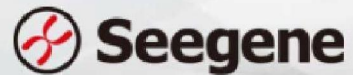


Seegene Solution for emerging COVID-19 Variants

Ver. 1.1

2021-02-01

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COVID-19 variants Alerts in the globe

- Health authorities warn the spread of three virus variants (VOC 202012/01, 501Y.V2, and P.1)
- The transmissibility of these variants is significantly higher than SARS-CoV-2 previously circulating
- In turn, it leads to higher hospitalization and mortality across all age, especially in older or with comorbidities
- At this stage, it is uncertain and no clinical data on their severity or vaccine match/effectiveness

→ The risk of variants is assessed as **HIGH/VERY HIGH**

Summary of variants

Variant information		VOC 202012/01	501Y.V2	501Y.V3
Country first reported		United Kingdom (UK)	South Africa (SA)	Japan (Brazilian traveler)
Nomenclature	GISAID clade	GR	GH	GR
	PANGOLIN lineage	B.1.1.7	B.1.351	P.1
No. Spike (S) gene mutation sites		9	10	12

- Above variants are quickly spreading out all around the world
- They are more likely to become the dominant type

Reference.

<https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/scientific-brief-emerging-variants.html>

<https://www.medicaldevice-network.com/features/covid-19-variant-tests/>



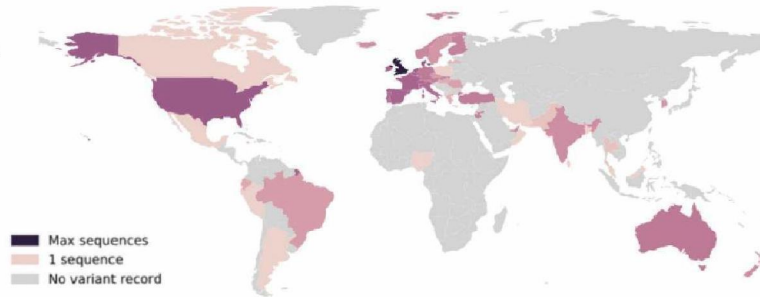
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Global distribution of Variant_VOC 202012/01 (UK)

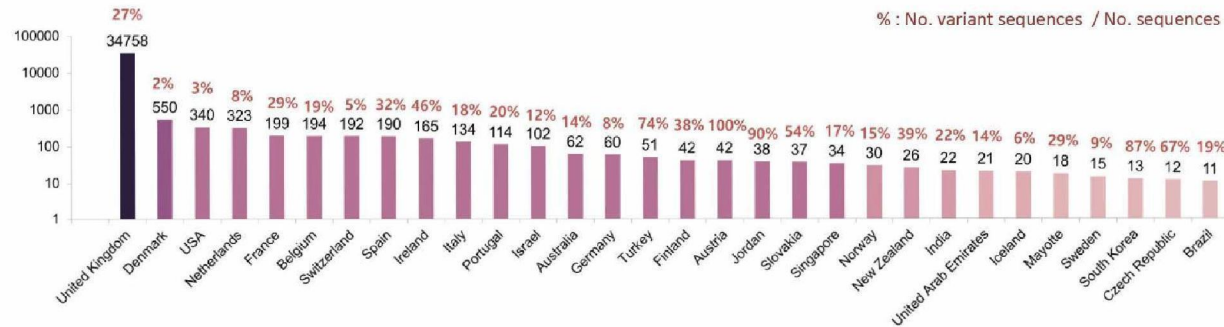
- Found in 73 countries
- Increase transmissibility
- Not related with the severity of disease or vaccine efficacy

As of Jan. 31, 2021

VOC 202012/01 (UK) map



VOC 202012/01 (UK) counts



References.

https://cov-lineages.org/global_report_B.1.351.html

<https://virological.org/t/transmission-of-sars-cov-2-lineage-b-1-1-7-in-england-insights-from-linking-epidemiological-and-genetic-data/576>

