



Blood Bank
Digital

IDEAS

Digital Health Hematology Services (DHHS in the near-future)



Blood Bank Digital

Dr Shoumen Palit Austin Datta

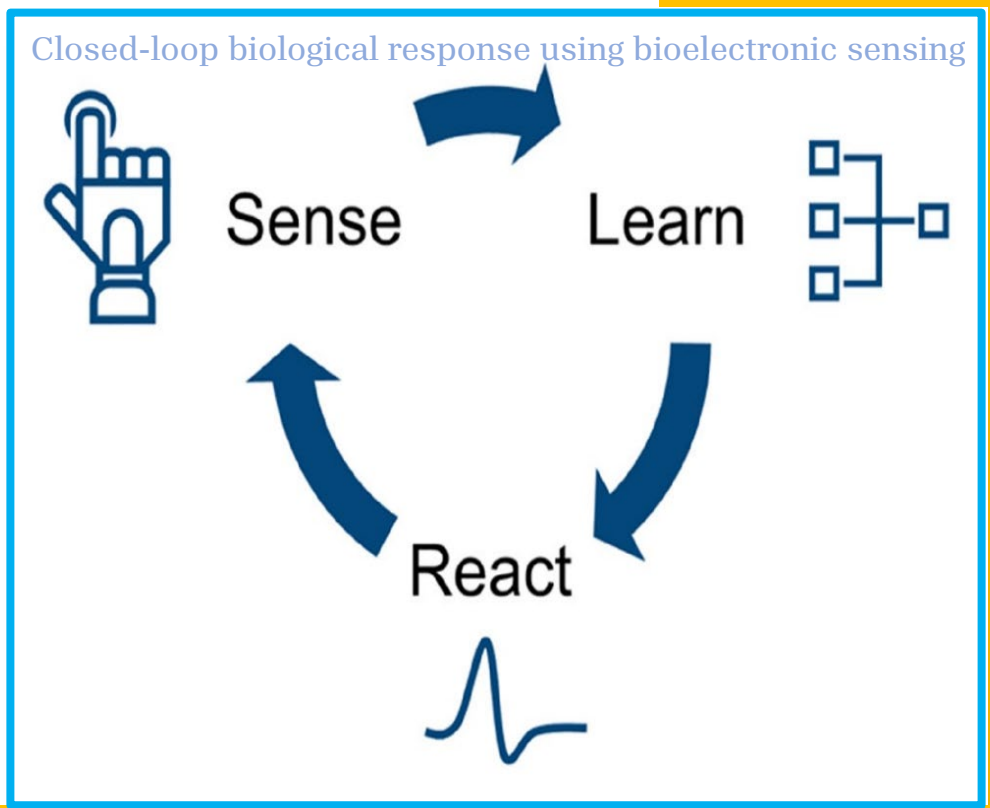
MIT Auto-ID Labs, Senior Member, Research Affiliate, Department of Mechanical Engineering, Massachusetts Institute of Technology ▪

shoumen@mit.edu

Senior Scientist, MDPnP Lab, Cybersecurity Program and SaAMS, Massachusetts General Hospital, Harvard Medical School ▪

sdatta8@mgh.harvard.edu

*Digital
Convergence
of
Biological
Transactions*



Data-Informed Decision Support (DIDS) Systems

Distributed Secure Near Real-time Mobile Digital Health Services

But, at a cost ...

Understanding the principle of transaction cost economics (TCE in DIGITAL HEALTH)

Transaction Cost

The Sveriges Riksbank Prize in
Economic Sciences in Memory of
Alfred Nobel 1991

Ronald H. Coase Facts

Ronald H. Coase



Photo from the Nobel
Foundation archive.

Ronald H. Coase

The Sveriges Riksbank Prize in Economic Sciences in
Memory of Alfred Nobel 1991

Born: 29 December 1910, Willesden, United Kingdom

Died: 2 September 2013, Chicago, IL, USA

Affiliation at the time of the award: University of Chicago,
Chicago, IL, USA

Prize motivation: “for his discovery and clarification of the
significance of transaction costs and property rights for the
institutional structure and functioning of the economy”

Foundation of DHHS ?

LIQUID BIOPSIES

SCALE POPULATION HEALTH USING LIQUID BIOPSIES VIA COMMUNITY BLOOD BANKS?

Angioni D, Delrieu J, Hansson O, Fillit H, Aisen P, Cummings J, Sims JR, Braunstein JB, Sabbagh M, Bittner T, Pontecorvo M, Bozeat S, Dage JL, Largent E, Mattke S, Correa O, Gutierrez Robledo LM, Baldivieso V, Willis DR, Atri A, Bateman RJ, Ousset PJ, Vellas B, Weiner M. *Blood Biomarkers from Research Use to Clinical Practice: What Must Be Done? A Report from the EU/US CTAD Task Force*. J Prev Alzheimers Dis. 2022; 9(4):569-579. doi: 10.14283/jpad.2022.85. PMID: 36281661; PMCID: PMC9683846. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9683846/pdf/nihms-1846920.pdf>

LIQUID BIOPSY (LB)

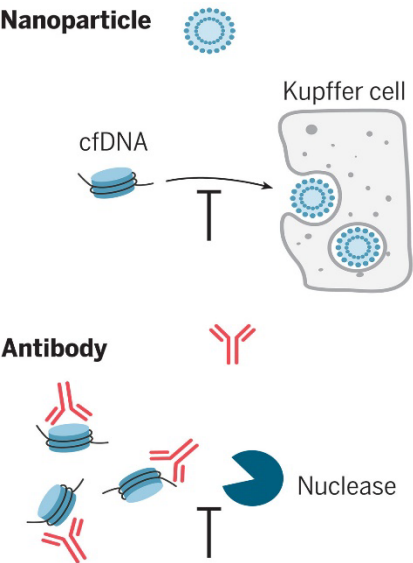
why it can scale

Liquid biopsies (LB) using blood can scale to reveal **personal** as well as **population health** signals (predictive) because blood draw in clinics and blood donation in community blood banks can be accomplished with relative ease and at a low cost even for resource constrained communities.

Key performance indicators (KPI) for liquid biopsies are sensitivity, predictive outcome (precision and accuracy). Key performance driver (KPD) is cost.

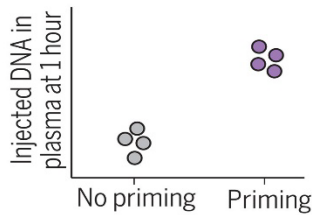
LIQUID BIOPSY - surpassing sensitivity limits by transiently augmenting the level of circulating tumor DNA (ctDNA) in blood (using nanoparticle priming agents) to attenuate clearance of cell-free DNA (cfDNA) in vivo.

Two priming agents for cfDNA

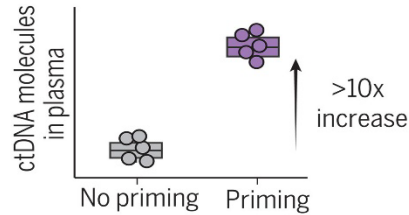


Higher ctDNA recovery in preclinical models

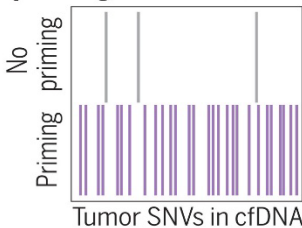
Increased circulation half-life of cfDNA



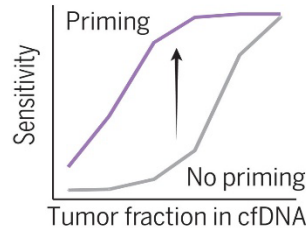
Recovery of more ctDNA



Better tumor molecular profiling from cfDNA

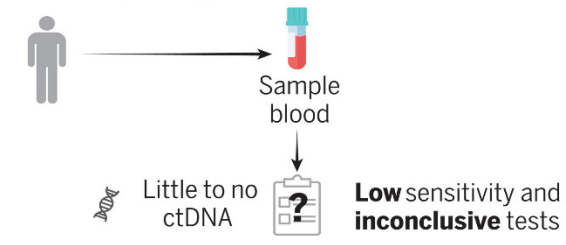


Higher sensitivity of ctDNA test

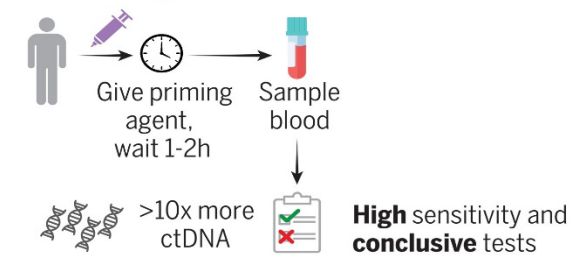


Envisioned clinical application

Without priming



With priming



<https://www.science.org/doi/10.1126/science.adf2341>

Priming agents (PA) reduce the clearance of cell-free (cf) DNA and enhance the sensitivity of liquid biopsies.

Priming agents transiently attenuate natural clearance mechanisms for cfDNA and consist of nanoparticles that act on the cells responsible for cfDNA clearance (top left) or DNA-binding antibodies that protect cfDNA from cellular uptake and enzymatic digestion (bottom left). In preclinical models, priming agents increased the half-life of cfDNA, enhanced recovery of circulating tumor (ct) DNA, and improved tumor molecular profiling from ctDNA and sensitivity of ctDNA testing (middle). PA's administered 1 to 2 hours prior to a blood draw, improves recovery of ctDNA and may boost the sensitivity of many types of liquid biopsy tests (right).

