July 7. 2020 – Moderna's Patent

Lipid Nanoparticles (LNPs) for mRNA Vaccines

has decreased binding affinity to major groove interacting partner, as compared to an unmodified nucleotide).

The polynucleotides, primary constructs, and mmRNA can optionally include other agents (e.g., RNAi-inducing agents, RNAi agents, siRNAs, shRNAs, miRNAs, antisense RNAs, ribozymes, catalytic DNA, tRNA, RNAs that induce triple helix formation, aptamers, vectors, etc.). In some embodiments, the polynucleotides, primary constructs, or mmRNA may include one or more messenger RNAs (mRNAs) and one or more modified nucleoside or nucleotides (e.g., mmRNA molecules). Details for these polynucleotides, primary constructs, and mmRNA follow.

https://www.modernatx.com/sites/default/files/US10703789.pdf

US010703789B2

(12) **United States Patent**
De Fougerolles et al.

(10) **Patent No.: US 10,703,789 B2**
(45) **Date of Patent: *Jul. 7, 2020**

(54) **MODIFIED POLYNUCLEOTIDES FOR THE PRODUCTION OF SECRETED PROTEINS**

(71) Applicant: **ModernaTX, Inc.**, Cambridge, MA (US)

(72) Inventors: **Antonin De Fougerolles**, Waterloo (BE); **Justin Guild**, Framingham, MA (US)

(73) Assignee: **ModernaTX, Inc.**, Cambridge, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **16/438,978**

(22) Filed: **Jun. 12, 2019**

(65) **Prior Publication Data**

US 2020/0017565 A1 Jan. 16, 2020

Related U.S. Application Data

(63) Continuation of application No. 14/987,328, filed on Jan. 4, 2016, now Pat. No. 10,385,106, which is a (Continued)

(51) **Int. Cl.**

A61K 48/00	(2006.01)
A61K 38/17	(2006.01)
A61K 47/54	(2017.01)
A61K 9/127	(2006.01)
C07K 14/535	(2006.01)
C12N 15/88	(2006.01)
A61K 9/50	(2006.01)
C07K 14/47	(2006.01)
A61K 31/7088	(2006.01)
C07K 19/00	(2006.01)
C12N 15/85	(2006.01)
A61K 38/18	(2006.01)
A61K 38/19	(2006.01)
A61K 38/48	(2006.01)
A61K 9/14	(2006.01)
A61K 47/10	(2017.01)
A61K 38/21	(2006.01)
A61K 38/36	(2006.01)
A61K 38/44	(2006.01)
A61K 39/395	(2006.01)

(Continued)

(52) **U.S. Cl.**

CPC ***C07K 14/535*** (2013.01); ***A61K 9/1271*** (2013.01); ***A61K 9/1272*** (2013.01); ***A61K 9/1277*** (2013.01); ***A61K 9/14*** (2013.01); ***A61K 9/5031*** (2013.01); ***A61K 31/7088*** (2013.01); ***A61K 38/1767*** (2013.01); ***A61K 38/1816*** (2013.01); ***A61K 38/1866*** (2013.01); ***A61K 38/191*** (2013.01); ***A61K 38/193*** (2013.01); ***A61K 38/212*** (2013.01); ***A61K 38/215*** (2013.01); ***A61K 38/36*** (2013.01); ***A61K 38/363*** (2013.01); ***A61K 38/44*** (2013.01); ***A61K 38/4833*** (2013.01); ***A61K 38/4846*** (2013.01); ***A61K 39/3955*** (2013.01); ***A61K 47/10*** (2013.01); ***A61K 47/54*** (2017.08); ***A61K 47/542*** (2017.08); ***A61K 48/0033*** (2013.01); ***A61K 48/0066*** (2013.01); ***A61K 48/0075*** (2013.01); ***C07K 14/47*** (2013.01); ***C07K 14/475*** (2013.01); ***C07K 14/505*** (2013.01); ***C07K 14/525*** (2013.01); ***C07K 14/56*** (2013.01); ***C07K 14/565*** (2013.01); ***C07K 14/745*** (2013.01); ***C07K 14/75*** (2013.01); ***C07K 16/2887*** (2013.01); ***C07K 16/32*** (2013.01); ***C07K 19/00*** (2013.01); ***C12N 9/0069*** (2013.01); ***C12N 9/644*** (2013.01); ***C12N 15/85*** (2013.01); ***C12N 15/88*** (2013.01); ***C12Y 113/12007*** (2013.01); ***C12Y 304/21005*** (2013.01); ***C12Y 304/21022*** (2013.01); ***A61K 9/0019*** (2013.01); ***A61K 48/00*** (2013.01); ***C12N 2840/00*** (2013.01)

(58) **Field of Classification Search**

CPC C07H 21/02; C12N 15/67; C12N 15/11

See application file for complete search history.

(56) **References Cited**

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(Continued)

Primary Examiner — Antonio Galisteo Gonzalez
(74) *Attorney, Agent, or Firm* — Clark & Elbing LLP

(57) **ABSTRACT**

A pharmaceutical composition which has a plurality of lipid nanoparticles that has a mean particle size of between 80 nm and 160 nm and contains a modified mRNA encoding a polypeptide. The lipid nanoparticles include a cationic lipid, a neutral lipid, a cholesterol, and a PEG lipid. The mRNA contains a 5'-cap, 5'-UTR, N1-methyl-pseudouridine, a 3'-UTR, and a poly-A region with at least 100 nucleotides.

14 Claims, 14 Drawing Sheets

Specification includes a Sequence Listing.

MODERNA US 10,703,789, B2. July 7, 2020

diameter particle that can remain stable at high temperatures (150° C.) (Grabow and Jaegar, Nature Materials 2012, 11:269-269; herein incorporated by reference in its entirety). Additionally these microsponges may be able to exhibit an extraordinary degree of protection from degradation by ribonucleases.

In another embodiment, the polymer-based self-assembled nanoparticles such as, but not limited to, microsponges, may be fully programmable nanoparticles. The geometry, size and stoichiometry of the nanoparticle may be precisely controlled to create the optimal nanoparticle for delivery of cargo such as, but not limited to, polynucleotides, primary constructs and/or mmRNA.

In one embodiment, the polymer based nanoparticles may comprise a core of the polynucleotides, primary constructs and/or mmRNA disclosed herein and a polymer shell. The polymer shell may be any of the polymers described herein and are known in the art. In an additional embodiment, the polymer shell may be used to protect the polynucleotides, primary construct and/or mmRNA in the core.

In yet another embodiment, the polymer based nanoparticle may comprise a non-nucleic acid polymer comprising

Articles 219, 220: LNP may be a gel, like Hydrogel

- Nanoparticles may form into a gel when injected into the subject
- Polymer-based self-assembled nanoparticles…may be fully programmable

In one embodiment, the semi-conductive and/or metallic nanoparticles may comprise a core of the polynucleotides, primary constructs and/or mmRNA disclosed herein and a polymer shell. The polymer shell may be any of the polymers described herein and are known in the art. In an additional embodiment, the polymer shell may be used to protect the polynucleotides, primary constructs and/or mmRNA in the core.

Gels and Hydrogels

In one embodiment, the polynucleotides, primary constructs and/or mmRNA disclosed herein may be encapsulated into any hydrogel known in the art which may form a gel when injected into a subject. Hydrogels are a network of polymer chains that are hydrophilic, and are sometimes

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found as a colloidal gel in which water is the dispersion medium. Hydrogels are highly absorbent (they can contain over 99% water) natural or synthetic polymers. Hydrogels also possess a degree of flexibility very similar to natural tissue, due to their significant water content. The hydrogel described herein may used to encapsulate lipid nanoparticles which are biocompatible, biodegradable and/or porous.

As a non-limiting example, the hydrogel may be an aptamer-functionalized hydrogel. The aptamer-functionalized hydrogel may be programmed to release one or more polynucleotides, primary constructs and/or mmRNA using nucleic acid hybridization. (Battig et al., J. Am. Chem. Society. 2012 134:12410-12413; herein incorporated by reference in its entirety).

As another non-limiting example, the hydrogel may be a shaped as an inverted opal.

The opal hydrogels exhibit higher swelling ratios and the swelling kinetics is an order of magnitude faster as well. Methods of producing opal hydrogels and description of opal hydrogels are described in International Pub. No. WO2012148684, herein incorporated by reference in its entirety.

In one embodiment, the nucleic acid self-assembled nanoparticles may comprise a core of the polynucleotides, primary constructs or mmRNA disclosed herein and a polymer shell. The polymer shell may be any of the polymers described herein and are known in the art. In an additional embodiment, the polymer shell may be used to protect the polynucleotides, primary constructs and mmRNA in the core.

Polymer-Based Self-Assembled Nanoparticles

Polymers may be used to form sheets which self-assembled into nanoparticles. These nanoparticles may be used to deliver the polynucleotides, primary constructs and mmRNA of the present invention. In one embodiment, these self-assembled nanoparticles may be microsponges formed of long polymers of RNA hairpins which form into crystalline 'pleated' sheets before self-assembling into microsponges. These microsponges are densely-packed sponge like microparticles which may function as an efficient carrier and may be able to deliver cargo to a cell. The microsponges may be from 1 um to 300 nm in diameter. The microsponges may be complexed with other agents known in the art to form larger microsponges. As a non-limiting example, the microsponge may be complexed with an agent to form an outer layer to promote cellular uptake such as polycation polyethyleneime (PEI). This complex can form a 250-nm

Polymer Journal

Review | Published: 08 May 2020

Graphene oxide-incorporated hydrogels for biomedical applications

Jongdarm Yi, Goeun Choe, Junggeon Park & Jae Young Lee

Polymer Journal **52**, 823–837 (2020) | Cite this article

1362 Accesses | **14** Citations | **31** Altmetric | Metrics

Abstract

Graphene and graphene derivatives (e.g., graphene oxide (GO)) have been incorporated into hydrogels to improve the properties (e.g., mechanical strength) of conventional hydrogels and/or develop new functions (e.g., electrical conductivity and drug loading/delivery). Unique molecular interactions between graphene derivatives and various small or macromolecules enable the fabrication of various functional hydrogels appropriate for different biomedical applications. In this mini-review, we highlight the recent progress in GO-incorporated hydrogels for biomedical applications while focusing on their specific uses as mechanically strong materials, electrically conductive scaffolds/electrodes, and high-performance drug delivery vehicles.

https://www.nature.com/articles/s41428-020-0350-9

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What is transfection?

Broadly defined, transfection is the process of artificially introducing nucleic acids (DNA or RNA) into cells, utilizing means other than viral infection. Such introductions of foreign nucleic acid using various chemical, biological, or physical methods can result in a change of the properties of the cell, allowing the study of gene function and protein expression in the context of the cell.

In transfection, the introduced nucleic acid may exist in the cells transiently, such that it is only expressed for a limited period of time and does not replicate, or it may be stable and integrate into the genome of the recipient, replicating when the host genome replicates. **Types of Transfection ›**

Transfection terminology

The terminology used for various gene delivery systems has evolved to keep pace with technological advances in the field and further refined to distinguish various methods and cell types.

https://www.thermofisher.com/us/en/home/references/gibco-cell-culture-basics/transfection-basics/introduction-to-transfection.html

July 7. 2020 – Moderna's Patent for Current Vaccine Modified Polynucleotide or Production of Secreted Proteins

(57) **ABSTRACT**

A pharmaceutical composition which has a plurality of lipid nanoparticles that has a mean particle size of between 80 nm and 160 nm and contains a modified mRNA encoding a polypeptide. The lipid nanoparticles include a cationic lipid, a neutral lipid, a cholesterol, and a PEG lipid. The mRNA contains a 5'-cap, 5'-UTR, N1-methyl-pseudouridine, a 3'-UTR, and a poly-A region with at least 100 nucleotides.

https://www.modernatx.com/sites/default/files/US10703789.pdf

US010703789B2

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(65) **Prior Publication Data**

US 2020/0017565 A1 Jan. 16, 2020

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(63) Continuation of application No. 14/987,328, filed on Jan. 4, 2016, now Pat. No. 10,385,106, which is a (Continued)

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A61K 38/44	(2006.01)
A61K 39/395	(2006.01)

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(58) **Field of Classification Search**

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See application file for complete search history.

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Primary Examiner — Antonio Galisteo Gonzalez
(74) *Attorney, Agent, or Firm* — Clark & Elbing LLP

(57) **ABSTRACT**

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14 Claims, 14 Drawing Sheets

Specification includes a Sequence Listing.