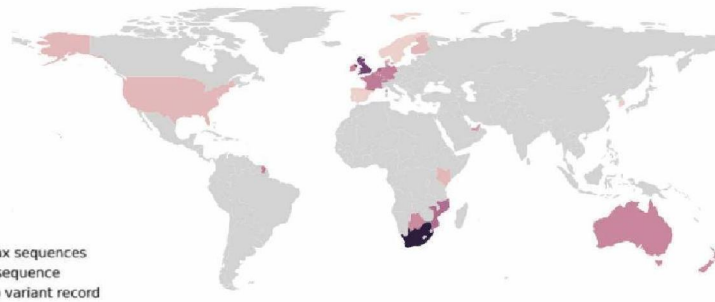


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Global distribution of Variant_501Y.V2 (SA)

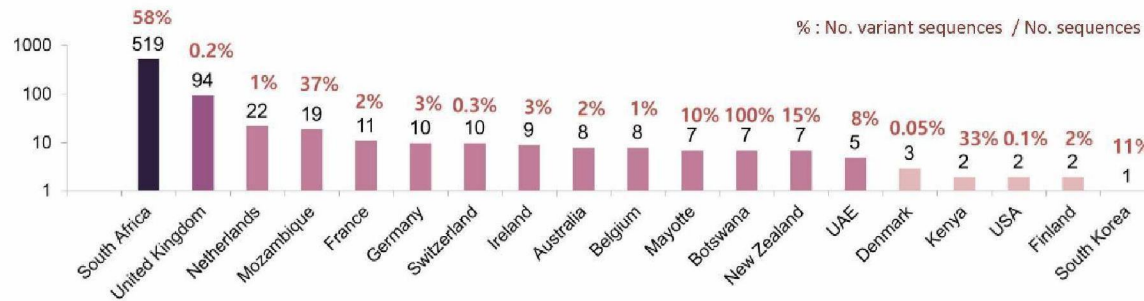
- Found in 31 countries
- Contain the multiple mutation (K417N, E484K, and N501Y) within the receptor-binding domain (RBD) of the S (spike) gene
- Some evidence on affecting antibody neutralization, leading to “evading immunity”

501Y.V2 (SA) map



As of Jan. 31, 2021

501Y.V2 (SA) counts



References.

https://cov-lineages.org/global_report_B.1.351.html

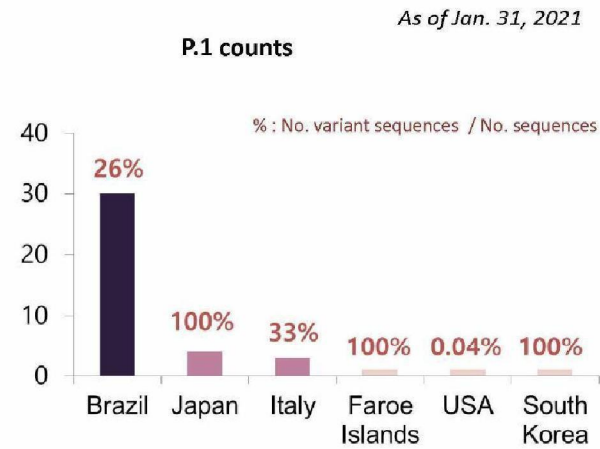
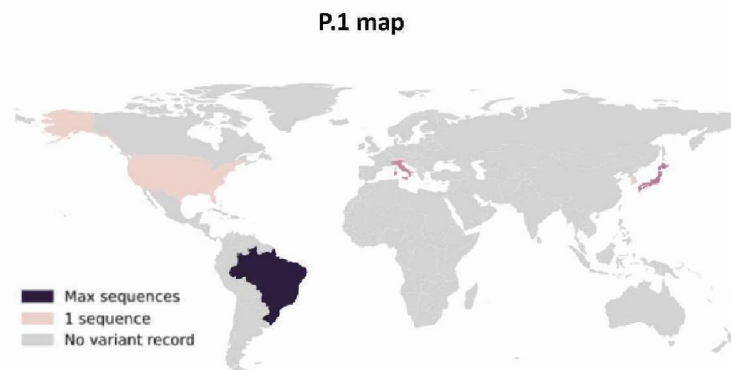
<https://virological.org/t/transmission-of-sars-cov-2-lineage-b-1-1-7-in-england-insights-from-linking-epidemiological-and-genetic-data/576>