Twitter Data Analytics from Geo Tagged Social Signals

Dr Monica Stephens

Humboldt State University

Browser address bar: http://users.humboldt.edu/mstephens/hate/hate_map.html#

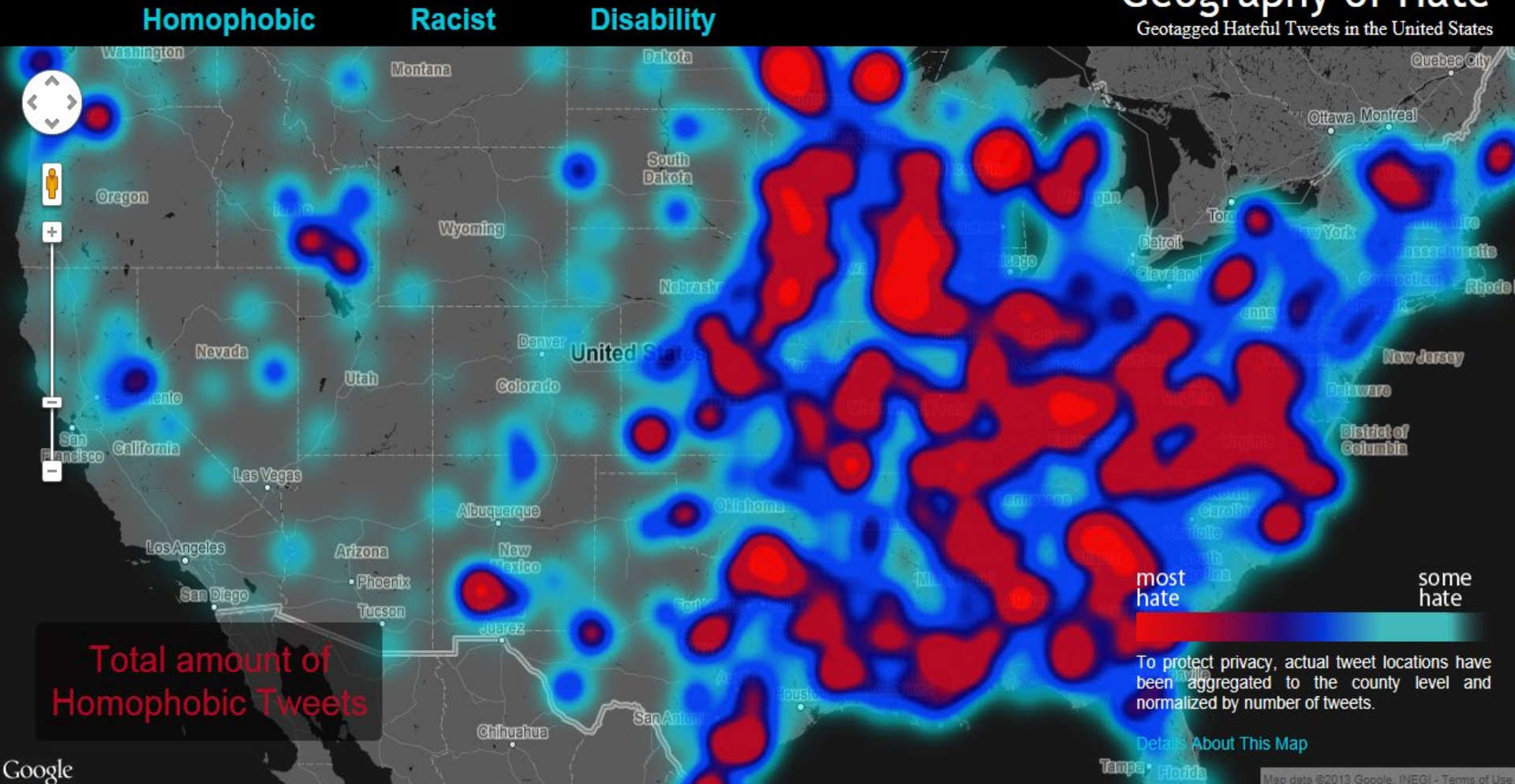
Search: Share More >>

Navigation: Back, Forward, Home, Stop, Refresh

Open tabs: Hate Map, Administrative-officers, chemistry58 - Handouts a..., General Chemistry for Stu..., IndraNooyiDavos2010ver2..., Future Energy (Boston) at ..., UNIVERSITY DATABASE, I...

Geography of Hate

Geotagged Hateful Tweets in the United States



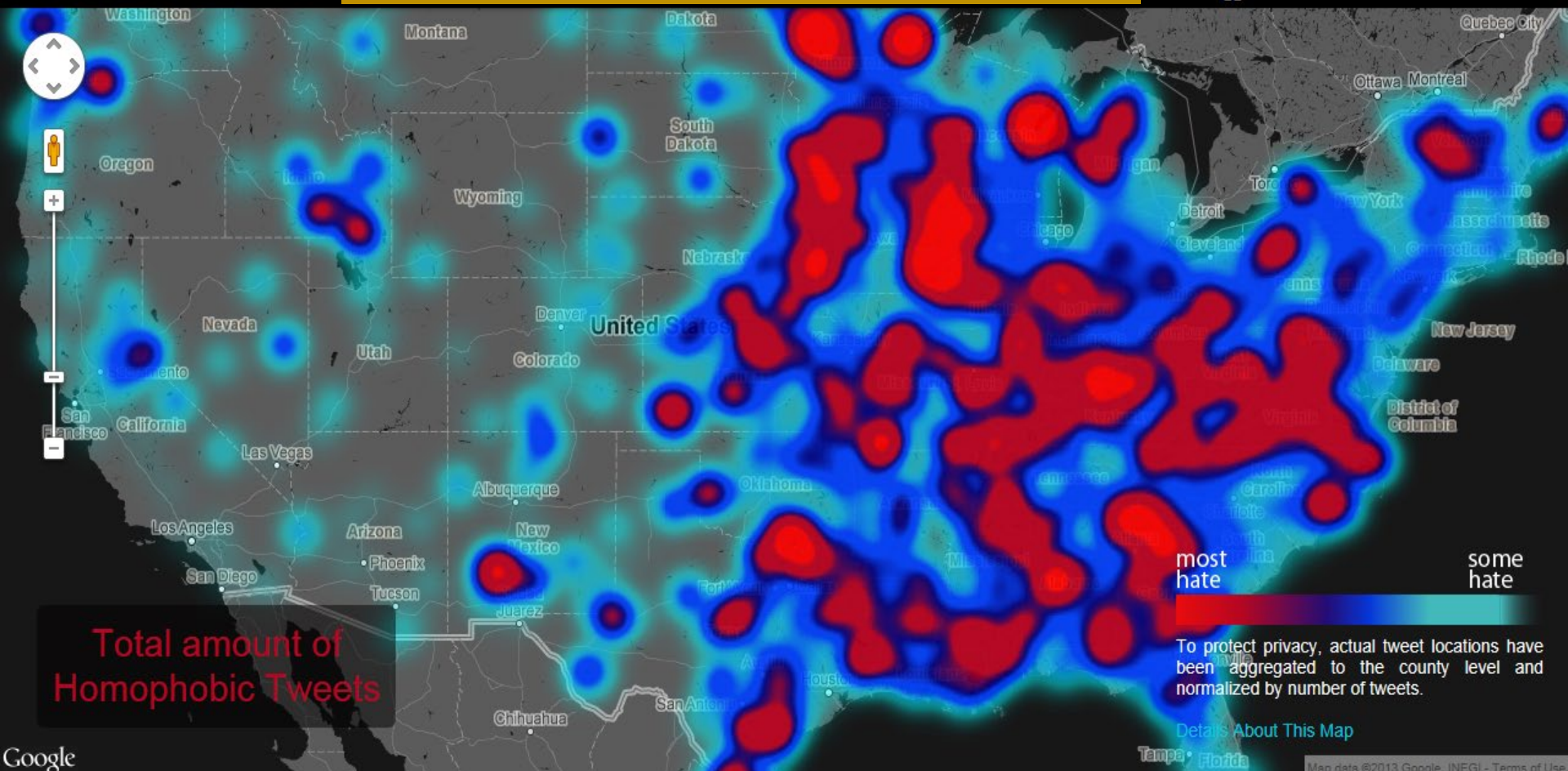
Instead of mapping hate, let us map anonymized liquid biopsy data by zip code (e.g., cancer clusters?)

Homophobic

Dr Monica Stephens <https://geog.space/> (mstephens@gmail.com)

Geography of Hate

Geotagged Hateful Tweets in the United States



LIQUID BIOPSY (population genetics?) from BLOOD BANKS ?

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MARCH 14, 2024

VOL. 390 NO. 11

A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening

Daniel C. Chung, M.D., Darrell M. Gray II, M.D., M.P.H., Harminder Singh, M.D., Rachel B. Issaka, M.D., M.A.S., Victoria M. Raymond, M.S., Craig Eagle, M.D., Sylvia Hu, Ph.D., Darya I. Chudova, Ph.D., AmirAli Talasaz, Ph.D., Joel K. Greenon, M.D., Frank A. Sinicrope, M.D., Samir Gupta, M.D., M.S.C.S., and William M. Grady, M.D.

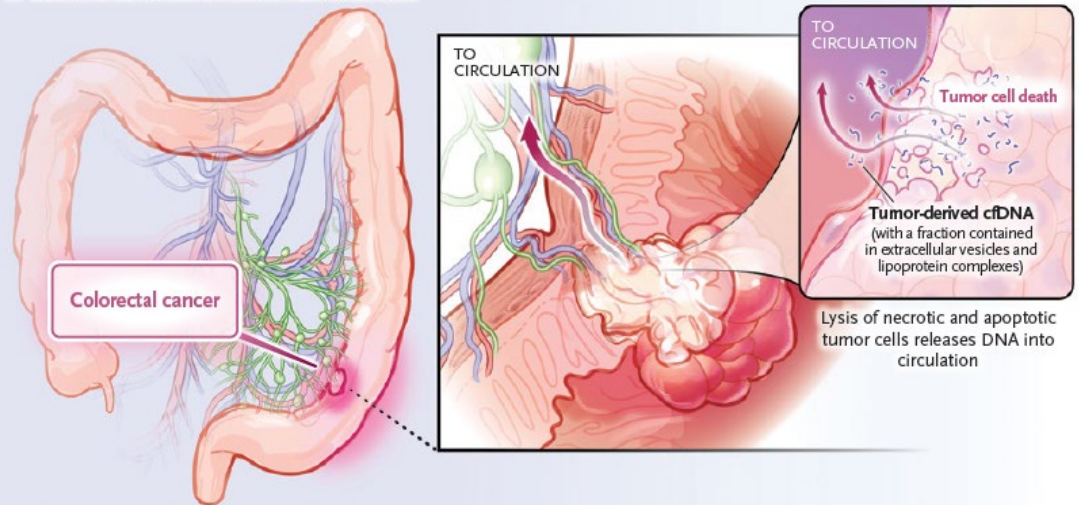
A Cell-free DNA Blood-Based Test
for Colorectal Cancer Screening

Daniel C. Chung, M.D., Darrell M. Gray II, M.D., M.P.H., Harinder Singh, M.D., Rachel B. Issaka, M.D., M.A.S.,
Victoria M. Raymond, M.S., Craig Eagle, M.D., Sylvia Hu, Ph.D., Darya I. Chudova, Ph.D., AmirAli Talasaz, Ph.D.,
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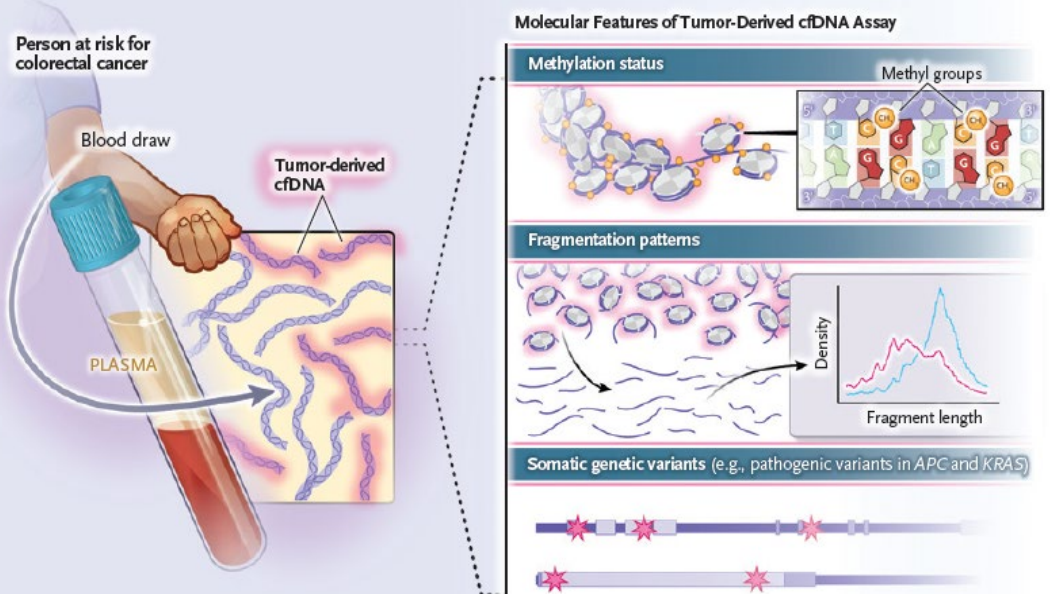
Chung DC, Gray DM 2nd,
Singh H, Issaka RB,
Raymond VM, Eagle C, Hu
S, Chudova DI, Talasaz A,
Greenson JK, Sinicrope
FA, Gupta S, Grady WM.
**A Cell-free DNA Blood-
Based Test for Colorectal
Cancer Screening.**

N Engl J Med. 2024 March
14; 390(11):973-983. doi:
10.1056/NEJMoa2304714.
PMID: 38477985.