TABLE 3-continued

3'-Untranslated Regions

3' UTR Identifier	Name/ Description	Sequence	SEQ ID NO.
		TCTGCTCCCTTCTCACCCACGCTGACCTCCTGC CGAAGGAGCAACGCAACAGGAGAGGGGTCTG CTGAGCCTGGCGAGGGTCTGGGAGGGACCAG GAGGAAGGCGTGCTCCCTGCTCGCTGTCCTGG CCCTGGGGGAGTGAGGGAGACAGACACCTGG GAGAGCTGTGGGGAAGGCACTCGCACCGTGC TCTTGGGAAGGAAGGAGACCTGGCCCTGCTC ACCACGGACTGGGTGCCTCGACCTCCTGAATC CCCAGAACACAACCCCCCTGGGCTGGGGTGG TCTGGGGAACCATCGTGCCCCCGCCTCCCGCC TACTCCTTTTTAAGCTT	
3UTR-015	Plod1; procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1	TTGGCCAGGCCTGACCCTCTTGGACCTTTCTT CTTTGCCGACAACCACTGCCCAGCAGCCTCTG GGACCTCGGGGTCCCAGGGAACCCAGTCCAG CCTCCTGGCTGTTGACTTCCCATTGCTCTTGGA GCCACCAATCAAAGAGATTCAAAGAGATTCC TGCAGGCCAGAGGCGGAACACACCTTTATGG CTGGGGCTCTCCGTGGTGTTCTGGACCCAGCC CCTGGAGACACCATTCACTTTTACTGCTTTGT AGTGACTCGTGCTCTCCAACCTGTCTTCCTGA AAAACCAAGGCCCCCTTCCCCCACCTCTTCCA TGGGGTGAGACTTGAGCAGAACAGGGGCTTC CCCAAGTTGCCCAGAAAGACTGTCTGGGTGA GAAGCCATGGCCAGAGCTTCTCCCAGGCACA GGTGTTGCACCAGGGACTTCTGCTTCAAGTTT TGGGGTAAAGACACCTGGATCAGACTCCAAG GGCTGCCCTGAGTCTGGGACTTCTGCCTCCAT GGCTGGTCATGAGAGCAAACCGTAGTCCCCT GGAGACAGCGACTCCAGAGAACCTCTTGGGA GACAGAAGAGGCATCTGTGCACAGCTCGATC TTCTACTTGCCTGTGGGGAGGGGAGTGACAG GTCCACACACCACACTGGGTCACCCTGTCCTG GATGCCTCTGAAGAGAGGGACAGACCGTCAG AAACTGGAGAGTTTCTATTAAAGGTCATTTAA ACCA	19
3UTR-016	Nucb1; nucleobindin 1	TCCTCCGGGACCCCAGCCCTCAGGATTCCTGA TGCTCCAAGGCGACTGATGGGCGCTGGATGA AGTGGCACAGTCAGCTTCCCTGGGGGCTGGTG TCATGTTGGGCTCCTGGGGCGGGGGCACGGC CTGGCATTTCACGCATTGCTGCCACCCCAGGT CCACCTGTCTCCACTTTCACAGCCTCCAAGTC TGTGGCTCTTCCCTTCTGTCCTCCGAGGGGCTT GCCTTCTCTCGTGTCCAGTGAGGTGCTCAGTG ATCGGCTTAACTTAGAGAAGCCCGCCCCCTCC CCTTCTCCGTCTGTCCCAAGAGGGTCTGCTCT GAGCCTGCGTTCCTAGGTGGCTCGGCCTCAGC TGCCTGGGTTGTGGCCGCCCTAGCATCCTGTA TGCCCACAGCTACTGGAATCCCCGCTGCTGCT CCGGGCCAAGCTTCTGGTTGATTAATGAGGGC ATGGGGTGGTCCCTCAAGACCTTCCCCTACCT TTTGTGGAACCAGTGATGCCTCAAAGACAGTG	20

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It should be understood that those listed in the previous tables are examples and that any UTR from any gene may be incorporated into the respective first or second flanking region of the primary construct. Furthermore, multiple wild-

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type UTRs of any known gene may be utilized. It is also within the scope of the present invention to provide artificial UTRs which are not variants of wild type genes. These UTRs or portions thereof may be placed in the same orientation as in the transcript from which they were selected or may be altered in orientation or location. Hence a 5' or 3' UTR may be inverted, shortened, lengthened, made chimeric with one or more other 5' UTRs or 3' UTRs. As used herein, the term "altered" as it relates to a UTR sequence, means that the UTR has been changed in some way in relation to a reference sequence. For example, a 3' or 5' UTR may be altered relative to a wild type or native UTR by the change in orientation or location as taught above or may be altered by the inclusion of additional nucleotides, deletion of nucleotides, swapping or transposition of nucleo-

Vector Amplification

The vector containing the primary construct is then amplified and the plasmid isolated and purified using methods known in the art such as, but not limited to, a maxi prep using the Invitrogen PURELINK™ HiPure Maxiprep Kit (Carlsbad, Calif.).

Plasmid Linearization

The plasmid may then be linearized using methods known in the art such as, but not limited to, the use of restriction enzymes and buffers. The linearization reaction may be purified using methods including, for example Invitrogen's PURELINK™ PCR Micro Kit (Carlsbad, Calif.), and HPLC based purification methods such as, but not limited to, strong

TABLE 4

Primers and Probes

Primer/ Probe Identifier	Sequence (5'-3')	Hybridization target	SEQ ID NO.
UFP	TTGGACCCTCGTACAG AAGCTAATACG	cDNA Template	22
URP	T_{x160}CTTCCTACTCAG GCTTTATTCAAAGACC A	cDNA Template	23
GBA1	CCTTGACCTTCTGGAA CTTC	Acid glucocere-brosidase	24
GBA2	CCAAGCACTGAAACGG ATAT	Acid glucocere-brosidase	25
LUC1	GATGAAAAGTGCTCCA AGGA	Luciferase	26
LUC2	AACCGTGATGAAAAGG TACC	Luciferase	27
LUC3	TCATGCAGATTGGAAA GGTC	Luciferase	28

A cDNA template may be synthesized by having a linearized plasmid undergo polymerase chain reaction (PCR). Table 4 is a listing of primers and probes that may be usefully in the PCR reactions of the present invention. It should be understood that the listing is not exhaustive and that primer-probe design for any amplification is within the skill of those in the art. Probes may also contain chemically modified bases to increase base-pairing fidelity to the target molecule and base-pairing strength. Such modifications may include 5-methyl-Cytidine, 2,6-di-amino-purine, 2'-fluoro, phosphoro-thioate, or locked nucleic acids.

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A new brilliantly blue-emitting luciferin-luciferase system from *Orfelia fultoni* and Keroplatinae (Diptera)

Vadim R. Viviani[1,2✉], Jaqueline R. Silva[1], Danilo T. Amaral[1], Vanessa R. Bevilaqua[2], Fabio C. Abdalla[1], Bruce R. Branchini[3] & Carl H. Johnson[4]

Larvae of *O. fultoni* (Keroplatidae: Keroplatinae), which occur along river banks in the Appalachian Mountains in Eastern United States, produce the bluest bioluminescence among insects from translucent areas associated to black bodies, which are located mainly in the anterior and posterior parts of the body. Although closely related to *Arachnocampa spp* (Keroplatidae: Arachnocampininae), *O.fultoni* has a morphologically and biochemically distinct bioluminescent system which evolved independently, requiring a luciferase enzyme, a luciferin, a substrate binding fraction (SBF) that releases luciferin in the presence of mild reducing agents, molecular oxygen, and no additional cofactors. Similarly, the closely related *Neoceroplatus spp*, shares the same kind of luciferin-luciferase system of *Orfelia fultoni*. However, the molecular properties, identities and functions of luciferases, SBF and luciferin of *Orfelia fultoni* and other luminescent members of the Keroplatinae subfamily still remain to be fully elucidated. Using *O. fultoni* as a source of luciferase, and the recently discovered non-luminescent cave worm *Neoditomiya* sp as the main source of luciferin and SBF, we isolated and initially characterized these compounds. The luciferase of *O. fultoni* is a stable enzyme active as an apparent trimer (220 kDa) composed of ~70 kDa monomers, with an optimum pH of 7.8. The SBF, which is found in the black bodies in *Orfelia fultoni* and in smaller dark granules in *Neoditomiya sp*, consists of a high molecular weight complex of luciferin and proteins, apparently associated to mitochondria. The luciferin, partially purified from hot extracts by a combination of anion exchange chromatography and TLC, is a very polar and weakly fluorescent compound, whereas its oxidized product displays blue

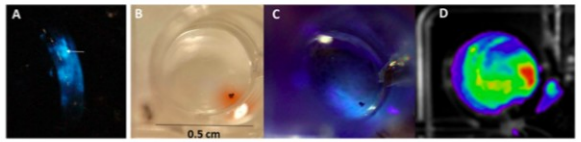
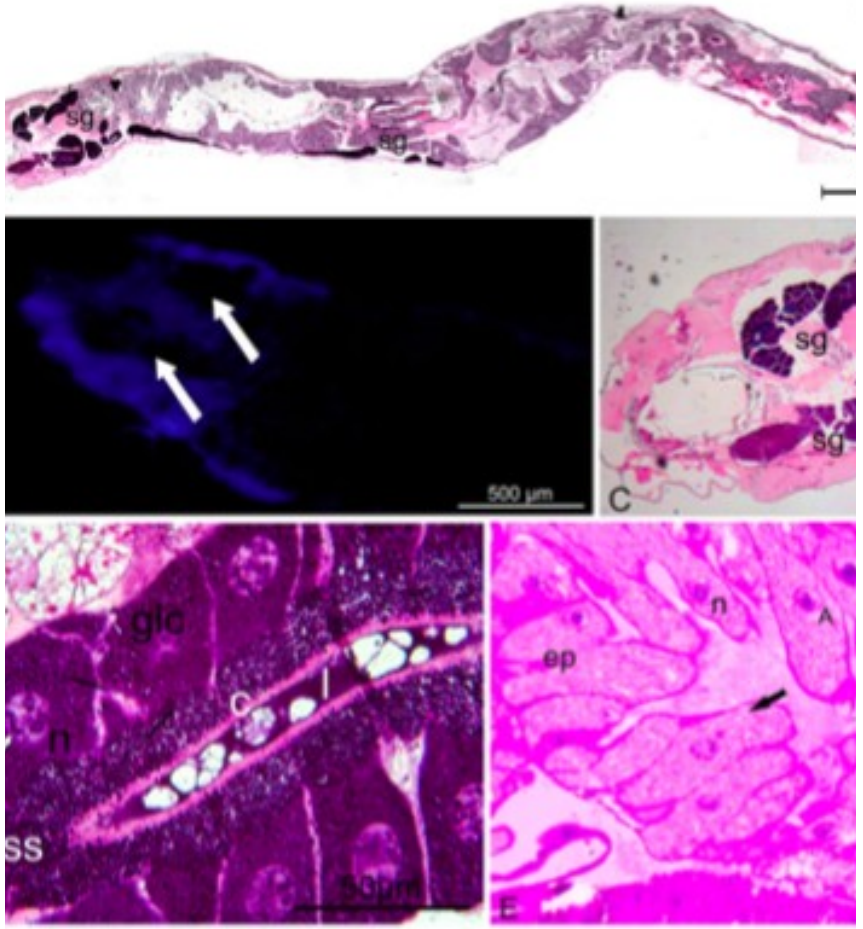
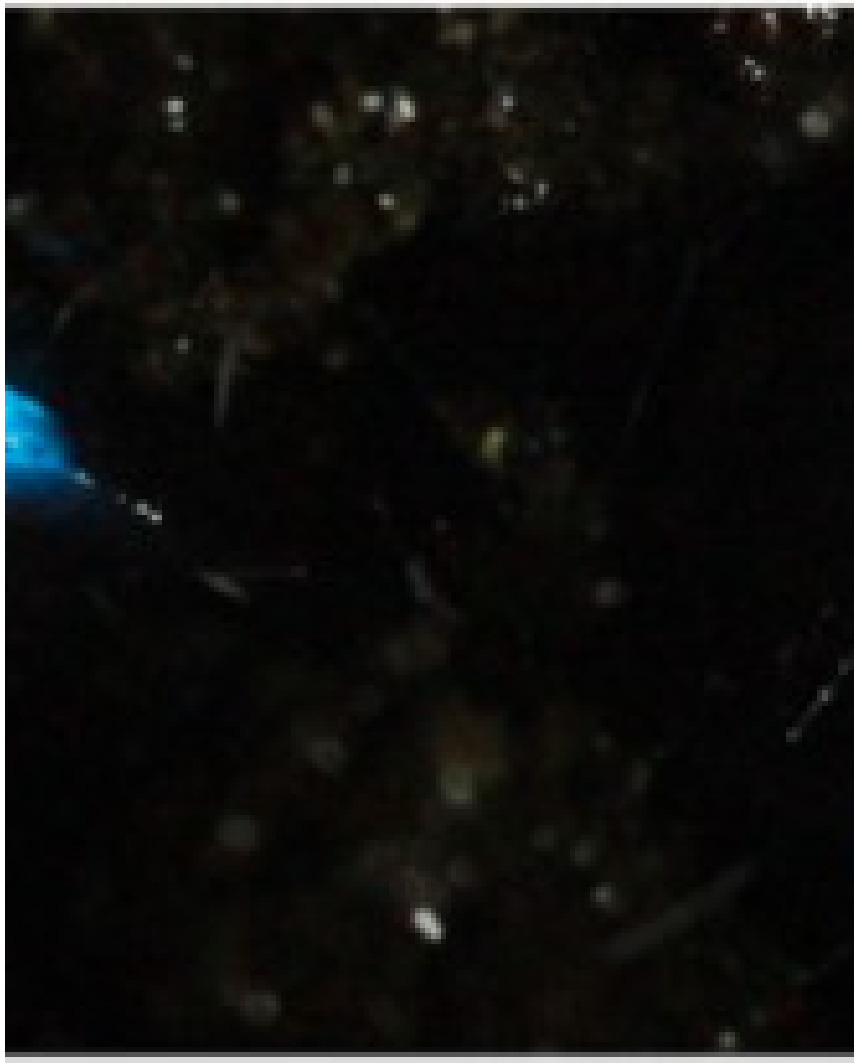


Figure 3. Bioluminescence, pigmentation and fluorescence associated with *Orfelia fultoni* black bodies: (**A**) *Orfelia* thorax evidencing bioluminescent areas surrounding the black bodies; (**B**) DTT-induced release of brownish-orange pigment; (**C**) associated blue fluorescence released by black bodies upon treatment with DTT and UV irradiation and (**D**) CCD-image of bioluminescence associated with the black bodies.