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Global distribution of Variant_P1

- Found in 9 countries
- Has the multiple mutation (K417T, E484K, and N501Y) within the receptor-binding domain (RBD) of the S (spike) gene
- Affect transmissibility and antibody-neutralization



References.

https://cov-lineages.org/global_report_P.1.html

 **Seegene**

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Allplex™ SARS-CoV-2 Variants I Assay

- Detect and Differentiate SARS-CoV-2 variants first reported from England, South Africa, and Japan
- Pre-screen new or existing SARS-CoV-2 variant/strain

Specification	Targets	FAM	S_E484K	
		HEX	RdRP	
		Cal 610	S_N501Y	
		Q 670	Endogenous IC	
		Q 705	S_HV69/70 deletion	
	PCR Turn around time	1 hr 55 min		
	Validated specimens	Nasopharyngeal swab, Nasopharyngeal aspirate, Oropharyngeal swab, BAL, Sputum		
	Validated system	Extraction	Seegene STARlet, Seegene NIMBUS, Seeprep32	
		Cycler	CFX96 IVD, CFX96 Dx	
	Regulation	RUO & CE-IVD		

Unique Feature I : Cutting-Edge technology

- Seegene's core technologies have been applied to the development of COVID-19 multiple variants assay
 - mTOCE : Able to detect multiple mutation sites
 - DPO : Able to increase the specificity of primer
 - AI-based *in silico* development : Able to monitor sequences of COVID-19 DB and design optimized diagnostic assay based on the proprietary algorithm by AI
 - And 7 more core technologies applied
- Accurate detection and differentiation three point mutations in S (Spike) gene and highly conserved region in RdRP gene in a single reaction

All in a tube

Mutation site in S gene	Major variant	Allplex SARS-CoV-2 variants I assay
HV 69/70 deletion	VOC 202012/01	Covered and distinguish ALL
E484K	501Y.V2 P.1	
N501Y	VOC 202012/01 501Y.V2 P.1	



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Unique Feature II : Identifying and pre-screening variant/strain

Key features

1. Qualitative detection of SARS-CoV-2
 2. Precisely identification of two mutation sites (i.e., N501Y, HV69/70 deletion) found in VOC 202012/01
 3. Accurately characterization of two mutation sites (i.e., N501Y, E484K) found in 501Y.V2
 4. Pre-screen a new variant or other strains
- ➔ Provide insight and qualified information for surveillance program in each country

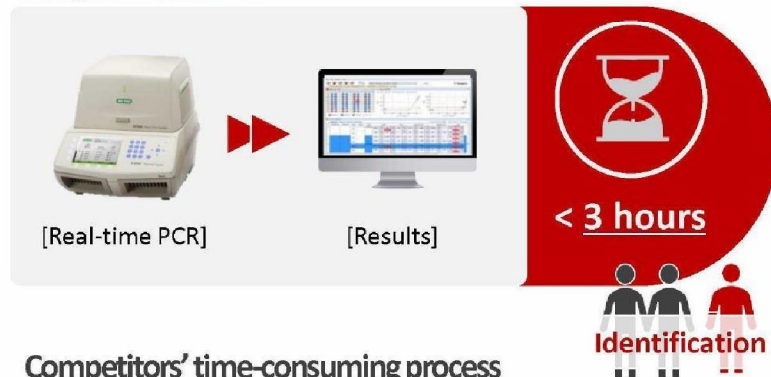
The example of interpretation

Targets	Case 1	Case 2	Case 3			
S_HV69/70 deletion	POS	-	-	-	POS	POS
S_E484K	-	POS	POS	-	POS	POS
S_N501Y	POS	POS	-	POS	-	POS
Interpretation	Variant detected	Variant detected	A new variant or existing strain detected			
Type	A variant with HV69/70 and N501Y found in VOC 202012/01 (UK)	A variant with E484K and N501Y found in 501Y.V2 (SA**) and P.1 (Japan)	Unknown variant/strain ➔ Sequencing for further analysis ➔ Report to surveillance system			