A Release of cfDNA into Circulation from Tumor Cells



B Characterization of Tumor-Derived cfDNA for Cancer Screening



LIQUID BIOPSY using samples from cord BLOOD BANKS

There is an **immense** (yet cryptic) potential for multi-generational epidemiologic studies to analyze bio-markers and specific precision changes in personal profiles over time and/or before/after any metabolic event (e.g., CoVID-19, CVD, COPD, PKD). The molecular metabolic signatures may be analyzed from stored blood in blood banks and pathology labs.

Proof is in the Pudding ?

FRAMINGHAM HEART STUDY

<https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs>

FHS began in 1948. This is what was reported in 2024

Li C, Stražar M, Mohamed AMT, Pacheco JA, Walker RL, Lebar T, Zhao S, Lockart J, Dame A, Thurimella K, Jeanfavre S, Brown EM, Ang QY, Berdy B, Sergio D, Invernizzi R, Tinoco A, Pishchany G, Vasan RS, Balskus E, Huttenhower C, Vlamakis H, Clish C, Shaw SY, Plichta DR, Xavier RJ. ***Gut microbiome and metabolome profiling in Framingham heart study reveals cholesterol-metabolizing bacteria.*** Cell. 2024 March 21: S0092-8674(24)00305-2. doi: 10.1016/j.cell.2024.03.014 <https://pubmed.ncbi.nlm.nih.gov/38569543/>

FRAMINGHAM HEART STUDY

<https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs>

Stool metagenomics and metabolomics from **1,429 Framingham Heart Study** participants revealed microbiome and metabolome composition. Specifically, the study found bacterial species from the *Oscillibacter* genus were associated with decreased fecal and plasma cholesterol levels. A bacterial enzyme called ismA can metabolize cholesterol into coprostanol, a lipid excreted, instead of absorbed by the body. Gut bacteria, including several *Oscillibacter* species, correlate with lower cholesterol levels in people. These bacteria could also metabolize cholesterol in lab experiments. Whether these bacteria can directly influence blood cholesterol in people needs to be confirmed. If delivered to the right place in the gut, it might lead to new treatments using [bacteria to transform artery-clogging cholesterol into a more harmless form](#). How about direct enzyme (ismA) delivery using mRNA?

FRAMINGHAM HEART STUDY - *started in 1948 and still helpful*

Li C, Stražar M, Mohamed AMT, Pacheco JA, Walker RL, Lebar T, Zhao S, Lockart J, Dame A, Thurimella K, Jeanfavre S, Brown EM, Ang QY, Berdy B, Sergio D, Invernizzi R, Tinoco A, Pishchany G, Vasani RS, Balskus E, Huttenhower C, Vlamakis H, Clish C, Shaw SY, Plichta DR, Xavier RJ. [Gut microbiome and metabolome profiling in Framingham heart study reveals cholesterol-metabolizing bacteria](#). Cell. 2024 March 21; S0092-8674(24)00305-2. doi: 10.1016/j.cell.2024.03.014 <https://pubmed.ncbi.nlm.nih.gov/38569543/>

<https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs>

What is the goal of the FHS?

The NHLBI has a long history of supporting large population and epidemiology studies that have transformed the way the public approaches heart disease. These studies involve studying the health of various populations to uncover patterns, trends, and outcomes that may be applicable to the general population. When it launched in 1948 the original goal of the Framingham Heart Study (FHS) was to identify common factors or characteristics that contribute to cardiovascular disease. Over the years, the FHS has become a successful, multigenerational study that analyzes family patterns of cardiovascular and other diseases, while gathering more genetic information from the two generations that followed the original study participants. The FHS also has expanded to include diverse populations so that risk factors in these different groups can be understood.



National Heart, Lung,
and Blood Institute



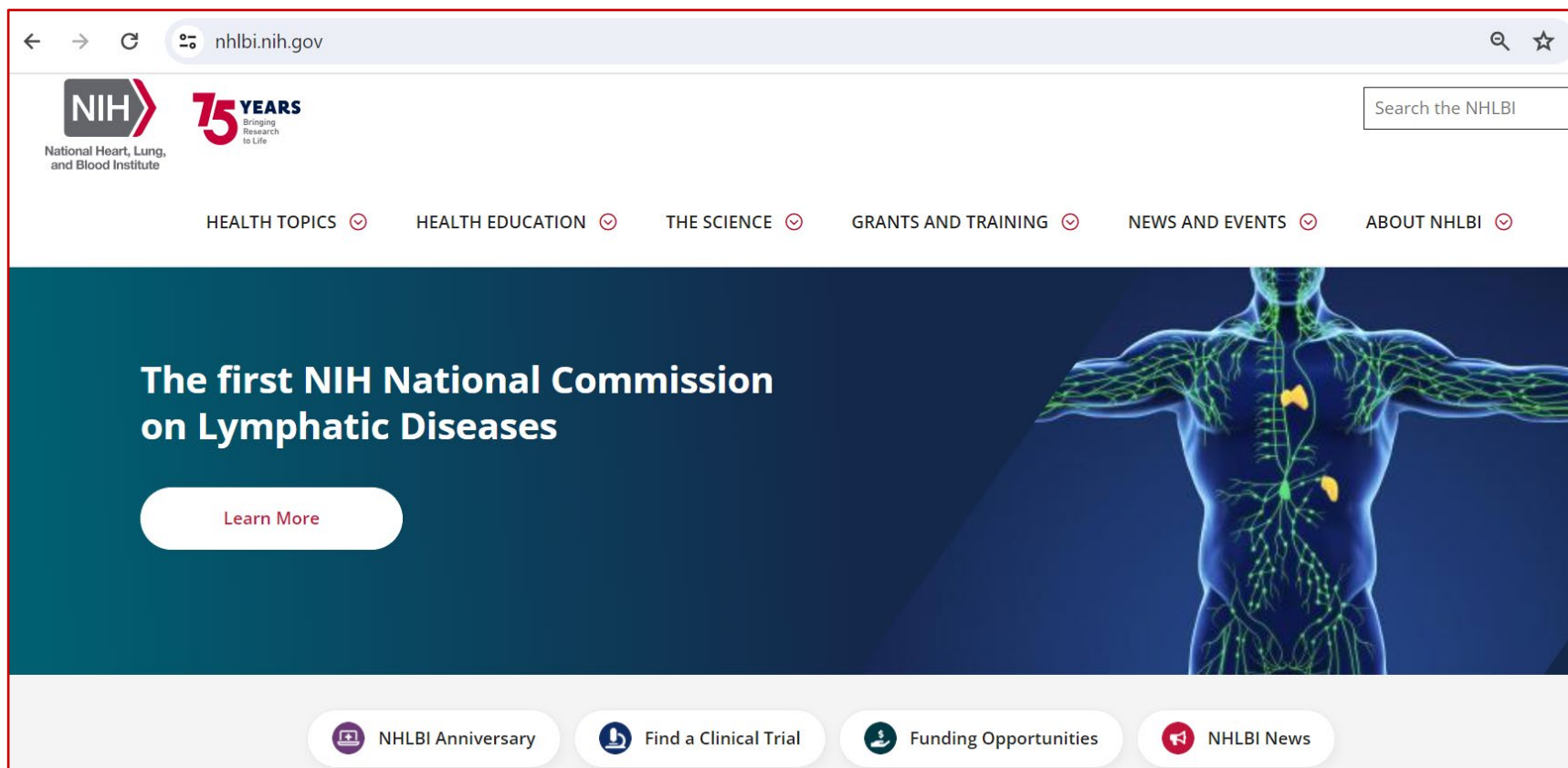
> *FHS is a longitudinal study*

- > *The FHS had over 15,000 people from three generations, including the original participants, their children, and their grandchildren at the start of each cohort.*
- > *FHS findings have informed the understanding of how cardiovascular health affects the rest of the body.*
- > *The study found high blood pressure and high blood cholesterol to be major risk factors for cardiovascular disease.*
- > *In the past half century, the study has produced approximately 6,000 articles in leading medical journals.*
- > *Data and biologic resources from the study are available for researchers to use, which continue to spur new scientific discoveries.*

What is possible using data
from research on stored
blood bank samples
(cord blood)?

*Molecular metabolomics,
proteomics & genetics of diseases?*

this is happening ...



The screenshot shows the NHLBI website homepage. At the top, there is a navigation bar with the NIH logo, the 75th anniversary logo, and a search bar. Below the navigation bar, there is a main banner with the text "The first NIH National Commission on Lymphatic Diseases" and a "Learn More" button. The banner features a 3D illustration of a human torso with a glowing green lymphatic system. At the bottom of the page, there are four circular icons with text: "NHLBI Anniversary", "Find a Clinical Trial", "Funding Opportunities", and "NHLBI News".