e 2. (**A**) Longitudinal section of the *Orfelia* larvae, showing paired tubular stru
om the anterior to the posterior part of the larvae, HE. (**B**) Total preparation of
a larvae under fluorescence. Notice blue fluorescence surround the black struct
alic-thorax section showing that the black structures saw in B are the silk glands
andular cells (glc) of *Orfelia* larvae filled with basophil granules (black arrows),
ticular space (ss), crossing the cuticle (c) into the lumen (l). Notice the polyteni
) into the nucleus (n). (**E**) Histological preparation of the epithelial cells (ep) of
ng polytenic chromosomes inside the nuclei (n) and vacuolization like (black a



a of *Orfelia fultoni* bioluminescence.

https://www.nature.com/articles/s41598-020-66286-1.pdf

Luciferase assay

Stephen T Smale

PMID: 20439408 DOI: 10.1101/pdb.prot5421

Abstract

When a transient or stable transfection assay is developed for a promoter, a primary objective is to quantify promoter strength. Because transfection efficiency in such assays can be low, promoters are commonly fused to heterologous reporter genes that encode enzymes that can be quantified using highly sensitive assays. The reporter protein's activity or fluorescence within a transfected cell population is approximately proportional to the steady-state mRNA level. A commonly used reporter gene is the luciferase gene from the firefly Photinus pyralis. This gene encodes a 61-kDa enzyme that oxidizes D-luciferin in the presence of ATP, oxygen, and Mg(++), yielding a fluorescent product that can be quantified by measuring the released light. Including coenzyme A in the reaction enhances the sensitivity of the assay and provides a sustained light reaction. In this protocol, cells transfected with a luciferase reporter plasmid are lysed using a detergent-containing buffer. Cell debris is removed by microcentrifugation and luciferase activity is measured using a luminometer. Some luminometers directly inject the reagents into the cell lysate. Such automation allows the signal to be measured at a precise time following injection, which can increase the consistency of the results. For manual luminometers, the substrate solution is mixed by hand with the cell lysate, and the fluorescence is read at a defined time following mixing. The luciferase assay is extremely rapid, simple, relatively inexpensive, sensitive, and possesses a broad linear range.

https://pubmed.ncbi.nlm.nih.gov/20439408/

miFiGHT

Cell Lysis Buffers

‹ Protein Extraction

Detergents for Protein Solubilization

Cell Fractionation and Organelle Isolation

Protease and Phosphatase Inhibitors

Cell Lysis Buffers

Membrane Protein Extraction and Isolation

Effective cell lysis and protein extraction for different species of organisms and different cell and tissue types require different buffer formulations. Thermo Scientific and Invitrogen lysis buffers have been optimized and validated with specific tissue types, as well as in primary and cultured mammalian cells. Protein extracts are compatible with most protein assays and typical downstream applications. These convenient single formulation reagents typically allow samples to be processed in 5–10 minutes and offer high protein yields.

Mammalian cell lysis buffers for cultured cells

Composition			
50 mM Tris, pH 7.4	10 mM Tris, pH 7.4	Non-denaturing	25 mM Tris-HCl,
250 mM NaCl	100 mM NaCl	detergent in 25 mM	pH 7.6
5 mM EDTA	1 mM EDTA	bicine buffer (pH	150 mM NaCl
50 mM NaF	1 mM EGTA	7.6)	1% NP-40
1 mM Na_3VO_4	1 mM NaF		1% sodium

Mammalian cell lysis buffers for cultured cells

	NP-40 Cell Lysis Buffer	Cell Lysis Buffer	M-PER Mammalian Protein Extraction Reagent	RIPA Lysis Buffer	IP Lysis Buffer
When to use					
	Recommended for extraction of **cytoplasmic** proteins	Need a harsher buffer than NP-40 or when **cytoplasmic and nuclear** protein extraction is needed	Mild, **non-denaturing** and efficient lysis for **cytoplasmic and nuclear** protein extraction	Extraction of **cytoplasmic and nuclear protein in denaturing** conditions	Formulated specially for **pull-down and immunoprecipitation** assays
Composition					
	50 mM Tris, pH 7.4 250 mM NaCl 5 mM EDTA 50 mM NaF 1 mM Na_3VO_4 1% NP-40 0.02% NaN_3	10 mM Tris, pH 7.4 100 mM NaCl 1 mM EDTA 1 mM EGTA 1 mM NaF 20 mM $Na_4P_2O_7$ 2 mM Na_3VO_4 1% Triton X-100 10% glycerol 0.1% SDS 0.5% deoxycholate	Non-denaturing detergent in 25 mM bicine buffer (pH 7.6)	25 mM Tris-HCl, pH 7.6 150 mM NaCl 1% NP-40 1% sodium deoxycholate 0.1% SDS	A modified RIPA buffer formulation without SDS

https://www.thermofisher.com/us/en/home/life-science/protein-biology/protein-purification-isolation/cell-lysis-fractionation/cell-lysis-total-protein-extraction.html

Vaccines and Related Biological Products Advisory Committee Meeting
October 26, 2021

FDA Briefing Document

EUA amendment request for Pfizer-BioNTech COVID-19 Vaccine for use in children 5 through 11 years of age

https://www.fda.gov/media/153447/download

5 EUA AMENDMENT REQUEST FOR THE PFIZER-BIONTECH COVID-19 VACCINE FOR USE IN CHILDREN 5-11 YEARS OF AGE

Vaccine formulation

Authorization is being requested for a modified formulation of the Pfizer-BioNTech COVID-19 Vaccine. Each dose of this formulation contains 10 µg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2 that is formulated in lipid particles and supplied as a frozen suspension in multiple dose vials.

To provide a vaccine with an improved stability profile, the Pfizer-BioNTech COVID-19 Vaccine for use in children 5-11 years of age uses tromethamine (Tris) buffer instead of the phosphate-buffered saline (PBS) as used in the previous formulation and excludes sodium chloride and potassium chloride. The packaged vials for the new formulation are stored frozen at -90°C to -60°C. The frozen vials may be thawed and stored at refrigerator at 2°C to 8°C for up to 10 weeks.

https://www.fda.gov/media/153447/download

INGREDIENTS AND APPEARANCE

miFiGHT

COMIRNATY
covid-19 vaccine, mrna injection, suspension

PRODUCT INFORMATION			
Product Type	VACCINE	**Item Code (Source)**	NDC:0069-2025
Route of Administration	INTRAMUSCULAR		

ACTIVE INGREDIENT/ACTIVE MOIETY		
Ingredient Name	**Basis of Strength**	**Strength**
TOZINAMERAN (UNII: 5085ZFP6SJ) (TOZINAMERAN - UNII:5085ZFP6SJ)	TOZINAMERAN	0.225 mg in 2.25 mL

INACTIVE INGREDIENTS	
Ingredient Name	**Strength**
ALC-0159 (UNII: PJH39UMU6H)	0.41 mg in 2.25 mL
ALC-0315 (UNII: AVX8DX713V)	3.22 mg in 2.25 mL
SUCROSE (UNII: C151H8M554)	231.8 mg in 2.25 mL
1,2-DISTEAROYL-SN-GLYCERO-3-PHOSPHOCHOLINE (UNII: 043IPI2M0K)	0.7 mg in 2.25 mL
CHOLESTEROL (UNII: 97C5T2UQ7J)	1.4 mg in 2.25 mL
WATER (UNII: 059QF0KO0R)	
TROMETHAMINE (UNII: 023C2WHX2V)	0.45 mg in 2.25 mL
TROMETHAMINE HYDROCHLORIDE (UNII: 383V75M34E)	2.97 mg in 2.25 mL

https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=48c86164-de07-4041-b9dc-f2b5744714e5&version=1

11 DESCRIPTION

SPIKEVAX (COVID-19 Vaccine, mRNA) is a sterile white to off-white suspension for intramuscular injection. Each 0.5 mL dose of SPIKEVAX contains 100 mcg of nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2 virus.

Each 0.5 mL dose of SPIKEVAX also contains the following ingredients: a total lipid content of 1.93 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.31 mg tromethamine, 1.18 mg tromethamine hydrochloride, 0.043 mg acetic acid, 0.20 mg sodium acetate trihydrate, and 43.5 mg sucrose.

https://www.fda.gov/media/155675/download

AGC Biologics' Heidelberg Facility to Further Supply Plasmid DNA for COVID-19 Vaccine

by **David Self** on 6/7/21 7:00 AM

AGC Biologics, a leading global Biopharmaceutical Contract Development and Manufacturing Organization (CDMO), has a
starting mater

"We are honor
make the vacci
Officer, Mark V
materials need

AGC Biologics
BioNTech's mR

"We are honored that BioNTech has entrusted us to become part of their global supply network in an effort to make the vaccine available to as many people as possible around the world," says AGC Biologics Chief Business Officer, Mark Womack. "We are very proud of our efforts to provide our global customers with the essential materials needed to rapidly deliver vaccines in the fight against the COVID-19 pandemic."

AGC Biologics will manufacture and supply BioNTech with pDNA starting material, an essential component of BioNTech's mRNA-based vaccine manufacturing process.

"The team at Heidelberg is enthusiastically embracing this important project with BioNTech," says AGC Biologics General Manager, Heidelberg, Dieter Kramer. "Every team member has a deep sense of pride in our COVID-19 teams and we look forward to supporting BioNTech in the production of their mRNA-based COVID-19 vaccine with Plasmid DNA."

AGC Biologics' Heidelberg facility has over 20 years of experience delivering a very wide range of microbial programs for our customers. In addition, the site is AGC's Center of Excellence for Plasmid DNA (pDNA) production, as part of their end-to-end Cell and Gene Therapy offering.

http://www.agcbio.com/news/agc-biologics-heidelberg-facility-to-further-supply-plasmid-dna-for-covid-19-vaccine

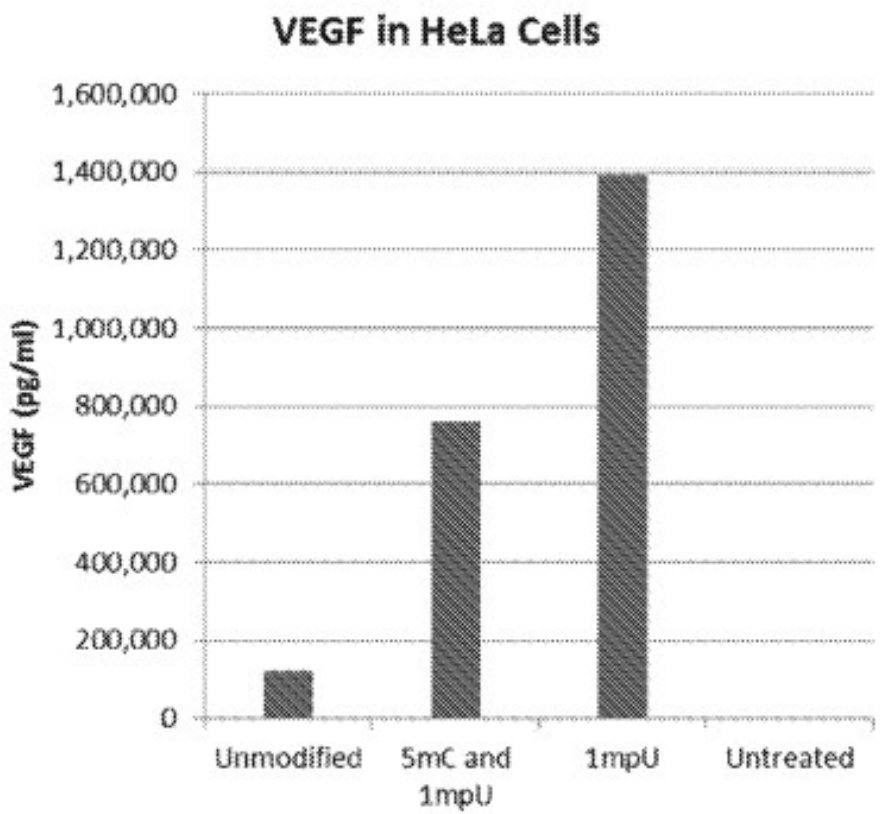
Plasmid DNA is used for a number of downstream applications such as **transfection, sequencing, screening clones, restriction digestion, cloning, and PCR**. A number of methods have been developed for the purification of plasmid DNA from bacteria.

https://www.sciencedirect.com › topics › neuroscience › p...

Plasmid DNA - an overview | ScienceDirect Topics

FIG. 9 is a histogram of VEGF protein production in HeLa cells from VEGF modified mRNA.