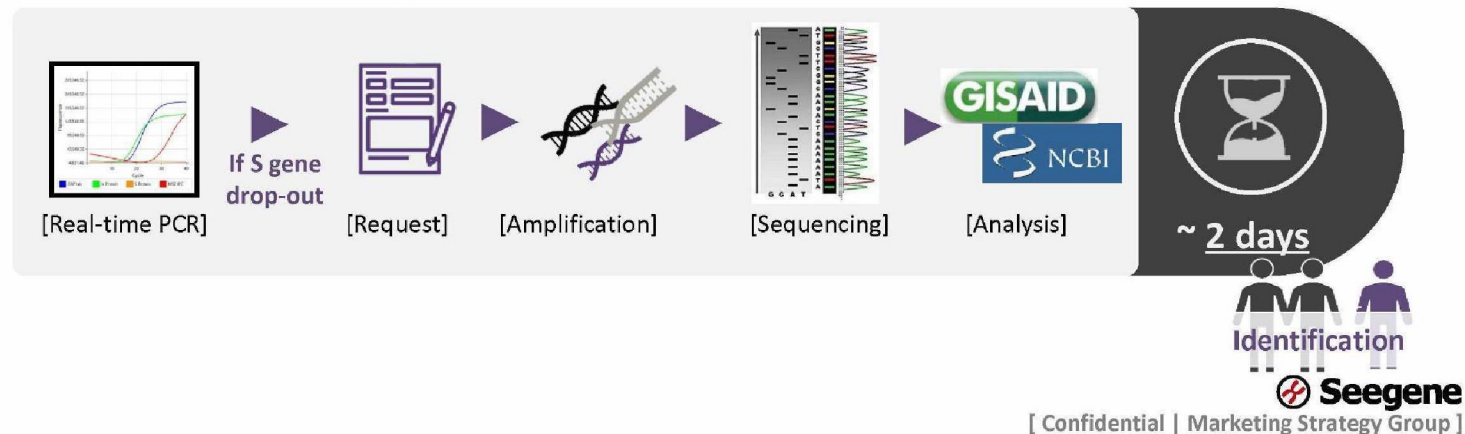
Unique Feature III : Time saving through mass screening

- Mass scaled analysis to filter out variants from COVID-19 positive cases
- Simplify a process to provide results in a half day
- Save time and cost through no need for further analysis

Seegene's solution



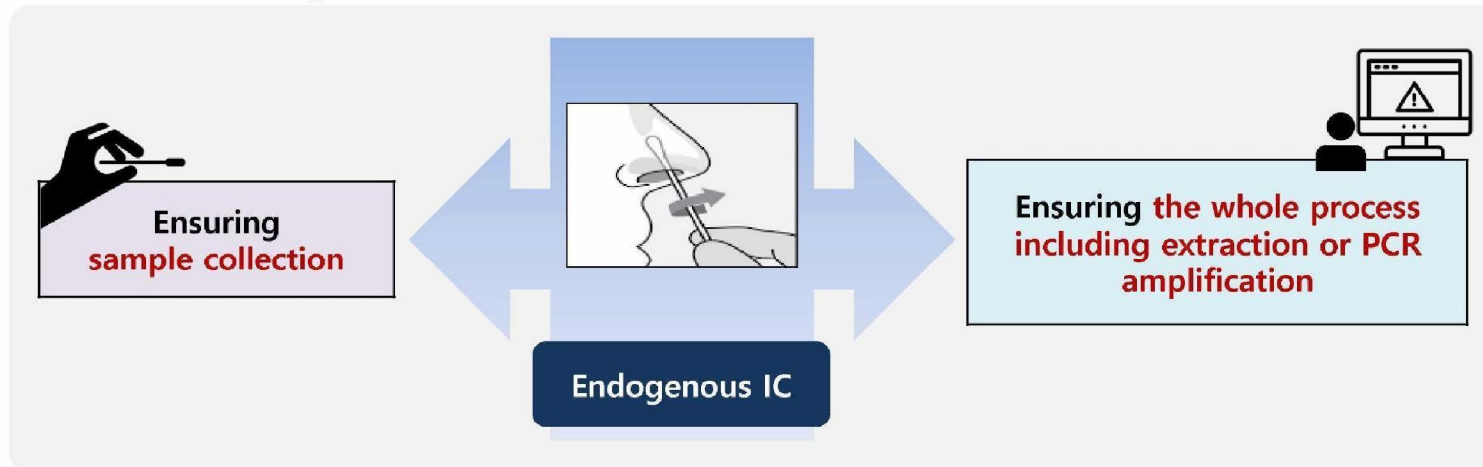
Competitors' time-consuming process



Unique Feature IV : Endogenous internal control (IC)