← → ↻ nhlbi.nih.gov 🔍 ☆





NIH 75 YEARS
National Heart, Lung, and Blood Institute
Bringing Research to Life

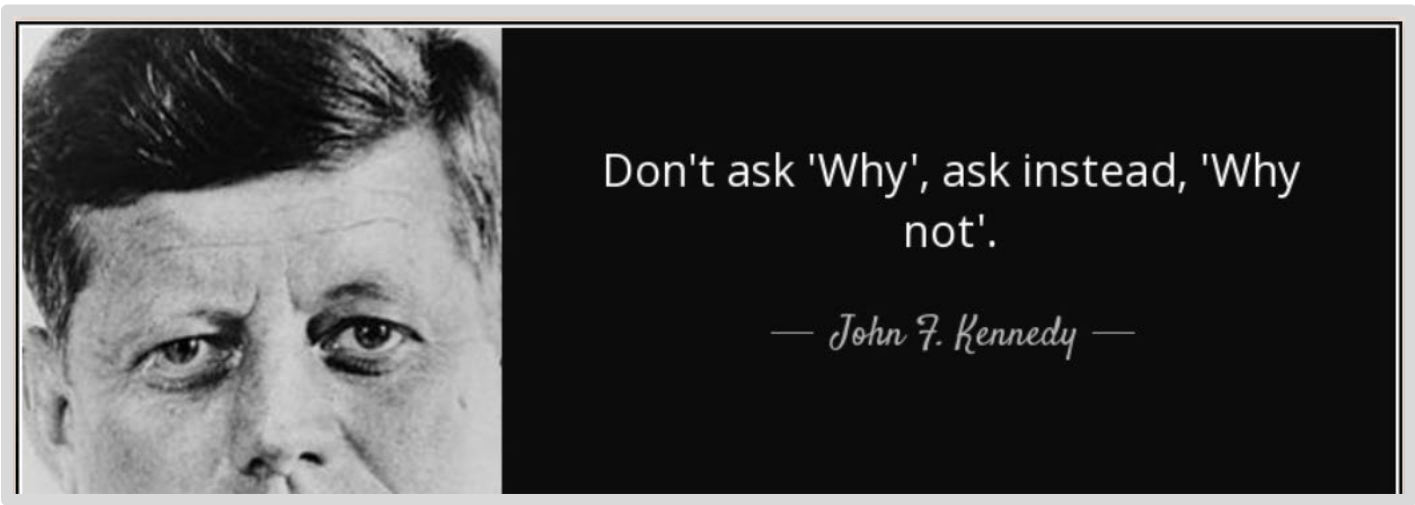
Search the NHLBI

HEALTH TOPICS ▾ HEALTH EDUCATION ▾ THE SCIENCE ▾ GRANTS AND TRAINING ▾ NEWS AND EVENTS ▾ ABOUT NHLBI ▾

The first NIH National Commission on Lymphatic Diseases

[Learn More](#)

 NHLBI Anniversary  Find a Clinical Trial  Funding Opportunities  NHLBI News



← → ↻ nhlbi.nih.gov 🔍 ☆


NIH **75 YEARS**
National Heart, Lung, and Blood Institute
Bringing Research to Life

Search the NHLBI

HEALTH TOPICS ▾ HEALTH EDUCATION ▾ THE SCIENCE ▾ GRANTS AND TRAINING ▾ NEWS AND EVENTS ▾ ABOUT NHLBI ▾

The first NIH National Commission

Blood Bank Repositories for Research



[NHLBI Anniversary](#) [Find a Clinical Trial](#) [Funding Opportunities](#) [NHLBI News](#)

Tsunami

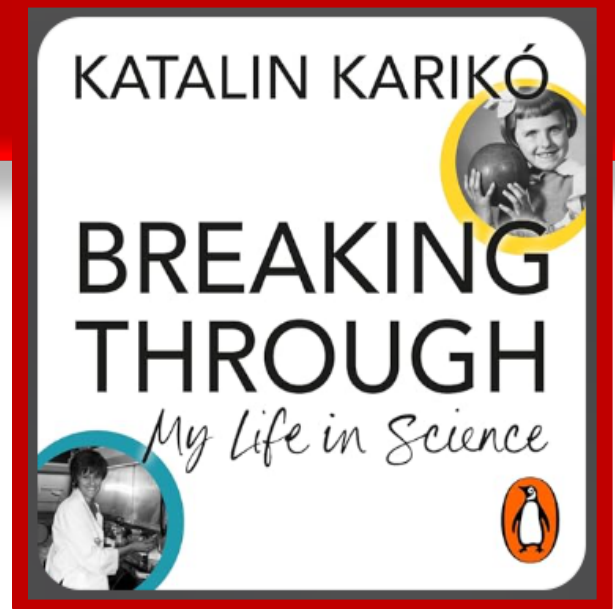
of research findings, waiting to happen!

Blood Bank Repositories for Research

Tsunami

of research findings, waiting to happen!

Tsunami needs to be triggered
Research needs leader to breakthrough



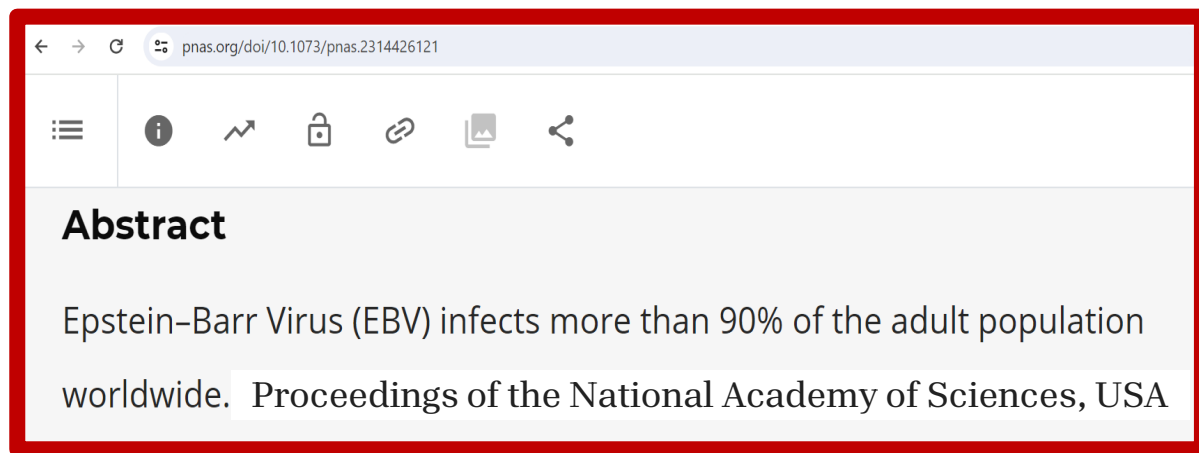
Tsunami

of research findings, waiting to happen!

Just think of one
example →



EBV



90% of the adult population is infected with Epstein-Barr Virus (EBV), worldwide.

Maroui MA, Odongo GA, Mundo L, Manara F, Mure F, Fusil F, Jay A, Gheit T, Michailidis TM, Ferrara D, Leoncini L, Murray P, Manet E, Ohlmann T, De Boevre M, De Saeger S, Cosset FL, Lazzi S, Accardi R, Herceg Z, Gruffat H, Khoueiry R. (2024) ***Aflatoxin B1 and Epstein-Barr virus-induced CCL22 expression stimulates B cell infection.***

Proceedings of the National Academy of Sciences U S A. 2024 April 16; 121(16):e2314426121. doi: 10.1073/pnas.2314426121. Epub 2024 April 4. PMID: 38574017 <https://pubmed.ncbi.nlm.nih.gov/38574017/>

Data

from cross-sectional research, still chained in blood banks and labs?

Can we detect EBV in
stored blood samples?

Yes
?

Gulley ML. ***Molecular diagnosis of Epstein-Barr virus-related diseases.*** J Mol Diagn. 2001 Feb; 3(1):1-10. doi: 10.1016/S1525-1578(10)60642-3. PMID: 11227065; PMCID: PMC1907346.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1907346/pdf/0043.pdf>

Ayee R, Ofori MEO, Wright E, Quaye O. (2020) **Epstein Barr Virus Associated Lymphomas and Epithelia Cancers in Humans**. J Cancer 2020; 11(7):1737-1750. doi:10.7150/jca.37282.
<https://www.jcancer.org/v11p1737.htm>

Establishment of latent infection by EBV has been implicated in several malignancies [30] due to the expression of limited sets of latent proteins, shown to play various biological roles discussed in Table 1.

EBV associated cancers

Table 1

Biological activities of Epstein Barr virus latency stage gene products and associated cancers

EBV latency protein	Type of latency	Biological activity	Associated cancers ^d
EBNA-1^a	Latency I, II, III	Segregation of viral genome in progenies, DNA replication, inhibition of MHC class I, enhances p53 degradation	Burkitt lymphoma, Gastric cancer, Breast cancer
EBNA-2	Latency III	Upregulation of host and viral proteins (transactivation), facilitate B cell immortalization	Posttransplant lymphoproliferative disorder
EBNA-3	Latency III	Transcription transactivation of both host and viral proteins, immortalization of B cell	Posttransplant lymphoproliferative disorder
EBNA-LP^b	Latency III	Transactivation of EBNA-2 to inactivate tumor suppressors, essential for immortalization of B cells	Posttransplant lymphoproliferative disorder
LMP-1/2^c	Latency II/III	B cell survival, upregulation of antiapoptotic proteins, mimics CD 40 ligand associated signaling, constitutively activate growth and cell survival promoting signaling pathways	Hodgkin lymphoma, Nasopharyngeal cancer, Posttransplant lymphoproliferative disorder, T/NK cell lymphoma, Breast cancer
EBV-Micro RNAs	Latency I, II, III	Target host mRNAs involved in apoptosis, proliferation and transformation. Suppress antigen presentation and activation of immune cells	Gastric cancer, T/NK cell lymphoma, nasopharyngeal cancer

^a EBNA-1 is expressed and detected in all EBV associated malignancies. ^b EBNA-LP is also known as EBNA-5. ^c LMP-1/2 are both involved in epithelia and B cell tumors, however, LMP 2 is frequently detected in a majority of all tumors as compared to LMP-1. ^d The associated tumors are not only limited to the ones discussed in this review.

Transmission of EBV through transplantation and blood transfusion has been reported. EBV establishes latent infection in B lymphocytes where it expresses limited sets of proteins (ETPs, EBNA, LMP) and EBER. Hematopoietic cell derived tumors include but not limited to Burkitt's lymphoma, Hodgkin lymphoma, post-transplant lymphoproliferative disorders, and natural killer (NK)/T cell lymphoma. EBV also causes epithelia derived malignancies such as nasopharyngeal cancer, gastric cancer, and breast cancer.

Information

from research findings just from one virus may save millions of lives.

If we can't detect, we can't treat, we can't cure

Blood
Banks
?

Real potential for cross-sectional data to feed and morph into longitudinal epidemiologic study.

60 YEARS AGO

> Lancet. 1964 Mar 28;1(7335):702-3. doi: 10.1016/s0140-6736(64)91524-7.

VIRUS PARTICLES IN CULTURED LYMPHOBLASTS FROM BURKITT'S LYMPHOMA

M A EPSTEIN, B G ACHONG, Y M BARR

PMID: 14107961 DOI: 10.1016/s0140-6736(64)91524-7

*That's why it is called **Epstein-Barr** Virus.*

90% of 8 billion people are infected with EBV

Sir Michael Anthony Epstein (1921–2024)

Codiscoverer of the Epstein-Barr virus

RICHARD F. AMBINDER AND RENA R. XIAN [Authors Info & Affiliations](#)

SCIENCE • 18 Apr 2024 • Vol 384, Issue 6693 • p. 274 • DOI: 10.1126/science.adp2961

> Lancet. 1964 Mar 28;1(7335):702-3. doi: 10.1016/s0140-6736(64)91524-7.