FIG. 9

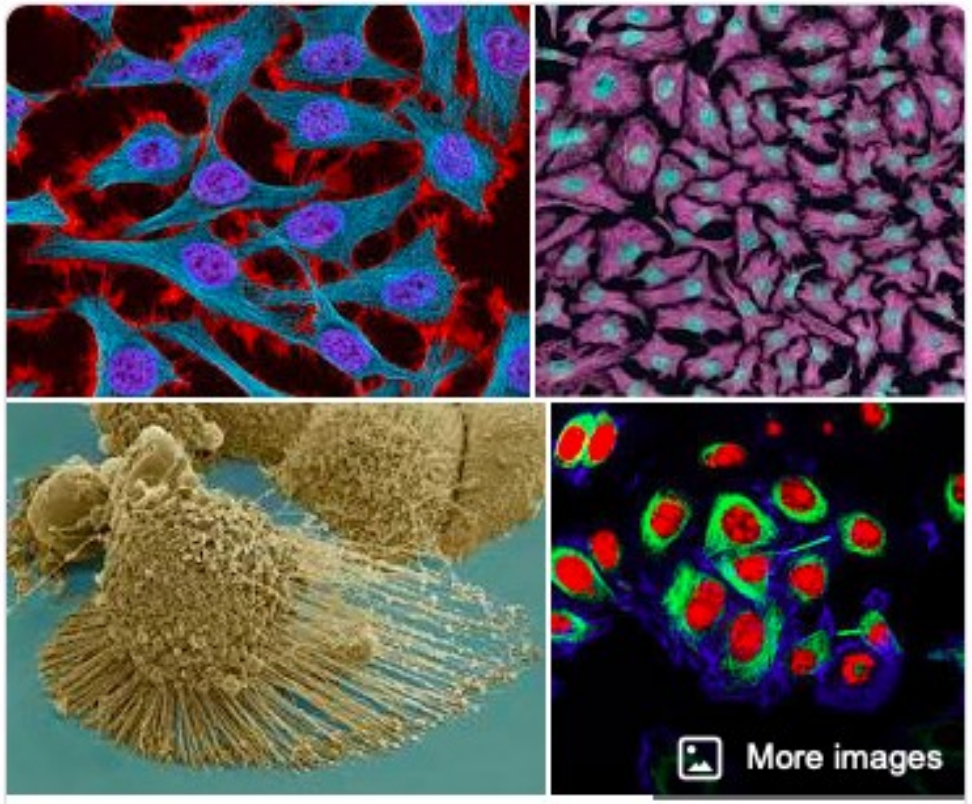


Why are the HeLa cells immortal?

3- HeLa cells are immortal, meaning **they will divide again and again and again**... This performance can be explained by the expression of an overactive telomerase that rebuilds telomeres after each division, preventing cellular aging and cellular senescence, and allowing perpetual divisions of the cells.

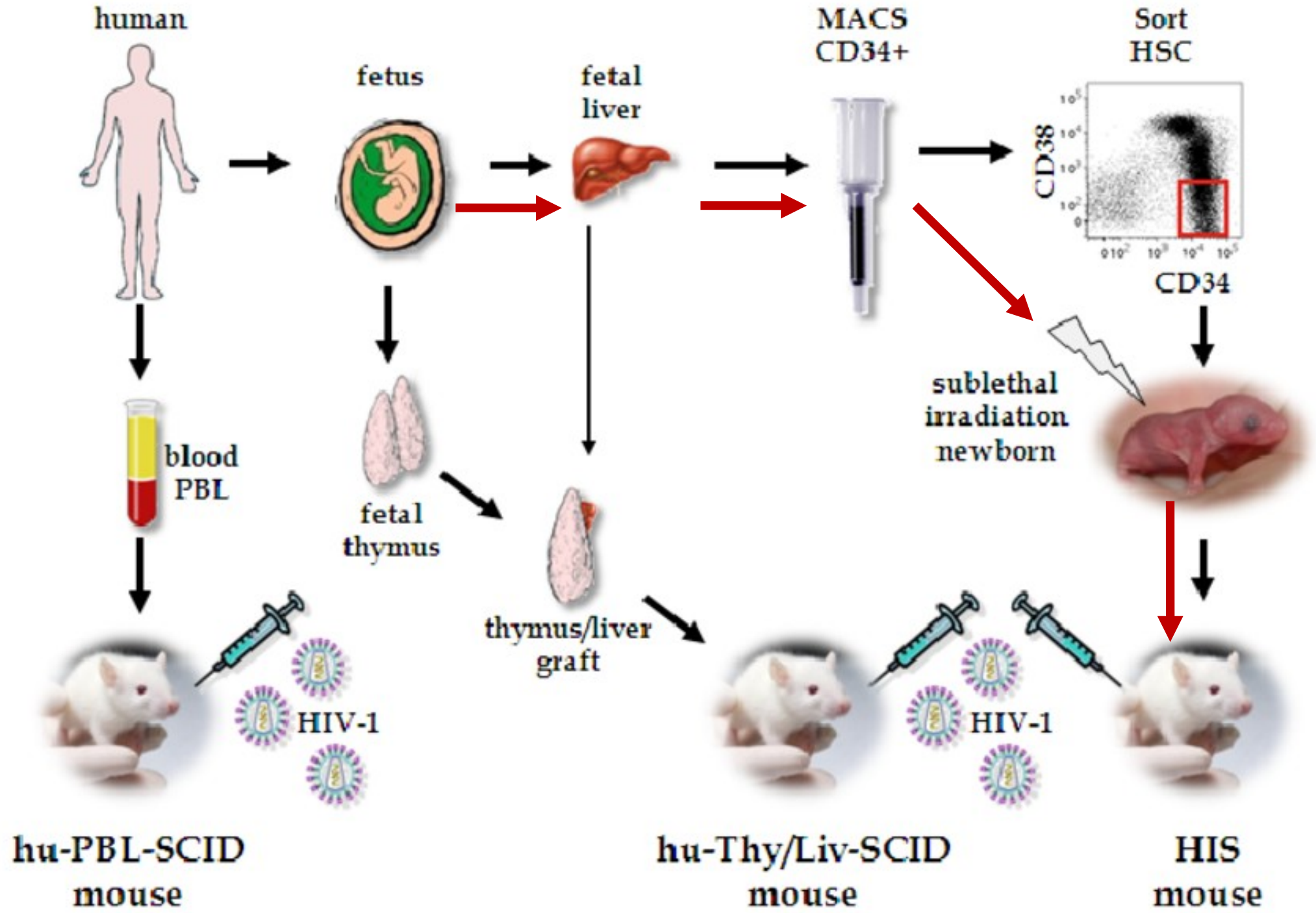
Nov 28, 2017

https://www.tebu-bio.com › blog › hela-cells-the-first-cell...



HeLa

HeLa is an immortal cell line used in scientific research. It is the oldest and most commonly used human cell line. The line is named after and derived from cervical cancer cells taken on February 8, 1951, from Henrietta Lacks, a 31-year-old African-American mother of five, who died of cancer on October 4, 1951. Wikipedia


human
fetus
fetal liver
MACS CD34+
Sort HSC
CD38
CD34
blood PBL
fetal thymus
thymus/liver graft
sublethal irradiation newborn
HIV-1
HIV-1
hu-PBL-SCID mouse
hu-Thy/Liv-SCID mouse
HIS mouse

IARPA Overview
Mr. Robert Rahmer, Director Office of Analysis Research
Intelligence Advanced Research Projects Activity

Intelligence Advanced Research Projects Activity

IARPA

Creating Advantage through Research and Technology

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

Office of the Director of National Intelligence

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

Point of Contact Information

Dr. Michael Patterson

Program Manager

Office of the Director of National Intelligence

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Washington, DC 20511

Phone: (301) 243-1812

Email: TEI-REX_ProposersDay@IARPA.gov

Website: https://www.iarpa.gov/index.php/research-programs/tei-rex

PROPOSERS' DAY DATE
September 29, 2021

BAA RELEASE DATE
October 19, 2021

PROPOSAL DUE DATE
Monday, 13 December 2021

Biodosimetry measures (KK Notes)

- biological responses to radiation exposure
- physiological, chemical, or biological changes due to radiation exposure

TEI REX
Advancing Biodosimetry

TEI-REX Problem Statement

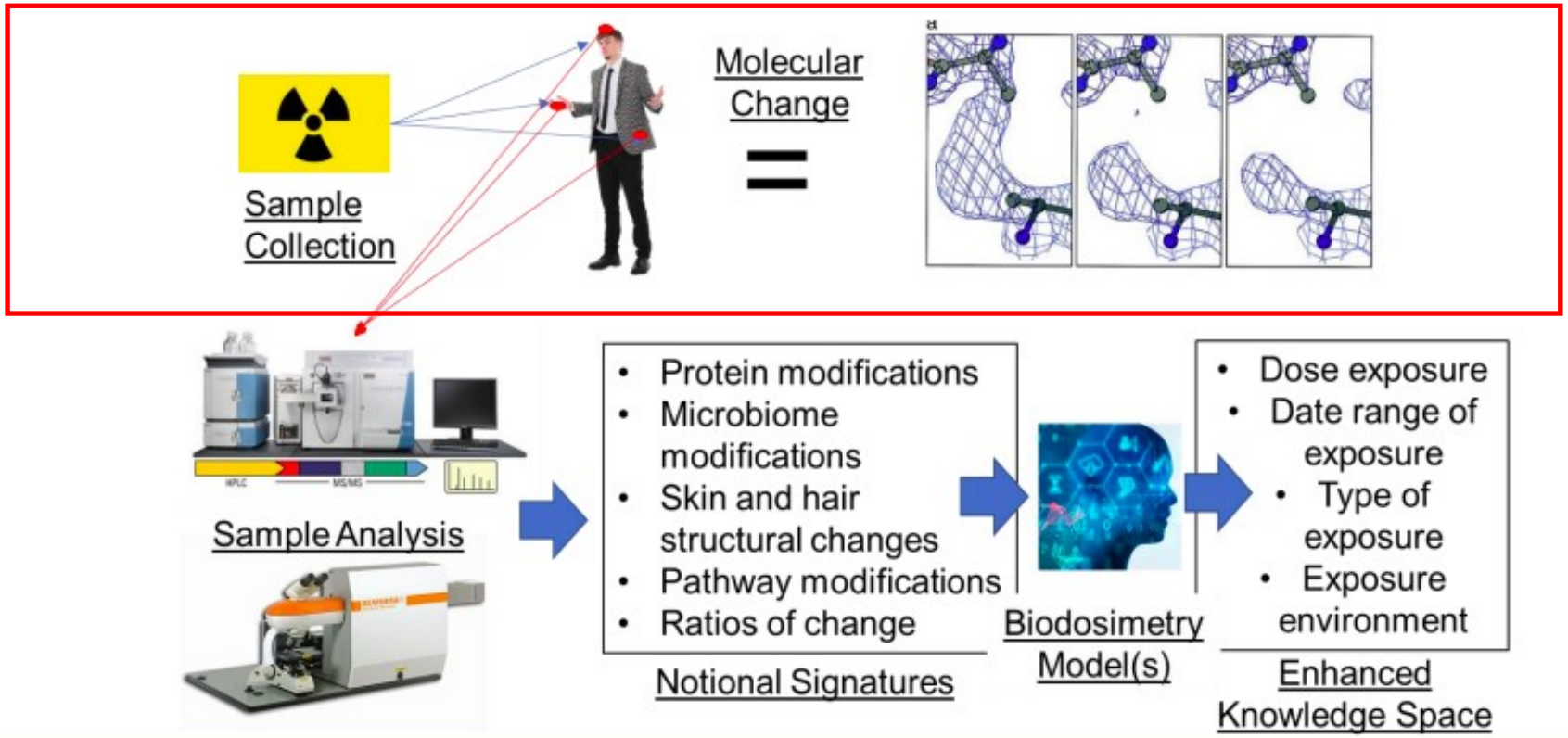
The Intelligence Community (IC) requires new capabilities to identify exposure events associated with lower-dose ionizing radiation which can also expand the overall knowledge of the exposure environment.

- TEI-REX will improve efforts:
  - Investigation of intentional or accidental exposures
  - Protection of IC, uniformed service, and other USG personnel
  - Biodosimetry in remote locations with limited supply chain
  - Counter-proliferation of radiological materials
- Limitations of current approaches:
  - Focus predominately on identifying high dose exposures
  - Reliant upon transient and/or extrapolated biomarkers
  - Require invasive, and often serial, sample collection

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

TEI-REX Program Overview

Develop methodologies and protocols for discovery and characterization of biomarker signatures associated with ionizing radiation exposure, demonstrate detection of robust biomarkers associated with TEI-REX samples, and generate computational biodosimetry models for evaluation of samples to inform towards exposure incidents.



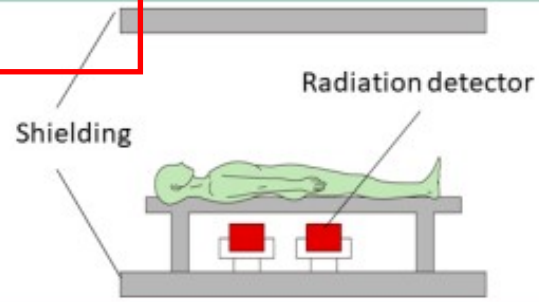
The Problem – Limitations

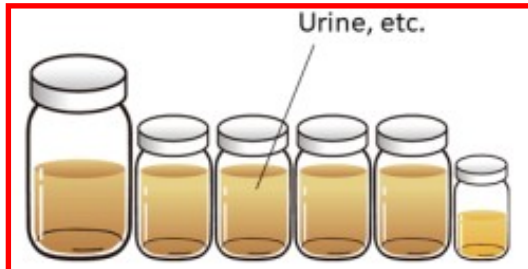
Approaches for retrospectively characterizing an exposure event are limited to mathematical modeling dependent upon extensive knowledge of the event, evaluation of sensors present at the time of exposure, evaluation of absorbed radionuclides, or analysis of transient biomarkers which provide limited information regarding the exposure environment.