- Monitor any trouble or mistake in a workflow
- Prevent false negative due to insufficient sampling or sampling error
- Verifying the ENTIRE process

Dual function of endogenous IC



Unique Feature V : Gold standard for SARS-CoV-2 diagnosis

- According to the UK PHE (public health England), popular commercial rapid antigen tests (RAT) below can detect VOC 202012/01 (UK) variant
- However, they all target the Nucleocapsid (N) protein, which means that their performance is not able to distinguish any variants generated by mutated in the Spike (S) protein

RAT Manufacturer	Target	The ability of COVID-19 variant differentiation
Abbott Panbio	Nucleocapsid (N) protein	No
Fortress		
Innova		
Roche / SD Biosensor		
Surescreen		
SEEGENE	3 mutation sites in Spike (S) gene	YES
	RdRP gene	

Reference.

<https://www.gov.uk/government/publications/sars-cov-2-lateral-flow-antigen-tests-evaluation-of-vui-20201201/sars-cov-2-lateral-flow-antigen-tests-evaluation-of-vui-20201201>



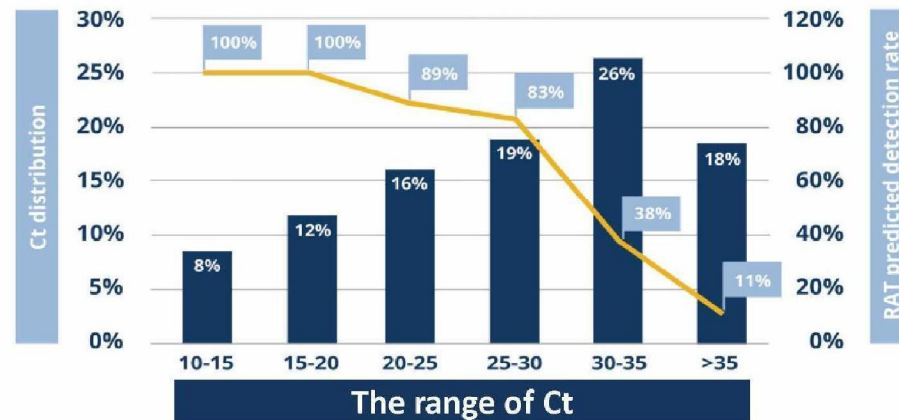
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(CONT'D)

Unique Feature VI : Gold standard for SARS-CoV-2 diagnosis

- The Real-Time PCR is considered as a gold standard because of the most accurate and reliable methods for SARS-CoV-2
- The rapid antigen tests (RAT) are getting popular in the supply chain limitation, but low sensitivity may cause severe results and loss in your community, typically in emerging various variants era

The high risk of false positive of RAT in Ct dependent manner



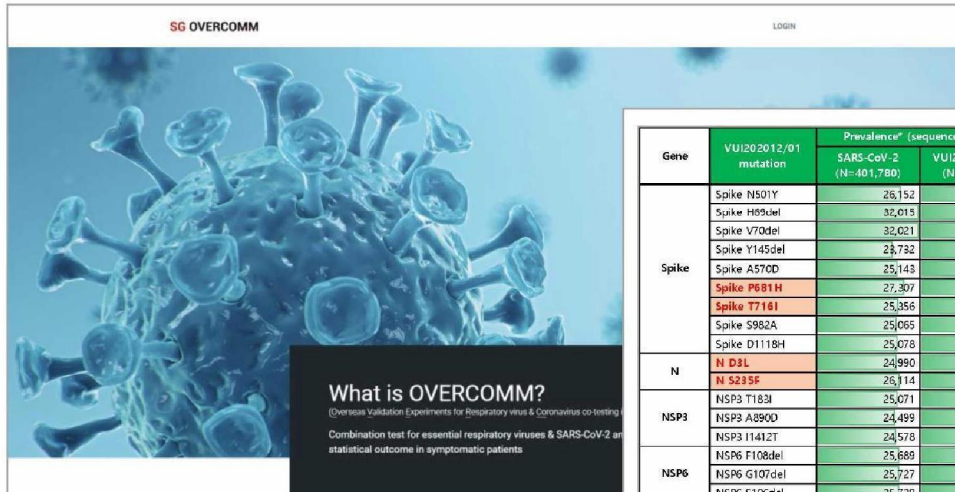
Reference.