VIRUS PARTICLES IN CULTURED LYMPHOBLASTS FROM BURKITT'S LYMPHOMA

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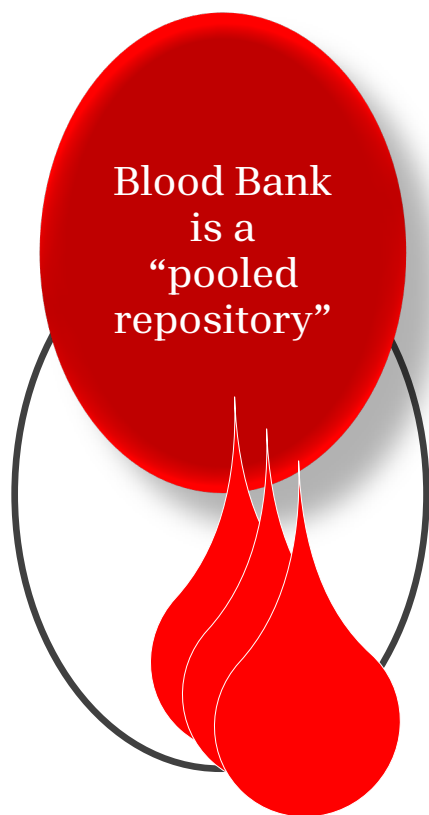
Sir Michael Anthony Epstein, pathologist who identified the first known human cancer-causing virus, died on **6 February 2024** at the age of 102. His team's pioneering work investigating primary tumor tissue and cultured tumor specimens from Ugandan children with jaw tumors identified the virus that now bears his name: the Epstein-Barr virus (EBV). EBV is associated with the tumor Epstein was studying, now known as Burkitt lymphoma, as well as a variety of other cancers and illnesses, including infectious mononucleosis and multiple sclerosis.





<https://doi.org/10.1126/science.adp2961>

Born in London, England, on 18 May 1921, Epstein studied medicine at Trinity College at the University of Cambridge and Middlesex Hospital Medical School in London. After national service with the Royal Army Medical Corps in India, he returned to the Middlesex Hospital, where there was interest in, as he wrote in his chapter of *Epstein Barr Virus Volume 1*, “the then deeply unfashionable chicken cancer viruses.” In 1911, Peyton Rous had characterized a virus in chickens that led to cancer, but there had been little interest in the implications. In 1956, Epstein spent a year studying electron microscopy with George Palade at the Rockefeller Institute in New York City. Palade convinced Epstein that viruses could be categorized on the basis of how they looked. Epstein again returned to the Middlesex Hospital, where he investigated the morphology of Rous sarcoma virus with electron microscopy and showed that it was an RNA virus.

Epstein was thus familiar with both cancer-causing viruses and electron microscopy when he happened to attend a lunchtime lecture by Denis Burkitt on a cancer prevalent in African children. Burkitt was a British Colonial Service medical officer based in Uganda, on leave in the UK. He described a tumor that typically arose in the jaw and quickly led to death, but what most interested Epstein was Burkitt's data showing that the geographical distribution of the tumor in Africa depended on temperature and rainfall. This suggested to Epstein that, as he wrote later, “a biological agent must play a part in causation,” and he immediately “postulated a climate-dependent arthropod vector spreading a cancer-causing virus.” Epstein decided to halt his current work and look for a virus in the lymphoma. He obtained funding from the British Empire Cancer Campaign (later Cancer Research UK) to travel to Uganda to, as he wrote, “work out how a regular supply of lymphoma samples” could be flown to his laboratory in London for testing.



→   ncbi.nlm.nih.gov/pmc/articles/PMC5618724/

Journal Article

T1-mapping using the Shortened Modified Look-Locker Inversion Recovery (ShMOLLI) technique has been validated in single- and multi-center clinical studies for a variety of cardiovascular diseases [17–28, 30–41]. It is also used in the UK Biobank (over 10,000 datasets acquired; projected total: 100'000, [42, 43]), and the ongoing multi-centre Hypertrophic Cardiomyopathy Registry study (HCMR; 2750 patients, [42–44]). We have a large resource of clinical and research scans with T1-mapping accumulated from pooled evidence from the past 7 years [18, 19, 23, 24, 26, 28, 30, 31, 34, 35, 39, 45]. In this study of 1291 subjects, we characterized commonly encountered clinical myocardial conditions using T1-mapping, derived native T1 ranges, and produced sample-size calculations to guide future clinical studies and trials.

Liu et al. *Journal of Cardiovascular Magnetic Resonance* (2017) 19:74
DOI 10.1186/s12968-017-0386-y

Journal of Cardiovascular
Magnetic Resonance

RESEARCH

Open Access



Measurement of myocardial native T1 in cardiovascular diseases and norm in 1291 subjects

Joanna M. Liu¹, Alexander Liu¹, Joana Leal¹, Fiona McMillan¹, Jane Francis¹, Andreas Greiser², Oliver J. Rider¹, Saul Myerson¹, Stefan Neubauer¹, Vanessa M. Ferreira¹ and Stefan K. Piechnik^{1*}

Table I

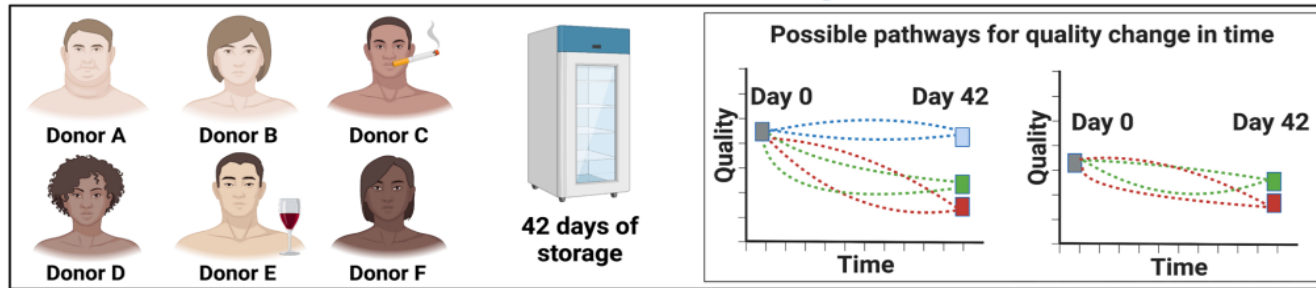
Delobel J, Rubin O, Prudent M, Crettaz D, Tissot JD, Lion N. (2010) **Biomarker analysis of stored blood products: emphasis on pre-analytical issues.** Int J Mol Sci. 2010 November 17;11(11):4601-4617. doi: 10.3390/ijms11114601. www.ncbi.nlm.nih.gov/pmc/articles/PMC3000103/pdf/ijms-11-04601.pdf

Parameters	Day 0	Day 3	Day 7	Day 14	Day 28	P value
Sodium	152.8 ± 4.01	150.1 ± 2.89	147.9 ± 1.41	143.1 ± 1.97	141.9 ± 3.99	<0.001
Potassium	4.33 ± 1.29	6.73 ± 2.43	9.93 ± 2.97	14.16 ± 4.56	19.89 ± 4.01	<0.001
Chloride	86.32 ± 1.96	89.55 ± 2.05	93.91 ± 2.44	96.83 ± 2.19	91.34 ± 1.09	<0.001
Calcium	0.06 ± 0.007	0.062 ± 0.005	0.063 ± 0.004	0.0067 ± 0.001	0.0066 ± 0.021	NS
Urea	27.71 ± 3.99	25.19 ± 2.70	26.11 ± 3.18	24.32 ± 2.45	24.17 ± 2.56	NS
Creatinine	0.99 ± 0.04	1.02 ± 0.02	1.07 ± 0.04	1.01 ± 0.06	1.02 ± 0.01	NS
AST (mg/dl)	21.95 ± 4.91	23.54 ± 6.32	28.43 ± 3.22	38.26 ± 9.90	44.31 ± 8.55	<0.001
ALT (mg/dl)	40.65 ± 13.65	40.43 ± 18.89	39.54 ± 23.66	44.87 ± 13.76	46.32 ± 10.87	0.487
LDH (mg/dl)	202.54 ± 17.87	289.21 ± 23.98	487.91 ± 97.93	523.65 ± 113.54	643.32 ± 187.8	<0.001
Proteins (g/dl)	6.76 ± 0.77	6.43 ± 0.76	5.99 ± 0.11	6.87 ± 0.3	6.7 ± 0.88	NS
PH	7.22 ± 0.18	7.01 ± 0.33	6.91 ± 0.44	6.89 ± 0.23	6.77 ± 0.54	<0.001

Will protein bio-markers suffer from storage lesions?

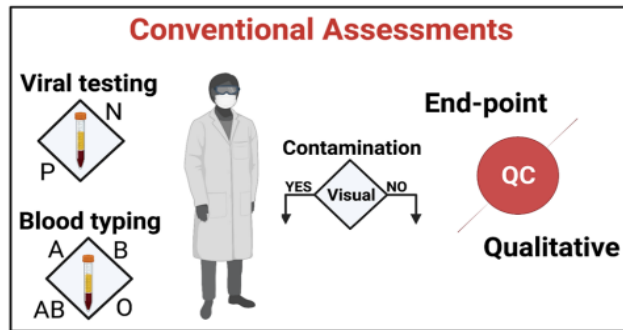
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6861460/pdf/PJMS-35-1697.pdf>

Donation and Storage

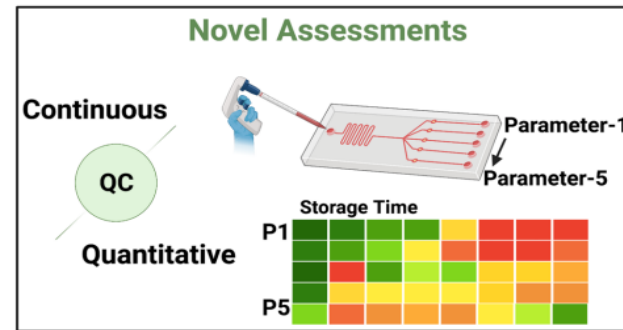


Transfusion

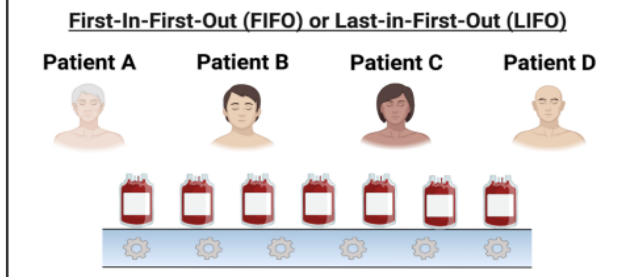
Current Workflow



Future Workflow



FIFO/LIFO Allocation



Data-driven Allocation

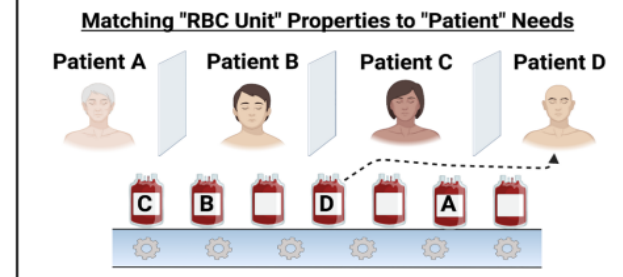




Fig. 1. The current and proposed future workflow for RBC storage and transfusion medicine.