Current Approaches:

- Mathematical modeling
- Personal Dosimetry
- Bioassay
  - Out of scope
  - Invasive, obvious, and serial
  - Focused on detecting radionuclide
  - Slow
- Biodosimetry

Direct counting	Bioassay
Directly measure the human body	Indirect measurement
Need to spare time to receive direct measurements	Submit samples (urine, feces, etc.)
Mainly target materials that emit γ-rays	Able to measure all radioactive materials
Short measuring time using the apparatus	Chemical analysis takes time.
Accurate dose assessment	Large margin of error in results of dose assessment





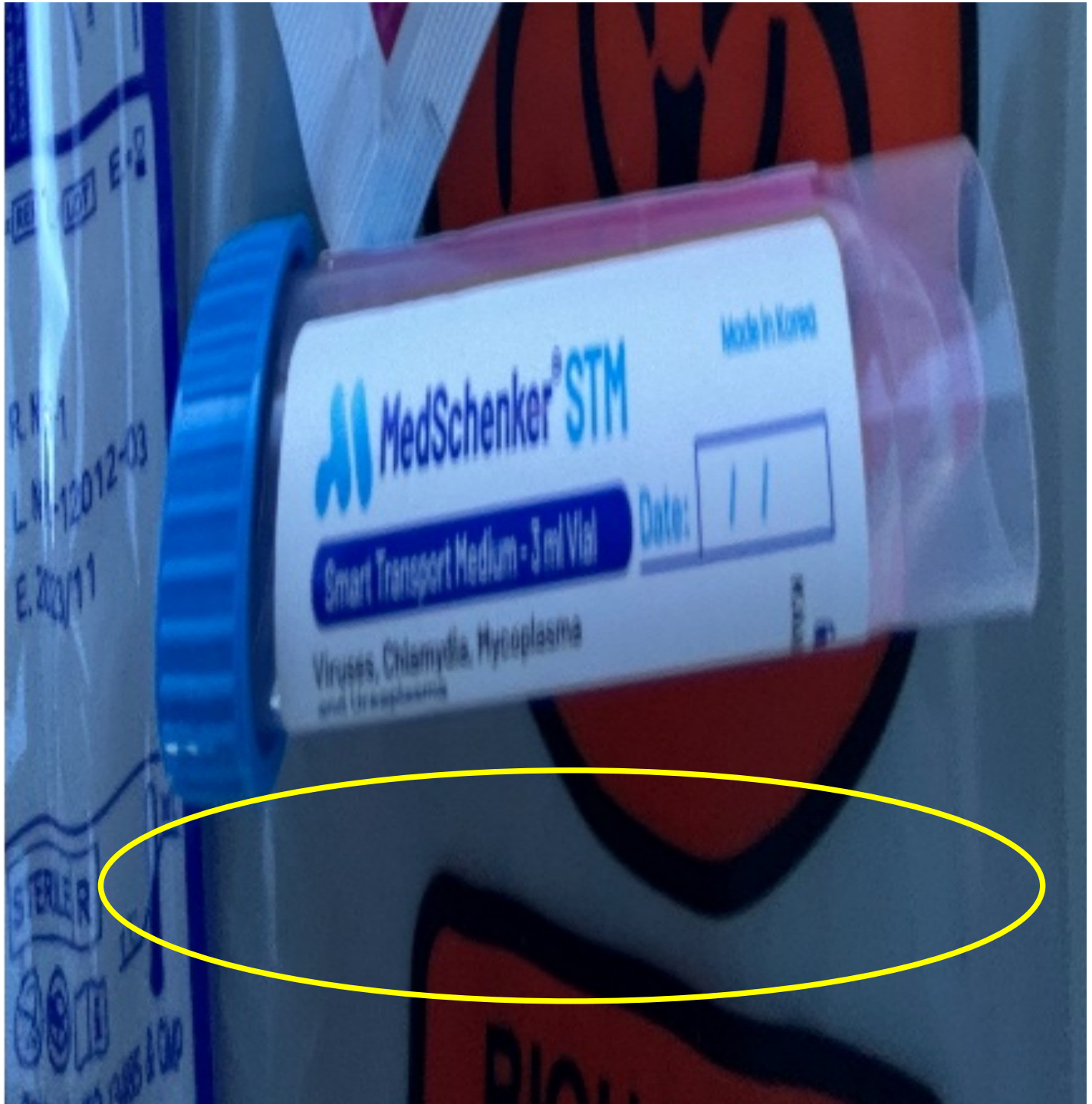
Japanese Ministry of the Environment

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

TEI-REX Potential Approaches

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

- Extensible and Novel Models
- Non-traditional samples
  - Hair
  - Skin
  - Interstitial Fluid
  - Saliva
  - Buccal and Mucosal cells
  - Sweat
  - Nails
- Robust Biomarkers
- Quantitative Analytical Platforms
- Advanced Computational Models


MedSchenker STM
Made in Korea
Smart Transport Medium - 3 ml Vial
Date: / /
Viruses, Chlamydia, Mycoplasma
STERILE R

MedSchenker®

Products Wholesale Contact Us

CAVSWAB™ NASOPHARYNGEAL

The MedSchenker® CavSwab™ tip is created with precision scalloped surface nylon fibers that create a 'cavum'. This design creates a larger surface area to absorb and help collect a large amount of specimen.

Specifications

Package	2000 units
Inner box	100 units
Length	153 mm
Breakpoint	101.3 mm
Shelf life	36 months

6 inches

FDA listed

https://medschenker.com/products/cavswab-nasopharyngeal/

GenBody COVID-19 Ag

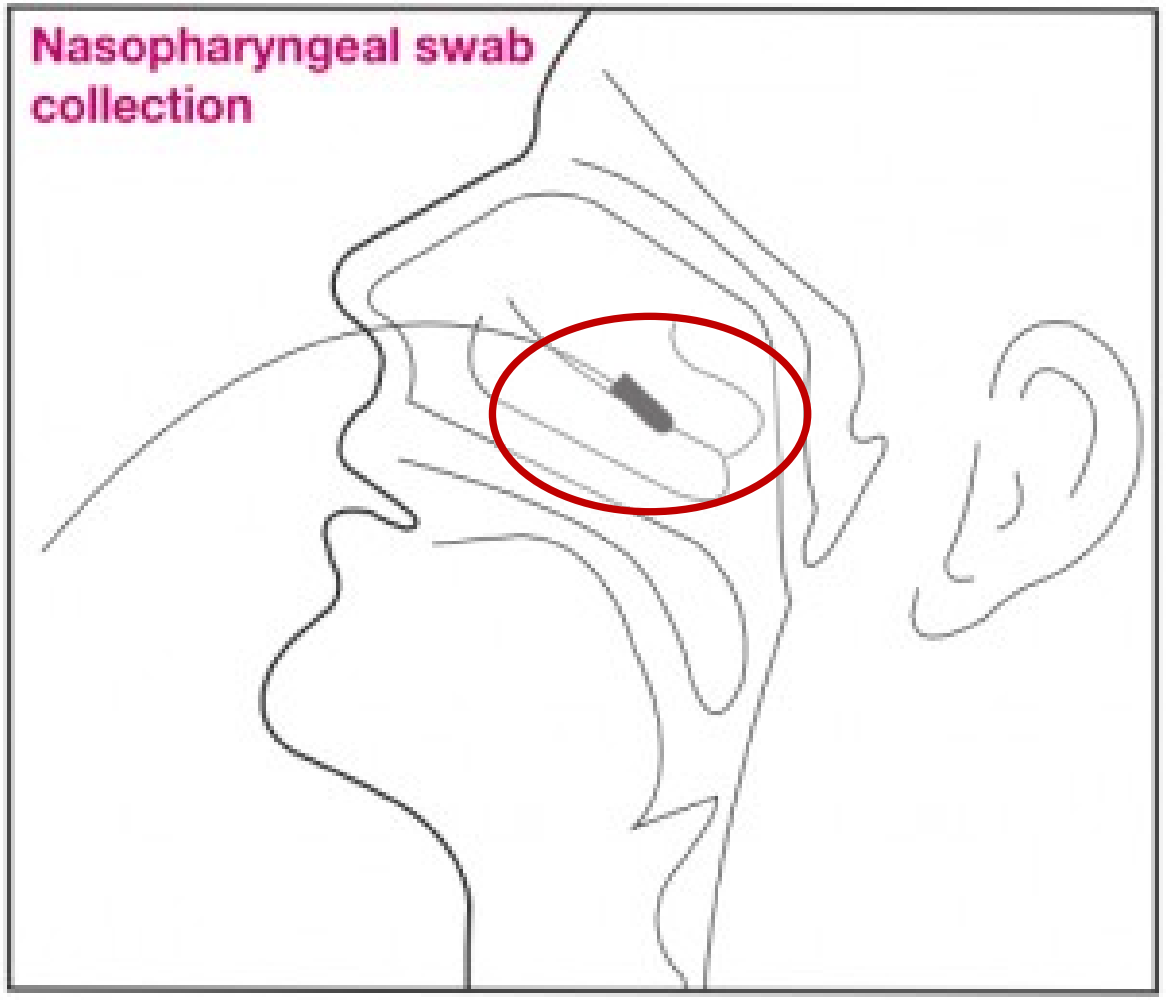
Detection kit for SARS-CoV-2 antigen in nasopharyngeal or anterior nasal swab specimens

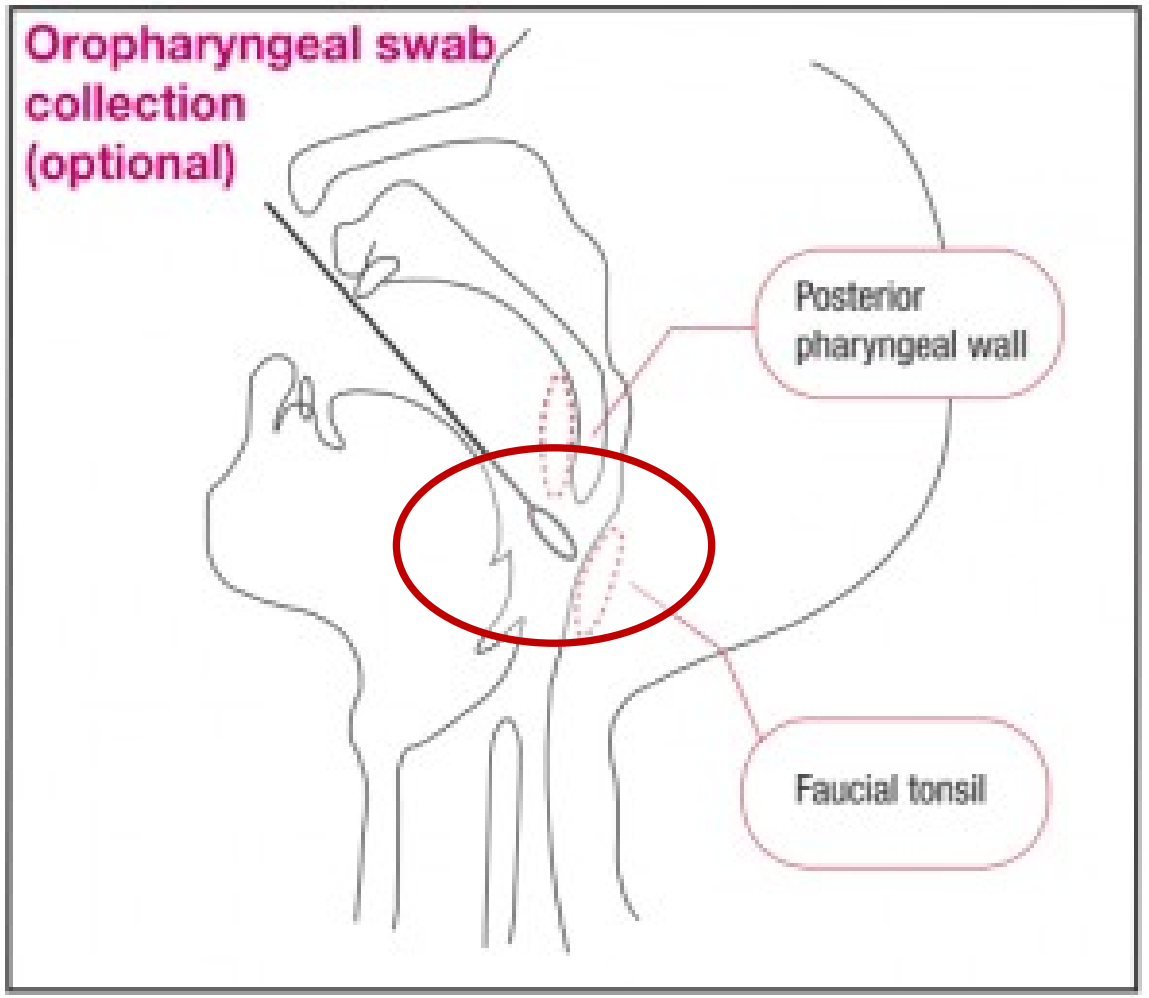
℞ ONLY IVD

2021.09.24 (Rev.1)

For use under the EUA Only

miFiGHT





https://www.fda.gov/media/150788/download

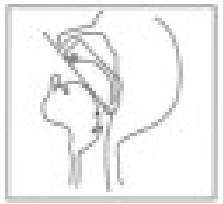
<Assay Procedure>

Preparation of Extraction solution

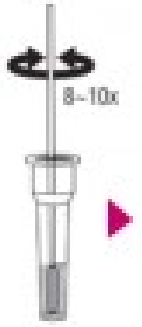
Fill the Extraction solution (400 μl)

Nasopharyngeal/Oropharyngeal swab

Nasopharyngeal swab collection



[Optional]
Oropharyngeal swab collection



Collect the specimens from the patient using provided swab

Mix the swab with extraction solution

Place the cap

Add 4 drops (~100 μl) of the solution into the sample well

Read the test results

Preparation of Extraction solution (VTM/UTM sample)

Drop 4 drops the Extraction solution (~100 μl)

Fill 100 μl VTM or UTM specimen

Mix strongly

Add 100 μl of the mixture to the sample well

When using samples from viral/universal transport media, it may cause inaccurate results due to decreasing the sensitivity of the test.

