

25000

Not sequenced

SSI + Hospitals

UFM (5 mio.) + Grundfos (5 mio.)

covid19genomics.dk/statistics

A brief history of SARS-CoV-2 sequencing in Denmark

A brief history of SARS-CoV-2 sequencing in Denmark

Mink-case
5000 samples pr. week

25000

Not sequenced

Per Michael Johansen @aaurektor · Mar 11
Verden kigger mod AAU's unikke sekventeringsforskning, der hjælper regeringer med at redde menneskeliv.
Minister @AneHalsboe tog sig i dag tid til at hylde de dygtige forskere @MadsAlbertsen85 og team. Tak for jeres enorme indsats og til ministeren for besøg #dkforsk #COVID19dk

Mads Albertsen
Professor MSO hos Aalborg University
4md. · 🌐

I dag havde vi Statsminister Mette Fredriksen på besøg i laboratoriet Aalborg Universitet til en snak om hvordan vi har opbygget et af verdens bedste programmer til overvågning af virus-varianter i Danmark i samarbejde i ... se mere

Mette F. 'totalt imponeret' af nordjyske forskere - nu takker hun dem
nordjyske.dk · 2 min. læsetid

Local Implementation
SSI + Hospitals

Feb   Mar   Apr   May   Jun   Jul   Aug   Sep   Oct   Nov   Dec   Jan   Feb   Mar   Apr   May   Jun   Jul   Aug   Sep

UFM (5 mio.) + Grundfos (5 mio.)

covid19genomics.dk/statistics

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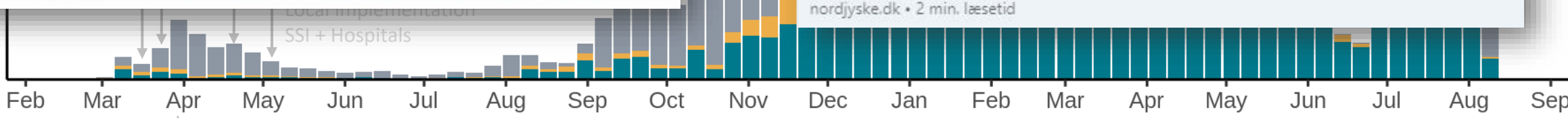
A brief history of SARS-CoV-2 sequencing in Denmark

Covariants.org

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Denmark has the worlds most comprehensive dataset

4,616,355 sequences shared via GISAID since 10 January 2020.
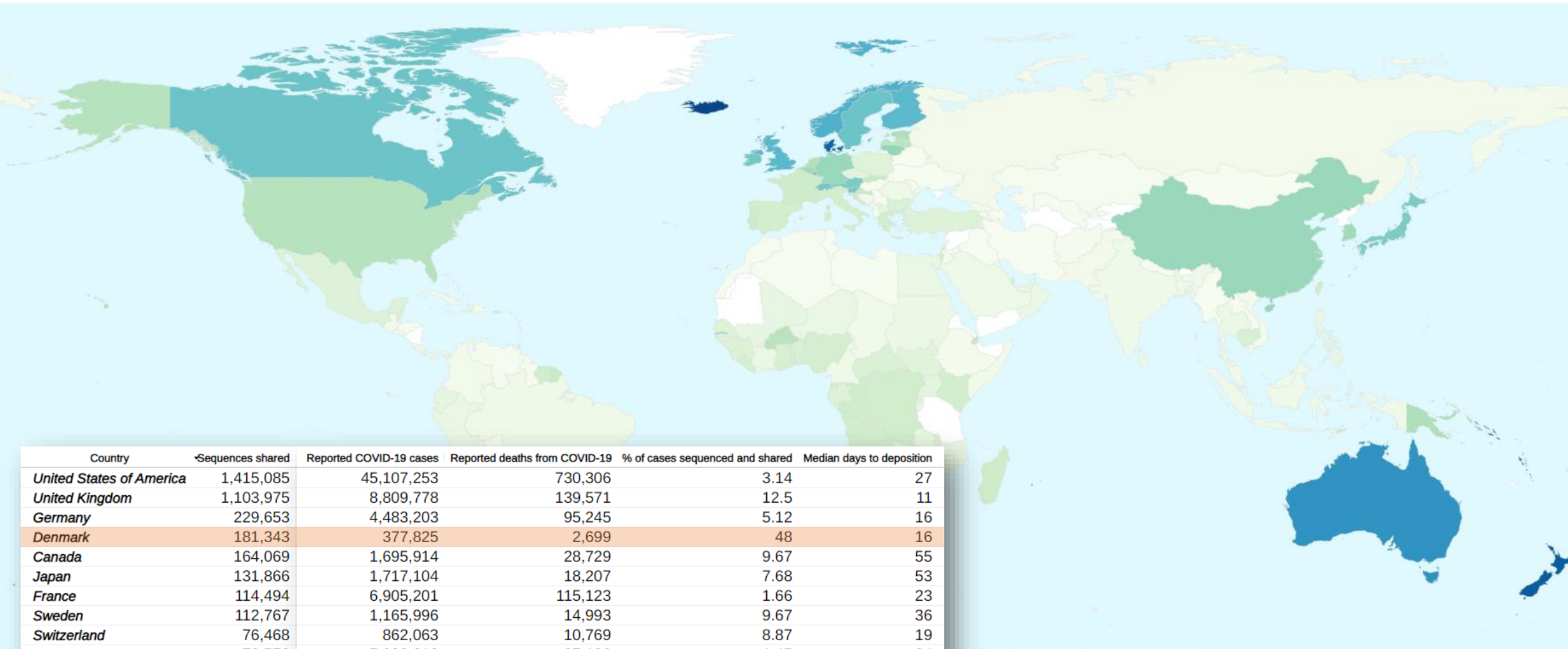
Country	Sequences shared	Reported COVID-19 cases	Reported deaths from COVID-19	% of cases sequenced and shared	Median days to deposition
United States of America	1,415,085	45,107,253	730,306	3.14	27
United Kingdom	1,103,975	8,809,778	139,571	12.5	11
Germany	229,653	4,483,203	95,245	5.12	16
Denmark	181,343	377,825	2,699	48	16
Canada	164,069	1,695,914	28,729	9.67	55
Japan	131,866	1,717,104	18,207	7.68	53
France	114,494	6,905,201	115,123	1.66	23
Sweden	112,767	1,165,996	14,993	9.67	36
Switzerland	76,468	862,063	10,769	8.87	19
Spain	72,576	5,002,218	87,186	1.45	34
India	70,720	34,202,202	455,068	0.207	61
Italy	69,022	4,743,720	131,856	1.46	17
Netherlands	67,335	2,087,859	18,320	3.23	21
Turkey	66,218	7,879,468	69,344	0.84	8

VID-19 cases shared via **GISAID**

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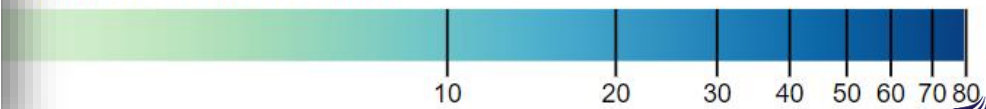
Danish Covid-19 Genome Consortium

Legend:
- Not sequenced
- Sequenced
- Genome

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