TRANSFUSION MEDICINE

Regulation of kynurenine metabolism by blood donor genetics and biology impacts red cell hemolysis invitro and in vivo

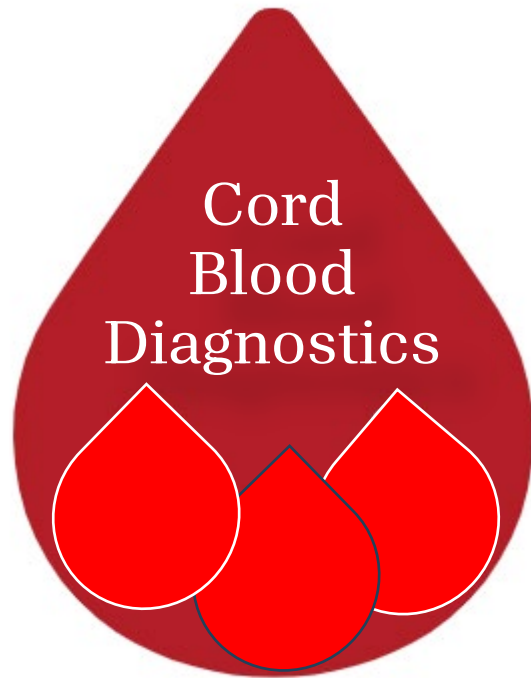
Travis Nemkov^{*1,2}, Daniel Stephenson^{*1}, Christopher Erickson¹,
Monika Dzieciatkowska¹, Alicia Key¹, Amy Moore³, Eric J. Earley³, Grier P. Page³,
Ian S. Lacroix¹, Mars Stone^{4,5}, Xutao Deng^{4,5}, Thomas Raife⁶, Steven Kleinman⁷,
James C. Zimring⁸, Nareg Roubinian^{4,5,9}, Kirk C. Hansen¹, Michael P. Busch^{4,5},
Philip J. Norris^{4,5}, Angelo D'Alessandro^{1,2}  ,

Recipient Epidemiology and Donor Evaluation Study-IV-P

Not only proteomic biomarkers but also genetic sign-posts using microarrays?

Kynurenine is a marker of osmotic fragility, and its levels are reproducible within a donor across donations. Polymorphisms in SLC7A5, **ATXN2** are associated with kynurenine levels in stored RBCs, Hgb increments, and in vivo hemolysis upon transfusion. <https://doi.org/10.1182/blood.2023022052>

Data analyses from cord blood are a cross-sectional study with potential for longitudinal research.



Bio-markers on-a-chip may lead to predictive/prognostic clues for personalized risk mitigation clinical strategies.

Guibert N, Pradines A, Favre G, Mazieres J. **Current and future applications of liquid biopsy in non-small cell lung cancer from early to advanced stages.** Eur Respir Rev. 2020 February 12; 29(155):190052. doi: 10.1183/16000617.0052-2019. PMID: 32051167; PMCID: PMC9488537. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9488537/pdf/ERR-0052-2019.pdf>

Šutić M, Vukić A, Baranašić J, Försti A, Džubur F, Samaržija M, Jakopović M, Brčić L, Knežević J. (2021) **Diagnostic, Predictive, and Prognostic Biomarkers in Non-Small Cell Lung Cancer (NSCLC) Management.** J Pers Med. 2021 October 27;11(11):1102. doi: 10.3390/jpm11111102. PMID: 34834454; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8624402/pdf/jpm-11-01102.pdf>

Imagine the treasure trove of data hiding in stored blood samples in blood banks

What epidemiology of blood donors can reveal about population public health

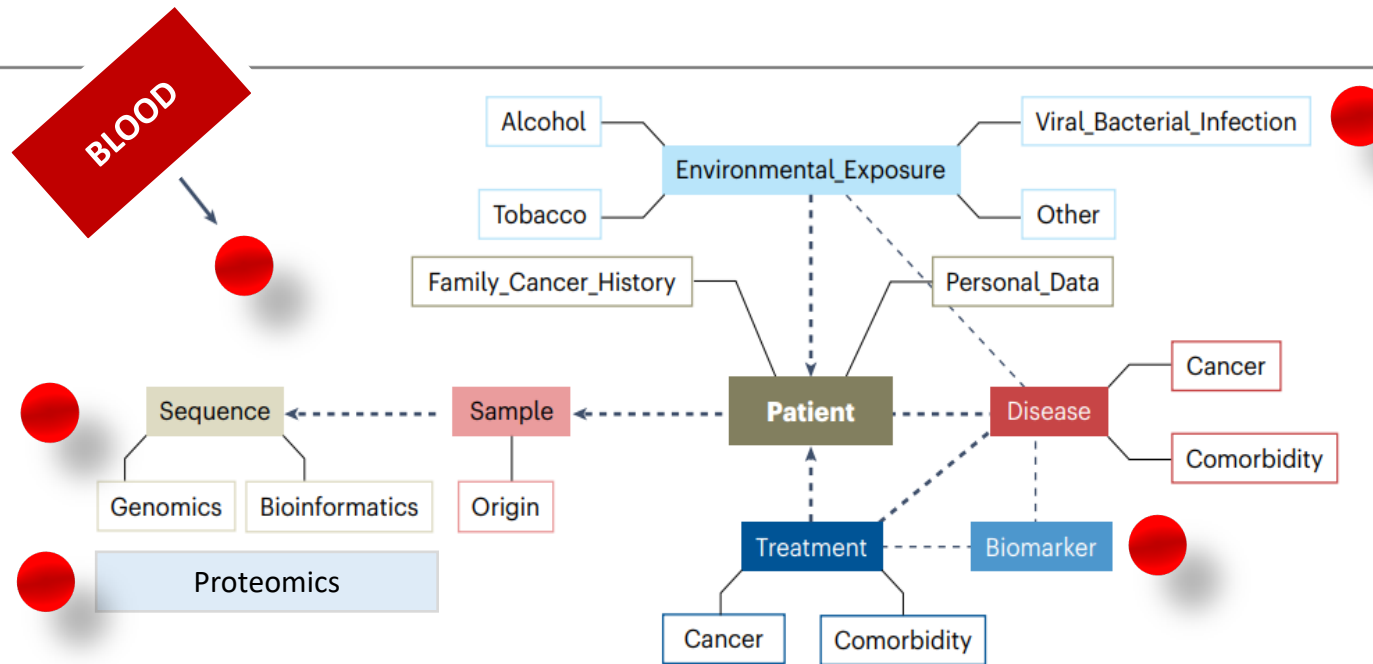


Fig. 1 | The 1+MG-MDC structure. Illustration of the 1+MG-MDC structure, comprising eight conceptual domains and related subdomains. Thick dotted lines indicate connections between domains, in some instances an additional arrowhead denotes directionality. Thin dotted lines indicate potential relationships between domains. Adapted from ref. 6.

<https://www.nature.com/articles/s41588-024-01721-x.pdf>

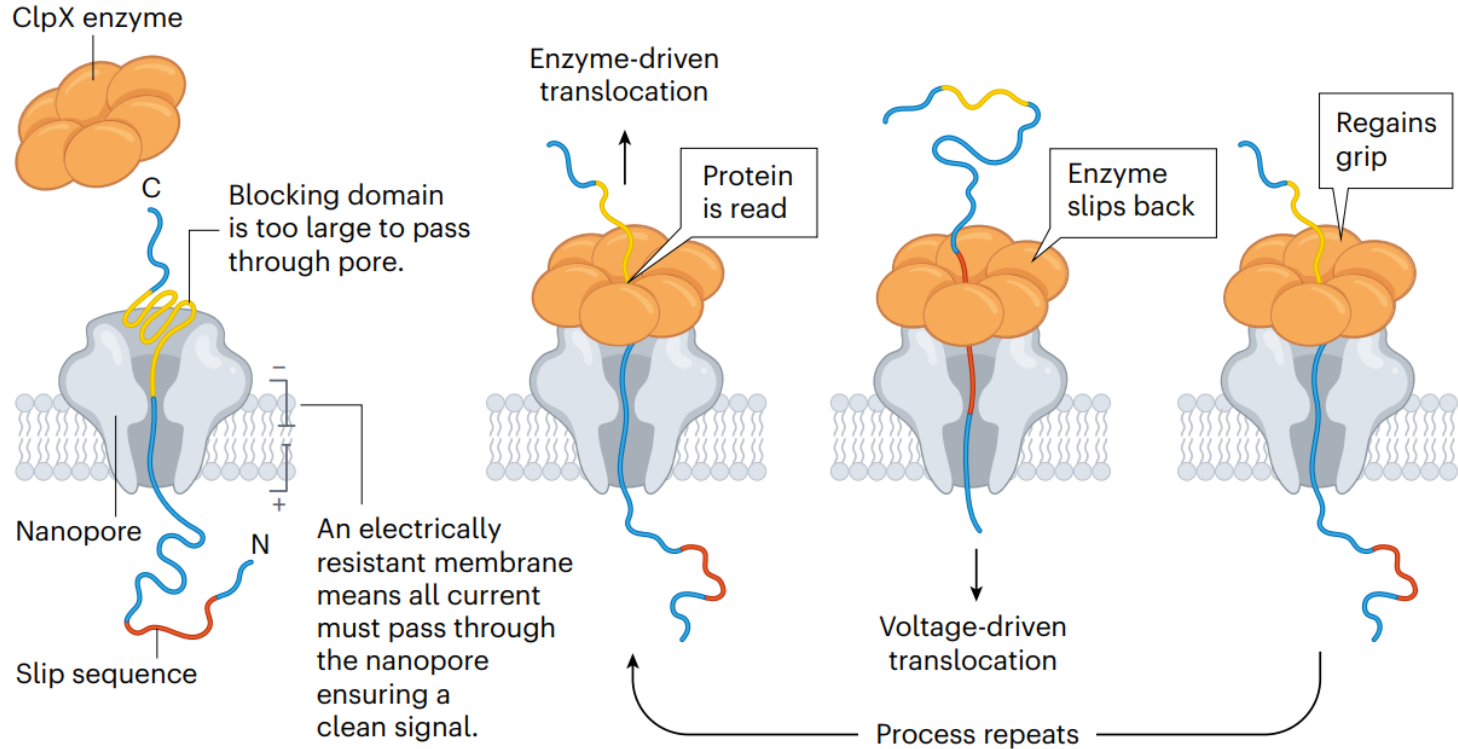
Riba M, Sala C, Culhane AC, Flobak Å, Patocs A, Boye K, Plevova K, Pospíšilová Š, Gandolfi G, Morelli MJ, Bucci G, Edsjö A, Lassen U, Al-Shahrour F, Lopez-Bigas N, Hovland R, Cuppen E, Valencia A, Poirel HA, Rosenquist R, Scollen S, Arenas Marquez J, Belien J, De Nicolo A, De Maria R, Torrents D, Tonon G. **The 1+Million Genomes Minimal Dataset for Cancer.** Nat Genet. 2024 May 3. doi: 10.1038/s41588-024-01721-x

Genomics (genotype) is not necessarily phenotype (proteomics)

<https://media.nature.com/original/magazine-assets/d41586-024-01280-5/d41586-024-01280-5.pdf>

READ AND REPEAT

One nanopore-based protein-sequencing strategy uses the push and pull of an electric field, the ClpX enzyme (orange) and a 'slip sequence' to move a protein back and forth across a membrane, providing multiple views of the protein sequence and increasing accuracy.



A nanopore sequencing device is typically used for sequencing DNA and RNA.

NANOPORE SEQUENCING COMES FOR PROTEINS

l'humanité a besoin de rêveurs

Will there be bumps on
the road to success?
Undoubtedly.