Read the test results

https://www.fda.gov/media/150788/download

COVID-19 Ag

GenBody COVID-19 Ag is an immunochromatographic assay kit for the qualitative detection of SARS-CoV-2 antigen in nasopharyngeal and oropharyngeal swab from human.

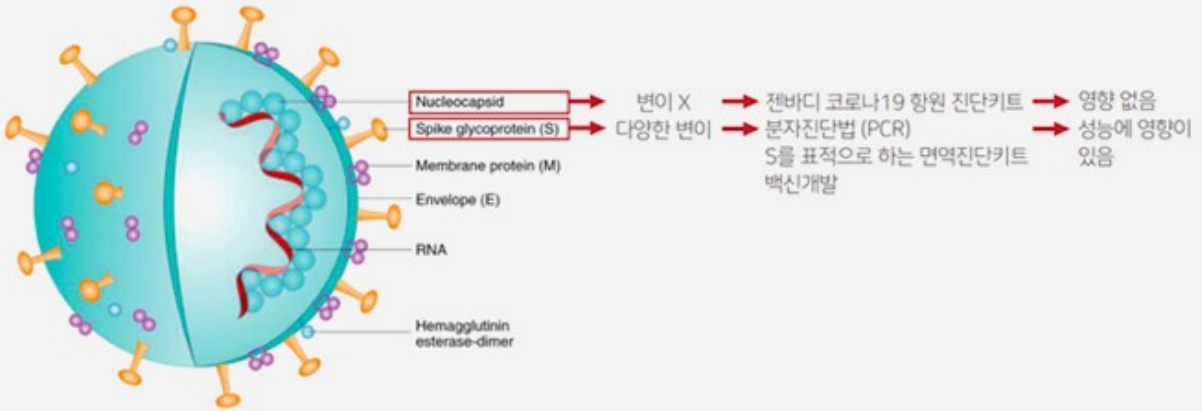
		Real-Time PCR		Total
		Positive	Negative	
GenBody COVID-19 Ag	Positive	72	2	74
	Negative	3	274	277
Total		75	276	351

- Sensitivity = 96.0% (95% CI = 88.75% to 99.17%)
- Specificity = 99.28% (95% CI = 97.41% to 99.91%)

https://www.fda.gov/media/150788/download

SARS-CoV-2 변종을 위한 GenBody COVID-19 Ag의 진단

- 사스코로나19의 다양한 변종(variant)들은 주로 스파이크단백질(S)의 돌연변이에 의해서 만들어짐.
- 때문에, 이 단백질을 진단 표적으로 하는 분자진단(molecular test, PCR)은 정확도가 영향을 받고, 백신개발 역시 영향을 받을 수 있음.
- 하지만, 젠바디 코로나19 항원 진단키트는 SARS-CoV-2의 변이가 없는 핵산단백질(N)를 표적으로 하기때문에 변종 코로나19 바이러스의 진단이 가능함



**참고문헌

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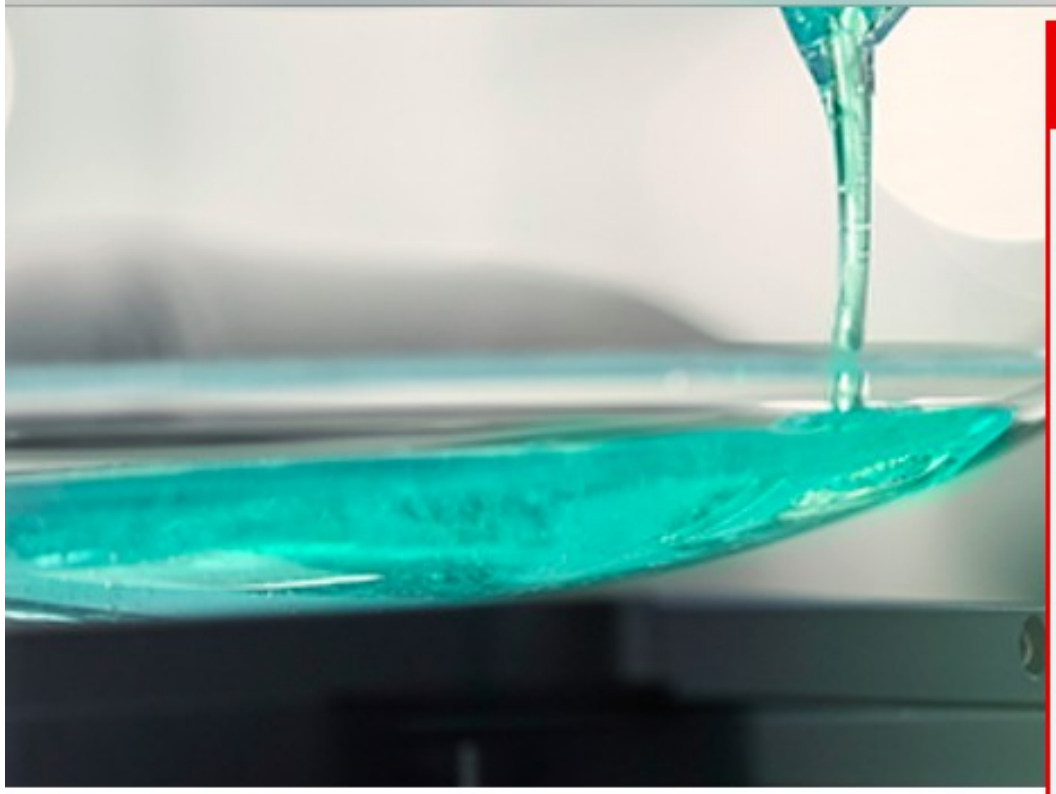
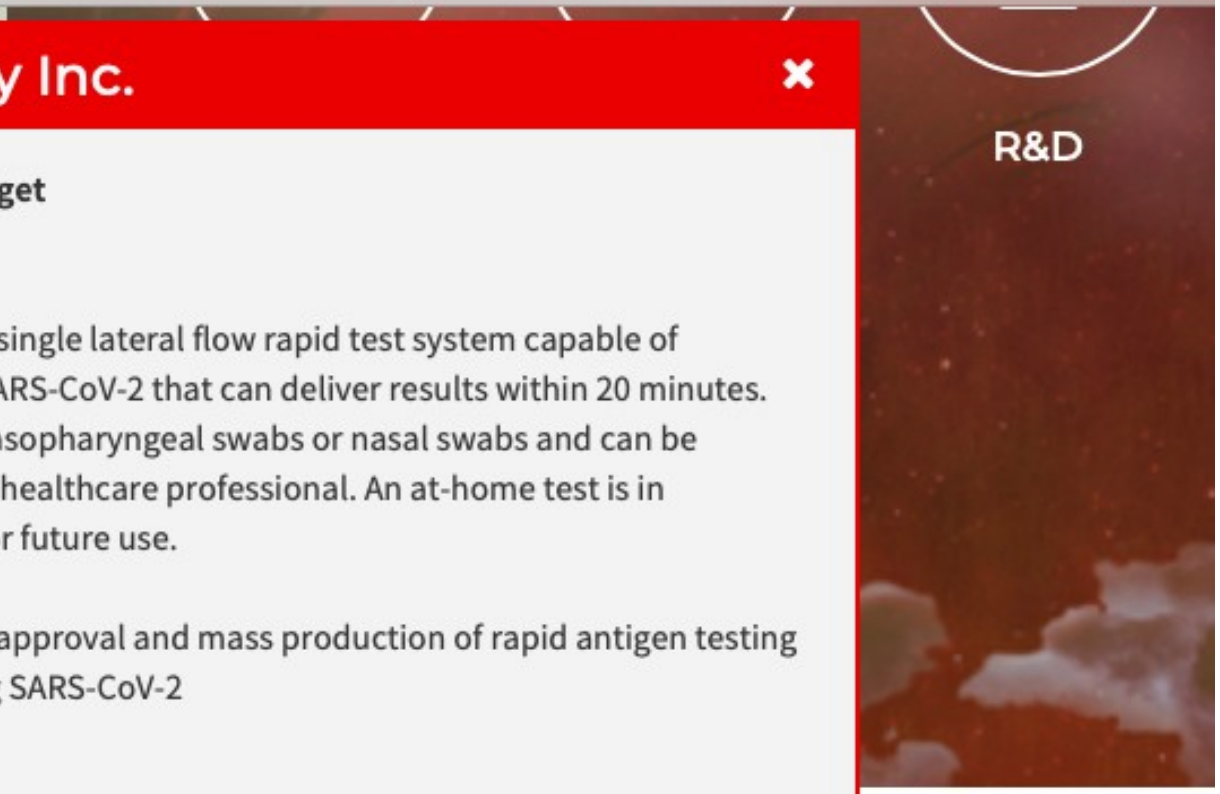
2. Andrew R. et al. Preliminary genomic characterization of an emergent SARS-CoV-2 lineage in the UK defined by a novel set of spike mutations. nCoV-2019 Genomic Epidemilology (2020) https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-the-uk-defined-by-a-novel-set-of-spike-mutations/563

COVID-19 Ag Brochure Download





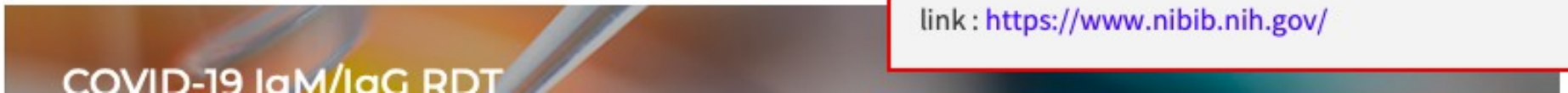
GenBody Inc.

Estimated Budget
10,000,000
Description
A visually read, single lateral flow rapid test system capable of detecting the SARS-CoV-2 that can deliver results within 20 minutes. The test uses nasopharyngeal swabs or nasal swabs and can be performed by a healthcare professional. An at-home test is in development for future use.
Project Title
U.S. regulatory approval and mass production of rapid antigen testing kit for detecting SARS-CoV-2
Sample Type
Nasal swab
Status
Active
Test Setting
POC
Type of test
Antigen
Sort By
POC Tests

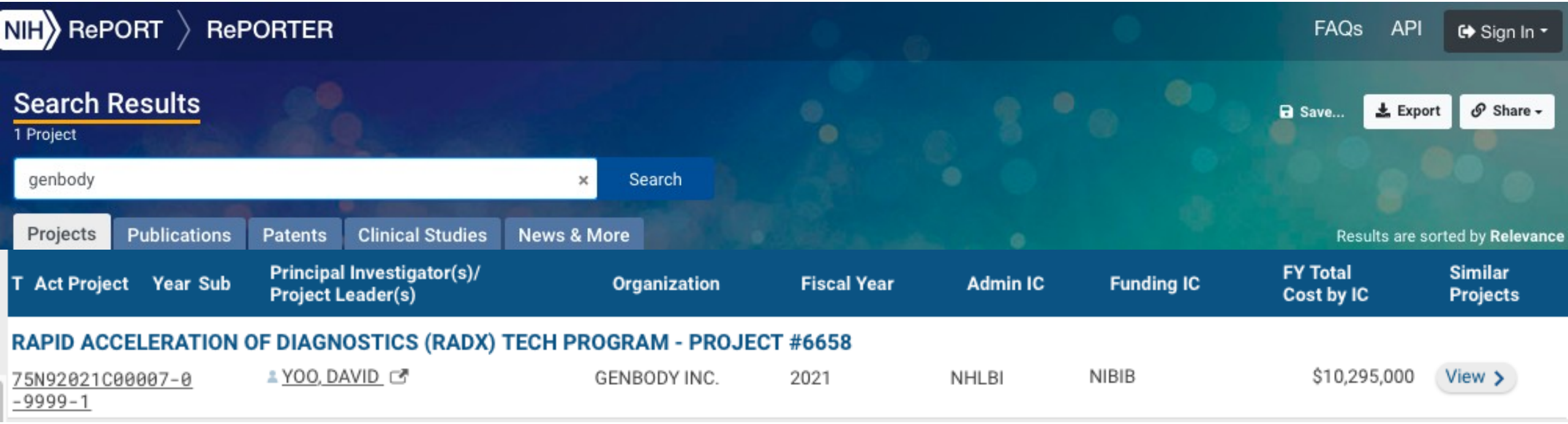
link : https://www.nibib.nih.gov/

Innovative
to make

MiFiGHT



Contiscope Series



https://reporter.nih.gov/search/FeobDHtnLUGTQJFFhE00yA/projects

RAPID ACCELERATION OF DIAGNOSTICS (RADX) TECH PROGRAM - PROJECT #6658

miFiGHT

Project Number	Contact PI/Project Leader	Awardee Organization
75N92021C00007-0-9999-1	YOO, DAVID	GENBODY INC.