SYNLAB_data_on_Rapid_Antigen_Tests_Press_Release_201125_(Germany)



[Confidential | Marketing Strategy Group]

Unique Feature VI : Web-based sharing on variants



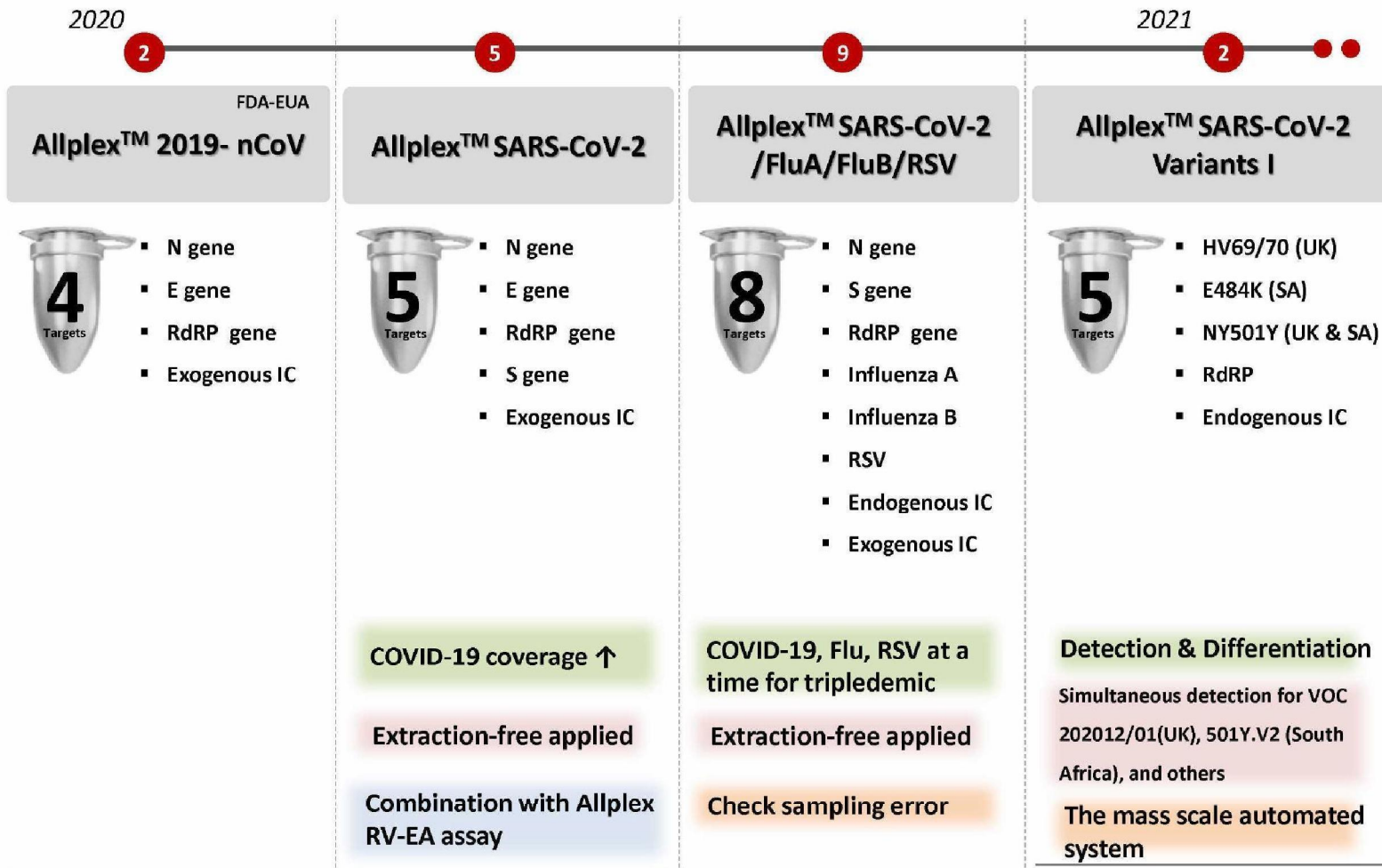
Gene	VUI202012/01 mutation	Prevalence* (sequence based)	
		SARS-CoV-2 (N=401,780)	VUI202012/01 (N=23,087)
Spike	Spike N501Y	26,152	23,087
	Spike H69del	32,013	23,087
	Spike V70del	32,021	23,085
	Spike Y145del	23,732	23,087
	Spike A570D	25,143	23,082
	Spike P681H	27,307	23,065
	Spike T716I	25,356	23,073
	Spike S982A	25,065	23,011
	Spike D1118H	25,078	23,013
	N	N D3L	24,990
N S235F		26,114	22,993
NSP3	NSP3 T183I	25,071	22,731
	NSP3 A890D	24,499	22,483
NSP6	NSP6 F108del	24,578	22,563
	NSP6 G107del	25,689	23,039
	NSP6 S106del	25,727	23,039
NS8	NS8 Q27stop	25,729	23,041
	NS8 R52I	24,766	22,479
	NS8 Y73C	24,629	22,478
		25,073	22,989