Humanity needs dreamers

<https://pccm.princeton.edu/events/humanity-needs-dreamers-visit-marie-curie-1>

<https://www.cambridgema.gov/cpl/calendarofevents/2018/04/19/humanityneedsdreamersavisitwithmariecurie>

www.colorado.edu/cuwizards/2020/11/14/december-5-2020-humanity-needs-dreamers-visit-marie-curie-susan-marie-frontczak

Article | **Separation Sample Preparation** 26 November 2012

Blood bank bias: Protein biomarkers of stored red blood cells



Overview

Several biomarkers of degradation in stored red blood cells have been identified in a proteomics study, providing an opportunity to estimate deterioration during storage as well as blood doping in sports.

Storage-induced changes of the cytosolic red blood cell proteome analyzed by 2D DIGE and high-resolution/high-accuracy MS.

Walpurgis K¹, Kohler M, Thomas A, Wenzel F, Geyer H, Schänzer W, Thevis M

Author information ▶

Proteomics, 09 Oct 2012, 12(21):3263-3272

<https://doi.org/10.1002/pmic.201200280> PMID: 22965759

BUT

If only 1% of the global population (~8 billion people) use diagnostics & treatment, imagine the business potential of research results!

If ethical profitability of social businesses can help improve healthcare for even 10% of the global population, then we helped ~800 million more!

Leukapheresis to enrich for T (CAR-T) lymphocytes for non-affluent nations?

CUTTING-EDGE CANCER THERAPY IS MADE IN INDIA — AT ONE-TENTH THE COST

The treatment, called NexCAR19, raises hopes that a transformative class of medicine will become more readily available in low- and middle-income countries.

By Smriti Mallapaty

A small Indian biotechnology company is producing a home-grown version of a cutting-edge cancer treatment known as chimeric antigen receptor (CAR) T-cell therapy that was pioneered in the United States. CAR-T therapies are used mainly to treat blood cancers and have burgeoned in the past few years. The Indian CAR-T therapy costs one-tenth that of comparable commercial products available globally.

A single treatment of NexCAR19, manufactured by Mumbai-based ImmunoACT, costs between US\$30,000 and \$40,000. The first CAR-T therapy was approved in the United States in 2017, and commercial CAR-T therapies currently cost between \$370,000 and \$530,000, not including hospital fees and drugs to treat side effects. These treatments have also shown promise in treating autoimmune diseases and brain cancer.

India's drug regulator approved NexCAR19 for therapeutic use in India in October. By

December, ImmunoACT was administering the therapy to paying patients, and it is now treating some two-dozen people a month in hospitals across the country.

"It's a dream come true," says Alka Dwivedi, an immunologist who helped to develop NexCAR19 and is now at the US National Cancer Institute (NCI) in Bethesda, Maryland. Her voice becomes tender as she describes seeing the first patient's cancer go into remission. These are people for whom all other treatments have failed, says Dwivedi.

<https://www.nature.com/articles/d41586-024-00809-y.pdf>

Nature | Vol 627 | 28 March 2024 | 709

The social business of medicine guided by ethical profitability for for-profit ventures? **Model for non-affluent non-OECD nations?**

NEWS | 21 March 2024 <https://www.nature.com/articles/d41586-024-00809-y>

Cutting-edge CAR-T cancer therapy is now made in India – at one-tenth the cost

The treatment, called NexCAR19, raises hopes that this transformative class of medicine will become more readily available in low- and middle-income countries.

COST IN USA

\$530,000

COST IN INDIA

\$30,000

A single treatment of NexCAR19, manufactured by Mumbai-based ImmunoACT, costs between US\$30,000 and \$40,000. The first CAR-T therapy was **approved** in the United States in 2017, and commercial CAR-T therapies in the US cost between \$370,000 and \$530,000, not including hospital fees and drugs to treat side effects. These treatments have also shown promise in treating **autoimmune diseases** and **brain cancer**. “It’s a dream come true,” says Alka Dwivedi, an immunologist who helped to develop NexCAR19 and is now at the US National Cancer Institute (NCI, NIH) in Bethesda, MD. These are people for whom all other treatments have failed, says Dwivedi. There is a “tremendous patient need”, says Nirali Shah, a paediatric oncologist at NCI, NIH who is also an academic collaborator of the researchers at ImmunoACT. “It’s positive news,” says Renato Cunha, a haematologist at the Grupo Oncoclínicas in São Paulo, Brazil. He says the Indian product could pave the way for making advanced cellular therapies accessible to other low- and middle-income countries. “Hope is the word that comes to mind.”

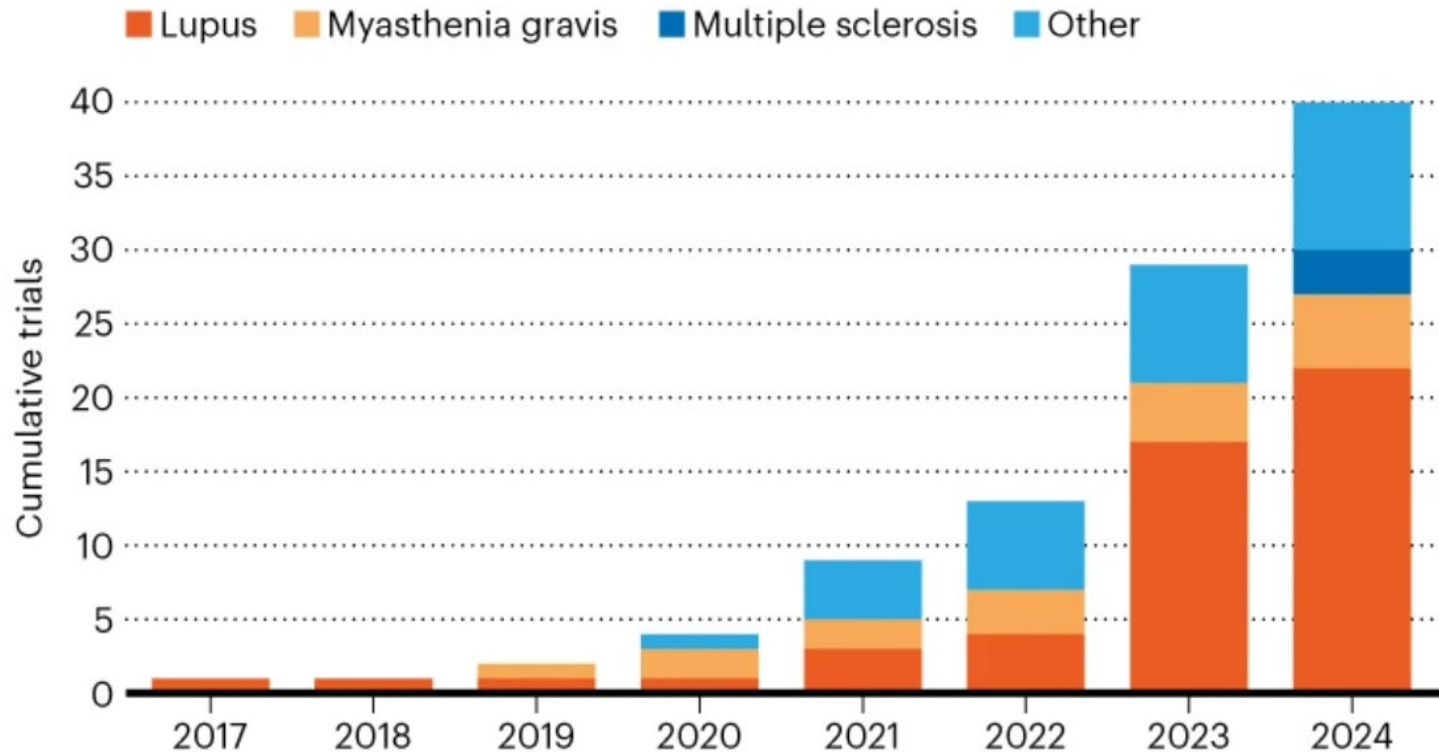
The potential for blood banks and blood donors as a source for CAR-T cells?

CAR-T therapy for multiple sclerosis enters US trials for first time

Hopes are high that engineered immune cells, which are already in use to treat blood cancer, will halt the progression of a degenerative autoimmune disorder.

ENLISTING IMMUNE CELLS TO TREAT AUTOIMMUNE DISEASE

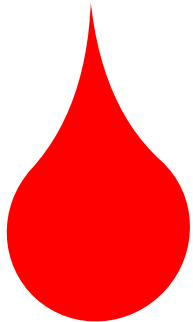
The number of clinical trials of CAR T cells — engineered immune cells — used to treat autoimmune disorders has grown rapidly over the past seven years. Testing of CAR-T therapy for the autoimmune disorder lupus accounts for the bulk of the trials.





ELSEVIER

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Review

Cord Blood Banking in the Arab World: Current Status and Future Developments

Monica M. Matsumoto¹, Rana Dajani², Kirstin R.W. Matthews^{1,*}¹James A. Baker III Institute for Public Policy, Science and Technology Policy Program, Rice University, Houston, Texas²Department of Biology and Biotechnology, Hashemite University of Jordan, Zarqa, Jordan**Table 3**

Timeline of Major CB Banking Developments in the Arab World

<http://dx.doi.org/10.1016/j.bbmt.2015.01.012> 1083-8791/

Year	Development
1998	First CB transplant is performed in Arab world
2003	SA: KFSH-RC begins performing CB transplants (from imported units) Muslim World League's Jurisprudential Council issues a <i>fatwa</i> approving CB for research and therapy
2006	UAE: DCRC opens first CB bank in the region, as a public–private hybrid model SA: KFSH-RC opens the Kingdom's first public CB bank UAE: Cryo-Save Arabia, the largest private CB storage facility in the region, opens in Dubai Healthcare City
2007	EG: National Blood Policy is approved with procedural guidelines for CB collection and storage
2009	QA: Virgin Health Bank moves its headquarters from London to Doha EG: CellSafe opens as the country's first private CB bank
2011	QA: Virgin Health Bank is granted the first (and only, to date) license for CB procurement, processing, and storage SA: KAIMRC opens the country's second public CB bank and creates the Saudi Donor Registry QA: Virgin Health Bank opens storage and processing facility at Qatar Science & Technology Park EG: National Stem Cell Committee is created and tasked with establishing regulations for stem cell research and therapy as well as a public CB bank
2012	EG: Stem cell research center opens at Sheikh Zayed Hospital QA: Stem cell research policy is enacted into legislation, allowing research using CB stem cells
2013	EG: Center for Stem Cell Research and Regenerative Medicine opens in Zewail City of Science & Technology
2014	JO: New stem cell research law is passed, including regulations for CB banking
2015	JO: Projected opening of the first in-country private CB storage facility by the company, BabyCord Jordan EG: Projected opening of the country's first public CB bank, located at Assiut University, in partnership with Zewail City of Science & Technology
2016	JO: Projected opening of the country's first public CB bank, located at KHCC

The potential for cord blood banks as an autologous source for CAR-T cells?