Description

Abstract Text

A method was developed to detect not only SARS-CoV-2, but also influenza A and Influenza B anigen at the same time in a single lateral flow rapid testing (LFRT) system. The kit is a single device that can detect SARS-CoV-2 antigen and influenza antigen simultaneously. Since Influenza with respiratory illness with symptoms of high fever is similar to COVID-19, there are many difficulties to distinguish it from clinical diagnosis. Influenza can be treated with antiviral drugs such as Tamiflu, and there are also defense measures such as vaccines, so the treatment method is different. We have developed and evaluated an analytical/clinical performance for rapid diagnosis kit of SARS-CoV-2 antigen, obtained approval from the Korean Food and Drug Administration, and diagnostic Kits for influenza A/B antigen have also been licensed and commercialized. This diagnostic kit is basically diagnosed through the naked eye, and a portable equipment (Confiscope G20 has CE but no FCC) can be used for accurate determination which can be applied to control systems using a network.

Public Health Relevance Statement

Data not available.

Project Terms

No Project Terms available.

https://reporter.nih.gov/search/FeobDHtnLUGTQJFFhE00yA/projects

GenBody Inc.
CHANGE AND INNOVATION

For use under the *Emergency Use Authorization* Only
For *in vitro diagnostic* Use
For *Prescription Use* only

GenBody COVID-19 Ag

Rapid Diagnostic Test for the Detection of SARS-CoV-2 Antigen

Instructions for Use
(IFU)

GenBody COVID-19 Ag
Detection kit for SARS-CoV-2 antigen in nasopharyngeal or anterior nasal swab specimens

℞ ONLY IVD
2021.09.24 (Rev.1)
For use under the EUA Only

https://www.fda.gov/media/150788/download

GenBody COVID-19 Ag

Detection kit for SARS-CoV-2 antigen in nasopharyngeal or anterior nasal swab specimens

Rx ONLY IVD

2021.09.24 (Rev.1)

For use under the EUA Only

The GenBody COVID-19 Ag is an immunochromatographic rapid diagnostic test (RDT) intended for the qualitative detection of nucleocapsid protein antigen from SARS-CoV-2 in direct nasopharyngeal (NP) or anterior nasal (AN) swab specimens from individuals who are suspected of COVID-19 by their healthcare provider within the first six days of symptom onset. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform moderate, high or waived complexity tests. This test is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance or Certificate of Accreditation.

Results are for the identification of SARS-CoV-2 nucleocapsid antigen. Antigen is generally detectable in nasopharyngeal (NP) or anterior nasal (AN) swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

Negative results should be treated as presumptive and may be confirmed with a molecular assay, if necessary, for patient management. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19.

https://www.fda.gov/media/150788/download

Finished Products

All | Viral Disease | DOA | Bacterial Disease | Parasitic Disease | Cardiac Marker | Cancer Marker

image available soon

Toxoplasma
Toksoplasmosis adalah infeksi pada manusia yang ditimbulkan oleh parasit protozoa (organisme bersel satu) Toxoplasma gondii
View Details

Malaria
Malaria disebabkan oleh parasit Plasmodium. Sebetulnya ada banyak jenis parasit Plasmodium, tapi hanya lima jenis
View Details

Chlamydia
Chlamydia disebabkan oleh bakteri Chlamydia trachomatis. Bakteri ini ditularkan oleh penderita melalui hubungan seksual tanpa
View Details

Typhoid
Salmonella typhi (S. typhi) adalah bakteri gram negatif dan merupakan agen penyebab demam tifoid, karakteristik
View Details

Syphilis
Sifilis adalah penyakit yang disebabkan oleh bakteri spirochetal Treponema pallidum (TP). Sifilis adalah salah satu infeksi
View Details

Drug Of Abuse (DOA)
Uji RDT terhadap obat-obatan terlarang yang mengandung metamfetamin, amfetamin, morfin, mariyuana, fensiklidin, metadon, kokain, ekstasi
View Details

Hepatitis
Hepatitis merupakan peradangan pada hati. Kondisi ini dapat berkembang menjadi fibrosis (luka), sirosis atau kanker
View Details

HIV
Virus HIV mengincar sistem kekebalan dan melemahkan sistem pertahanan manusia terhadap infeksi dan beberapa jenis
View Details

Leptospira
Leptospira adalah penyakit bakteri yang menyerang manusia dan hewan
View Details

Malaria
Malaria merupakan penyakit yang disebabkan oleh parasit Plasmodium
View Details

miFiGHT

https://patentimages.storage.googleapis.com/68/80/73/6a17a66e9ec8c5/US11107588.pdf

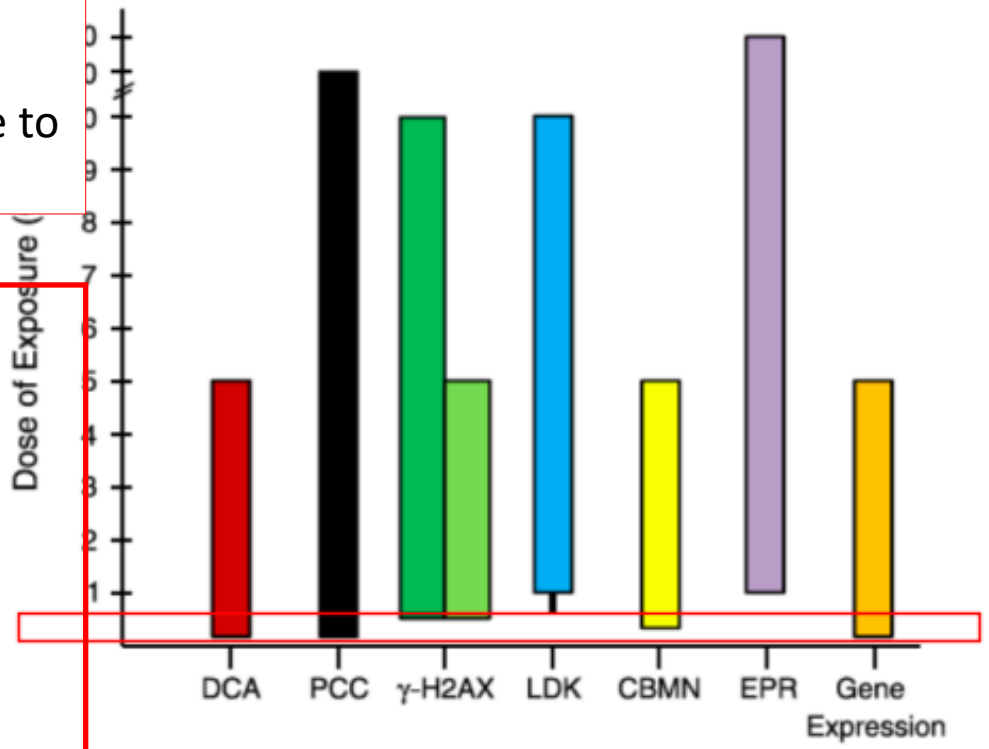
The Problem – Limitations

Approaches for retrospectively characterizing an exposure event are limited to mathematical modeling dependent upon extensive knowledge of the event, evaluation of sensors present at the time of exposure, evaluation of absorbed radionuclides, or analysis of transient biomarkers which provide limited information regarding the exposure environment.

Biodosimetry measures

- biological responses to radiation exposure
- physiological, chemical, or biological changes due to radiation exposure

- Bioassay
- Biodosimetry
  - Invasive samples
  - Transient signatures
  - Supply-chain requirements
  - High standard deviations at low-doses
  - Limited environment characterization



2021, remm.hhs.gov, Optimizing the Use of Biodosimetry Tools

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

New Biodosimetry Capabilities

Approach	Dose Range (Gray)	Analysis Time	Time period test is effective	Sample Type	Key Implementation Factors
DCA	0.1* – 5 0.5 – 5 (triage)	~3 days	3-6 months	Blood	-Can identify partial body exposures -Multi-day processing
LDK	0.5 - 10	~2 days	~ 9 days	Blood	-Multiple blood draws -Early baseline is best
Gamma-H2AX foci	0.5 - 10	2-6 hours	~2 days	Blood and buccal cells	-Immediate collection -Single blood draw
Gene expression profiles	0.1* – 5	9-36 hours	2-3 days	Blood, saliva, interstitial fluid	-Multiple blood draw -Baseline recommended
miRNA profiling	0.5* - 8	~2 days	1-7 days	Blood, saliva, interstitial fluid, urine, plasma, serum	-Single or multiple blood draw -Baseline recommended
TEI-REX Methods	0.1 - 10	3 hours	Immediate – variable yrs (noncumulative)	Minimally and non-invasive	-Single sample collection -Informs to environment

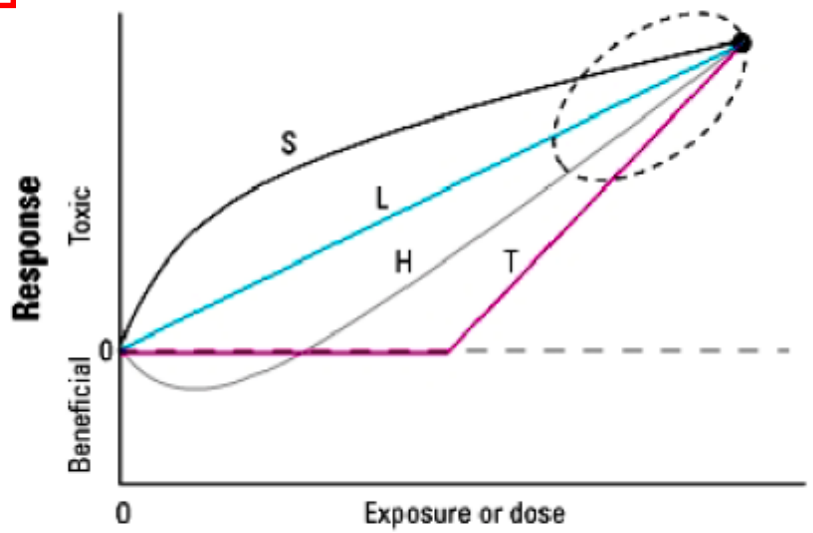
*standard deviations reported around 0.5 Gray

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

The Problem – Assumptions

Proposers should feel comfortable addressing, technically supported, established assumptions in this community.

- TEI-REX is **NOT** focused on clinical outcomes but proposals may leverage parallel research efforts.
- The assumptions made for whole-organism, clinical outcomes may not be appropriate assumptions for cellular or molecular scale ionizing radiation exposures.
- Assumptions associated with linear, no-threshold; non-linear, no-threshold; and non-linear, threshold theories must be scientifically supported from a molecular perspective.



Australasian Physical & Engineering Sciences in Medicine, 2009

TEI-REX will focus upon molecular and physical changes, which *may* inform towards physiological and clinical impact in future research.

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

How Can We Solve the TEI-REX Challenge?

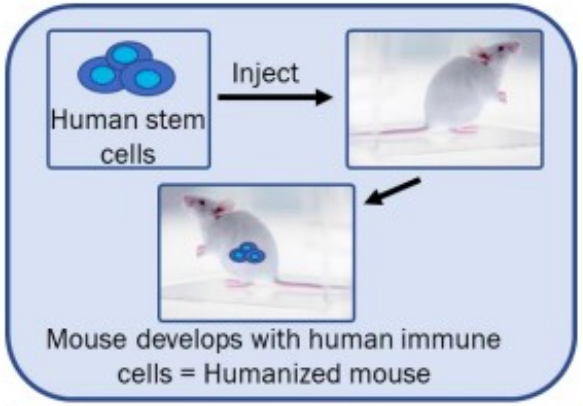
You tell us!

- Agnostic to research approach
- Propose what is needed to meet objectives
  - Research approach
  - Staff
  - Resources
  - Teaming plans
- Highlighting innovative, novel, and scientifically supported research and development approaches

TEI-REX Potential Approaches

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

- Extensible Traditional and Novel Models
  - Traditional models: cell lines, mice, pig, guinea pig, canines, NHPs
  - Non-traditional models: organs-on-a-chip, multi-layer cell cultures, humanized mice, 3-D printed cultures or follicles
- Non-traditional samples
- Robust Biomarkers
- Quantitative Analytical Platforms
- Advanced Computational Models



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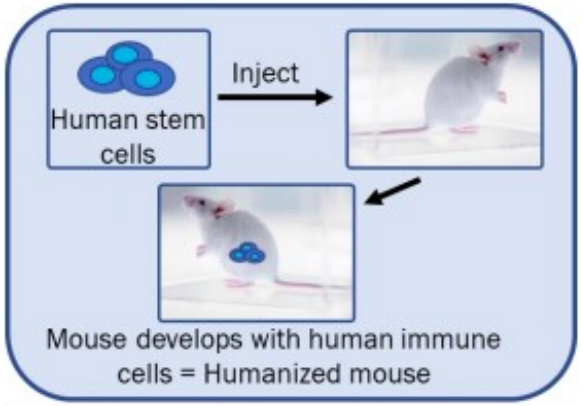
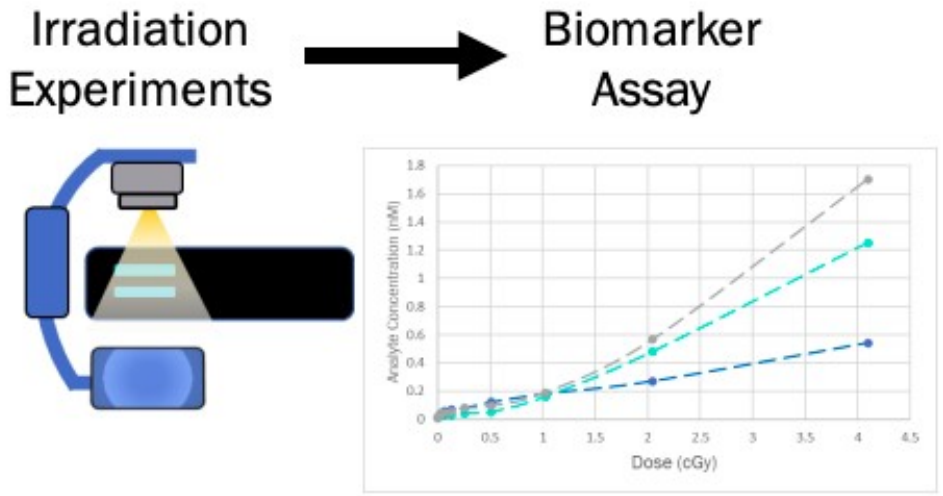
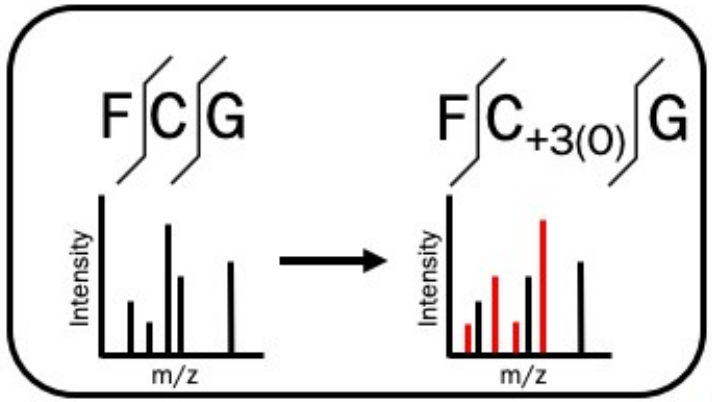