Gene	501Y.V2 mutation	Prevalence* (sequence based)		
		SARS-CoV-2 (N=401,781)	501Y.V2 (N=500)	
Spike	Spike N501Y	26,152	500	
	Spike L18F	37,945	139	
	Spike E484K	871	500	
	Spike K417N	545	500	
	Spike D60A	522	464	
	Spike D215G	494	379	
	Spike L242del	533	465	
	Spike L243del	587	465	
	Spike L244del	590	465	
	Spike A701V	999	499	
	Spike R246I	101	86	
	E	E P71L	815	498
	N	N T205I	4,305	500
NSP2	NSP2 T85I	56,299	497	
NSP3	NSP3 K837N	1,164	493	
NSP5	NSP5 K90R	5,389	499	
NS3	NS3 Q57H	85,392	477	
	NS3 S171L	1,942	413	

Regular analysis of SARS-CoV-2 database

- Providing information on a webpage (<https://overcomm.seegene.com/>)
- Fluctuation rate of the major mutation
- Status of product coverage for emerging mutations

Unique Feature VII : Streamlined COVID-19 product portfolio



THANK YOU

Appedix. Mutation sites in S gene of major variants

Variant information		VOC 202012/01	501Y.V2	P.1
No. Spike (S) gene mutation sites		9	10	12
	L18F		YES	YES
	T20N			YES
	P26S			YES
	HV 69/70 deletion	YES		
	D80A		YES	
	D138Y			YES
	Y144 deletion	YES		
	R190S			YES
	D215G		YES	
	L:L 242/244 deletion		YES	
	R246I		YES	
RBD	K417N		YES	
RBD	K417T			YES
RBM in RBD	E484K		YES	YES
RBM in RBD	N501Y	YES	YES	YES
	A570D	YES		
	D614G	YES	YES	YES
	H655Y			YES
	P681H	YES		
	A701V		YES	
	T716I	YES		
	S982A	YES		
	T1027I			YES
	D1118H	YES		
	V1176F			YES

RDB mutations

SARS-CoV-2 RBD	UK	South Africa	Japan
K417	-	K417N	K417T
G446	-	-	
Y449	-	-	
Y453	-	-	
L455	-	-	
F456	-	-	
A475	-	-	
E484		E484K	E484K
F486	-	-	
N487	-	-	
Y489	-	-	
Q493	-	-	
G496	-	-	
Q498	-	-	
T500	-	-	
N501	N501Y	N501Y	
G502	-	-	
Y505	-	-	

RBM