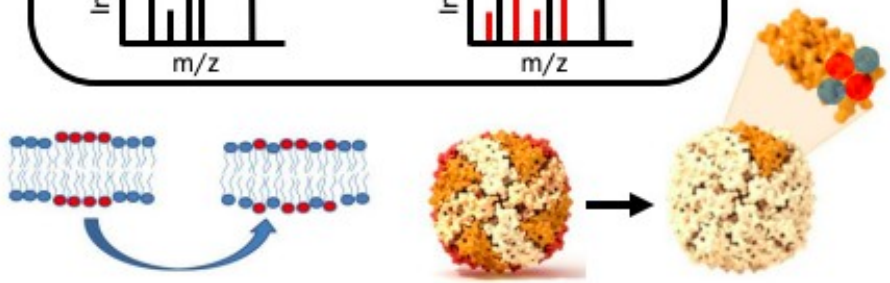
TEI-REX Potential Approaches

https://www.iarpa.gov/images/ProposersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

- Extensible and Novel Models
- Non-traditional samples
- Robust Biomarkers
  - Protein and peptide modifications
  - Amino acid modifications
  - Lipids
  - Structural changes
  - Modifications of microbiome
  - Metabolites
- Quantitative Analytical Platforms
- Advanced Computational Models







Elements Out of Scope

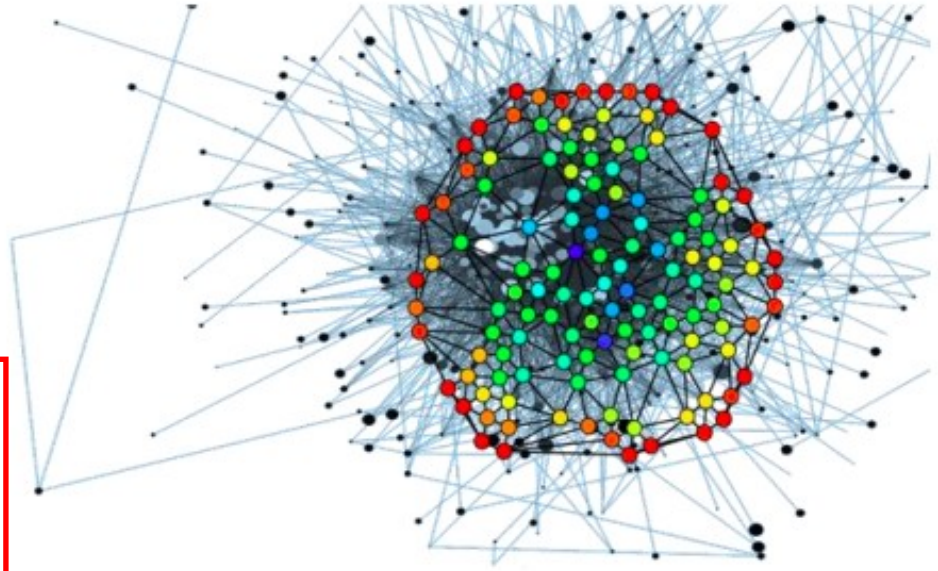
https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

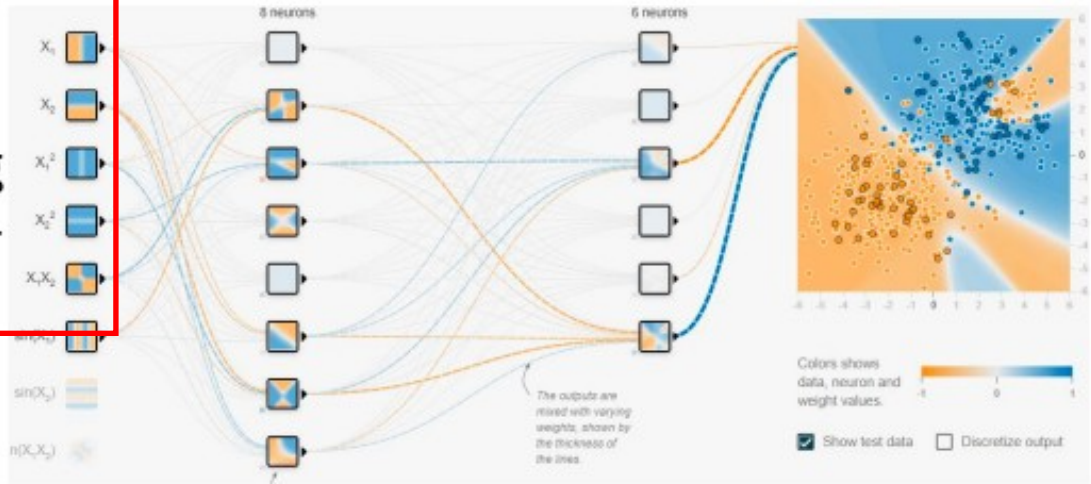
- Samples which cannot be collected through minimally- or non-invasive means
  - More intrusive samples may be used for early research and development but must lead towards appropriate TEI-REX sample types
  - Detection of radionuclides
- Biomarkers or Signatures
  - Research focused on signatures of DNA damage, to include single or double stranded breaks and/or associated repair activation signatures
    - Use of traditional biodosimetry tools for validation is permitted
  - Ratiometric expression profiling of DNA, RNA, and/or proteins
  - Biomarkers that require multiple serial sample collections from the same biological organism
    - Population level baselines are permitted

TEI-REX Potential Approaches

https://www.iarpa.gov/images/PropsersDayPDFs/TEI-REX/CLEANED_TEI-REX_ProposersDay_Final_20210928.pdf

- Extensible and Novel Models
- Non-traditional samples
- Robust Biomarkers
- Quantitative Analytical Platforms
- **Advanced Computational Models**
  - Trained neural network models using in-house and public biomarker databases
  - Integration with established biodosimetry models, including explicitly programmed, physics-based models





2:22

2035

Karen Kingston
659 subscribers

Technicians work at a genetic testing laboratory of BGI in Kunming, Yunnan Province, China, on Dec. 26, 2018.... MORE

THINKING ABOUT CHINA

Chinese Military-Linked Firm Gathers American DNA, Provides COVID Tests

Karen Kingston was "The Stew Peters Show" in Oct 2021, and then again in Nov breaking this info when they tested her son and sent his data to Korea!

We have been MONTHS ahead of everything, labeled as "conspiracy theorists" and fact-checked by the dishonest satan-worshiping regime "media" all along.

But, all along, we've been right.

China is "developing the world's largest bio database," said Edward You, who is the U.S. national counterintelligence officer for Emerging and Disruptive Technologies. "Once they have access to your genetic data, it's not something you can change like a pin code."

Racing to dominate the bioeconomy, the Chinese Communist Party (CCP) is compiling a massive database of medical, health, and genetic information from people around the world, including Americans.

The CCP enlists the help of private companies to aid in gathering genetic data, which can be combined with top military supercomputing capabilities, to discover genetic weaknesses in a population. Bioweapons can then be developed, which prey on these weaknesses. As part of Beijing's military-civil fusion policy, Chinese scientists, along with the military, have been conducting research in the areas of brain science, gene editing, and the creation of artificial genomes.

Similar research could be used to enhance the performance of Chinese soldiers. BGI Group, formerly Beijing Genomics Institute, is the leader of the CCP's genome project, as well as one of the leading producers of COVID-19 tests. BGI also has ties to China's People's Liberation Army (PLA), according to a Jan. 30 report by Reuters.

BGI operates the largest pig cloning project in the world. After manipulating generations of pig DNA, intentionally producing pigs that are smaller or larger, more susceptible to certain diseases, or less susceptible to others, the CCP is zeroing in on the ability to produce "super soldiers." Among the projects currently underway is BGI's attempt to make China's Han ethnic soldiers less susceptible to altitude sickness.

https://www.theepochtimes.com/chinese-military-linked-firm-gathers-american-dna-provides-covid-tests_4250811.html?utm_source=uschinanoe&utm_campaign=uschina-2022-02-03&utm_medium=email&est=E69q1XOCvRiG6nCJ1VzI4Bk0GrLDcs4Mee2TTekzm42otMewDwTHHbH7DBI%3D

China Is Collecting DNA From Tens of Millions of Men and Boys, Using U.S. Equipment

Even children are pressed into giving blood samples to build a sweeping genetic database that will add to Beijing's growing surveillance capabilities, raising questions about abuse and privacy.

Published June 17, 2020 Updated July 30, 2020

阅读简体中文版 · 閱讀繁體中文版

The police in China are collecting blood samples from men and boys from across the country to build a genetic map of its roughly 700 million males, giving the authorities a powerful new tool for their emerging high-tech surveillance state.

They have swept across the country since late 2017 to collect enough samples to build a vast DNA database, according to a new study published on Wednesday by the Australian Strategic Policy Institute, a research organization, based on documents also reviewed by The New York Times. With this database, the authorities would be able to track down a man's male relatives using only that man's blood, saliva or other genetic material.

An American company, Thermo Fisher, is helping: The Massachusetts company has sold testing kits to the Chinese police tailored to their specifications. American lawmakers have criticized Thermo Fisher for selling equipment to the Chinese authorities, but the company has defended its business.

The project is a major escalation of China's efforts to use genetics to control its people, which had been focused on tracking ethnic minorities and other, more targeted groups. It would add to a growing, sophisticated surveillance net that the police are deploying across the country, one that increasingly includes advanced cameras, facial recognition systems and artificial intelligence.

The San Diego Union-Tribune

SCIENCE

Jacobs family gives Salk Institute historic $100M gift for science center

LA JOLLA — Philanthropists Irwin and Joan Jacobs, whose gifts have profoundly influenced health, science and the arts across San Diego County for decades, are giving the Salk Institute up to $100 million to help build a major center for science and technology.

The gift is the largest in the La Jolla institute's history and represents the focal point of a $500 million fundraising campaign to expand the campus and deepen research in areas such as cancer, plant biology, aging and neurodegenerative diseases.

The Salk specializes in basic science. But it has begun to do more to help translate its findings into therapeutic drugs and to work on practical ways to fight climate change, such as developing plants that absorb greater amounts of carbon dioxide.

As part of the change, the institute has been heavily investing in computational biology, a field where the ever-growing ability to analyze massive data sets enabled scientists to quickly determine the genetic makeup of the various strains of COVID-

The Jacobs gift is a timely one "because the faculty are working together on larger problems with deep implications," said Salk President Fred "Rusty" Gage, who shook science in the 1990s when he discovered that adult humans can generate new brain cells.

Irwin M. Jacobs, the founding chairman and CEO Emeritus of Qualcomm, and his wife Joan Jacobs, pose for a portrait in their San Diego home in 2019. (Sam Hodgson/The San Diego Union-Tribune)

The couple will donate $1 for every $2 raised by the Salk during a period that will end on June 30, 2022

https://www.sandiegouniontribune.com/news/science/story/2021-11-12/jacobs-family-salk-institute-100-million

Per the PREP Act:

3. Are There Any Limitation on Immunity from Liability?

WILLFUL MISCONDUCT* is misconduct that is greater than any form of recklessness or negligence. It is defined in the PREP Act as an act or failure to act that is taken:

- *intentionally to achieve a wrongful purpose;*
- *knowingly without legal or factual justification; and*
- ***in disregard of a known or obvious risk that is so great as to make it highly probable that the harm will outweigh the benefit***

**All three of these conditions must be proven with clear and convincing evidence.*

WILLFUL MISCONDUCT cannot be found against:

- *A manufacturer or distributor for actions regulated by HHS under the Public Health Service Act or the Federal Food, Drug and Cosmetic Act,* ***if HHS chooses not to take an enforcement action against the manufacturer or distributor****, or if HHS terminates or settles an enforcement action without imposing a criminal, civil, or administrative penalty; or*
- ***A program planner or qualified person who acts in accordance with applicable directions, guidelines, or recommendations issued by the HHS regarding administration and use of a countermeasure as long as HHS or the State or local health authority is notified about the serious injury or death within seven days of its discovery.***

https://www.phe.gov/Preparedness/legal/prepact/Pages/prepqa.aspx#immune3