Table 1

Relevant Demographic, Health, and Economic Indicators of 5 Arab Countries Studied: Jordan, Saudi Arabia, UAE, Egypt, and Qatar

Country	Population	Arab	Fert	GNI	Health \$	Hosp Beds	Leukemia	Lymphoma
Jordan	7.93M	98%	3.16	\$4.95k	8.4%	1.8	6.1	8.2
Saudi Arabia	27.3M	90%	2.17	\$26.2k	3.7%	2.2	3.8	7.9
UAE	5.63M	13% ^{ll}	2.36	\$38.6k	3.3%	1.9	3.7	6.7
Egypt	86.9M	99%	2.87	\$3.16k	4.9%	1.7	5.9	9.3
Qatar	2.12M	40%	1.92	\$85.5k	1.9%	1.2	4.9	7.7

Table 2

Current CB Banking Options in the Arab World

CB Bank	Type	Storage Location	Collection Office Location(s)
BabyCord	Priv	USA (Boston), Jordan (Amman)*	Jordan
Biovault Family	Priv	UK (Plymouth)	Lebanon, UAE
CellSafe	Priv	Egypt (Cairo)	Egypt
Cells4Life	Priv	UK (Burgess Hill, Essex)	Bahrain, Egypt, Jordan, Kuwait, Lebanon, Qatar, Saudi Arabia, UAE
Center for Stem Cell Research & Regenerative Medicine	Publ	Egypt (Assiut)*	Egypt
Cryo-Save	Priv	UAE (Dubai), Belgium (Niel)	Egypt, Kuwait, Oman, Saudi Arabia, UAE
DCRC [†]	Hybr	UAE (Dubai)	UAE
Future Health Biobank	Priv	UK (Nottingham), Switzerland (Châtel-St-Denis)	Bahrain, Egypt, Jordan, Kuwait, Lebanon, Morocco, Qatar, Saudi Arabia, Syria, UAE
KAIMRC	Publ	Saudi Arabia (Riyadh)	Saudi Arabia
KFSH-RC [†]	Publ	Saudi Arabia (Riyadh)	Saudi Arabia
KHCC	Publ	Jordan (Amman)*	Jordan
Precious Cells	Priv	UK (Middlesex)	Jordan, Lebanon, UAE
Smart Cells	Priv	UK (West Drayton)	Egypt, Jordan, Kuwait, Lebanon, Syria, UAE
Sultan Qaboos Univ. Hospital	Publ	Oman (Muscat)	Oman
Virgin Health Bank	Priv, Hybr	Qatar (Doha)	Qatar

Matsumoto MM, Dajani R, Matthews KR. **Cord Blood Banking in the Arab World: Current Status and Future Developments. Biol Blood Marrow Transplant.** 2015 July; 21(7):1188-94. doi: 10.1016/j.bbmt.2015.01.012. Epub 2015 Feb 14. PMID: 25687797.

2024 Warren Alpert Prize Honors Four Pioneers in CAR T-Cell Therapy

Lab-made immune cells offer a lifeline for patients with blood cancers

www.penmedicine.org/news/news-blog/2023/august/carl-june-on-the-boundless-potential-of-car-t-cell-therapy

Kalos M, Levine BL, Porter DL, Katz S, Grupp SA, Bagg A, June CH. **T cells with chimeric antigen receptors have potent antitumor effects and can establish memory in patients with advanced leukemia.** Sci Transl Med.

2011 August 10; 3(95):95ra73. doi: 10.1126/scitranslmed.3002842

www.ncbi.nlm.nih.gov/pmc/articles/PMC3393096/pdf/nihms384661.pdf

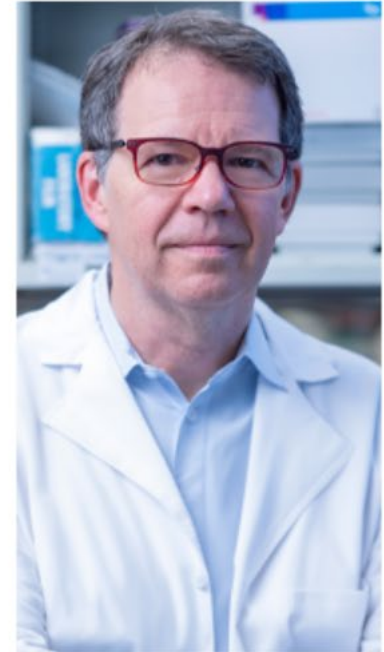
Porter DL, Levine BL, Kalos M, Bagg A, June CH. **Chimeric antigen receptor-modified T cells in chronic lymphoid leukemia.** N Engl J Med. 2011 Aug

25;365(8):725-33. doi: 10.1056/NEJMoa1103849. Epub 2011 Aug 10. Erratum in: N Engl J Med. 2016 Mar 10;374(10):998. doi: 10.1056/NEJMs160005

www.ncbi.nlm.nih.gov/pmc/articles/PMC3387277/pdf/nihms-320786.pdf

2024 Warren Alpert Prize Honors Four Pioneers in CAR T-Cell Therapy

Lab-made immune cells offer a lifeline for patients with blood cancers



- [Renier Brentjens](#), Katherine Anne Gioia Endowed Chair of Medicine and deputy director of Roswell Park Comprehensive Cancer Center
- [Zelig Eshhar](#), professor emeritus, the Weizmann Institute of Science, chair of Immunology, Division of R&D, Sourasky Medical Center, Israel
- [Carl June](#), Richard W. Vague Professor in Immunotherapy, University of Pennsylvania Perelman School of Medicine
- [Michel Sadelain](#), Stephen and Barbara Friedman Chair, founding director of the Center for Cell Engineering at Memorial Sloan Kettering Cancer Center

<https://hms.harvard.edu/news/2024-warren-alpert-prize-honors-four-pioneers-car-t-cell-therapy>

Potential for blood banks / cord blood banks in cellular & molecular therapy

FUTURE FORWARD RESEARCH – THINK VERY FAR BEYOND THE HORIZON

- Take any blood and transform HLA gene expression to match recipient (HLA typing) for transfusion medicine
- Apheresis of donor blood to enrich for desired cell types (e.g., CAR-T) and induce HLA gene expression for immune match
- Use CD34+ cord blood cells and induce (iPSC) to make immuno-compatible tissue (any tissue, organoid) for transplantation

To: Shoumen Pa Datta

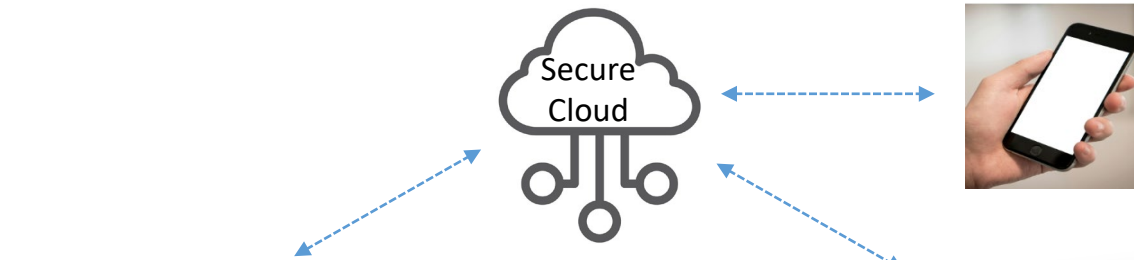


Sun 4/7/2024 3:58 PM

Are you asking if blood banks can do this? If so, the answer is yes.

I'd like to talk to you about the possibility and problems. Many of the blood centers are very conservative.

Digital Health Hematology Services (DHHS is far closer at hand)



Local Wireless Sensor Mesh Network

DHHS IN THE NEAR-FUTURE OF BLOOD BANKS ?



Data-Informed Decision Support (DIDS) Systems
Distributed Secure Near Real-time Mobile Digital Health Services

← → ↻ nhlbi.nih.gov/news/2021/future-medicine-lab-chip-devices-starting-make-impact

 An official website of the United States government [Here's how you know](#) ▾



National Heart, Lung,
and Blood Institute



[Home](#) / [News and Events](#) / [All News](#) / Future of medicine: Lab-on-a-chip

RESEARCH FEATURE

Future of medicine: Lab-on-a-chip devices starting to make an impact

September 27, 2021

Article

<https://doi.org/10.1038/s41467-024-48910-0>

Mucus production, host-microbiome interactions, hormone sensitivity, and innate immune responses modeled in human cervix chips

Received: 22 April 2023

Zohreh Izadifar^{1,5}, Justin Cotton¹, Siyu Chen², Viktor Horvath¹,

Accepted: 22 March 2024

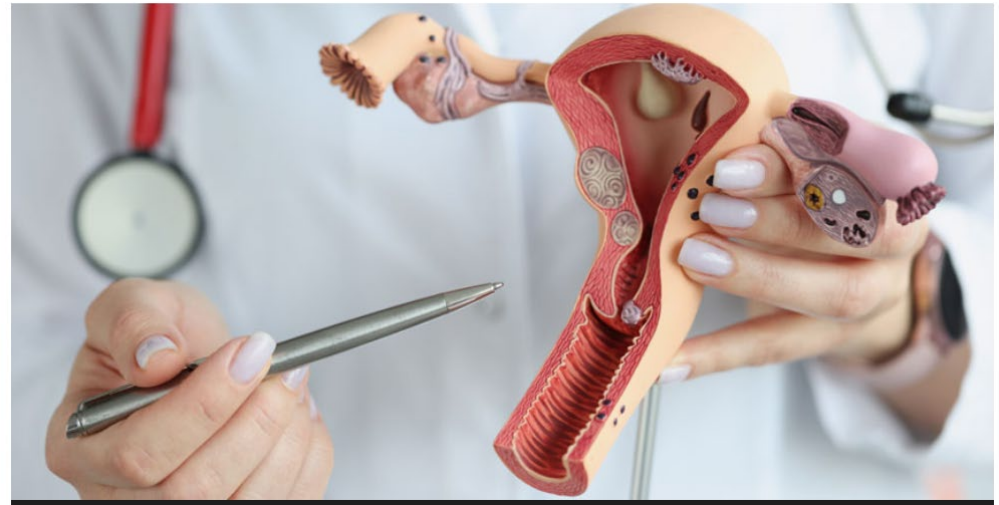
Anna Stejskalova³, Aakanksha Gulati¹, Nina T. LoGrande¹, Bogdan Budnik¹,
Sanjiv Shahriar¹, Erin R. Doherty¹, Yixuan Xie², Tania To¹, Sarah E. Gilpin¹,
Adama M. Sesay¹, Girija Goyal¹, Carlito B. Lebrilla^{1,4} & Donald E. Ingber^{1,3,4}✉

Published online: 29 May 2024

Cervix-on-a-Chip to Accelerate Research on Women's Health

New model could lead to better understanding of, treatments for diseases of female reproductive tract

June 6, 2024 | Research



<https://hms.harvard.edu/news/cervix-chip-accelerate-research-womens-health>



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Mahajan G, Doherty E, To T, Sutherland A, Grant J, Junaid A, Gulati A, LoGrande N, Izadifar Z, Timilsina SS, Horváth V, Plebani R, France M, Hood-Pishchany I, Rakoff-Nahoum S, Kwon DS, Goyal G, Prantil-Baun R, Ravel J, Ingber DE. **Vaginal microbiome-host interactions modeled in a human vagina-on-a-chip**. *Microbiome*. 2022 Nov 26; 10(1):201. doi: 10.1186/s40168-022-01400-1

Mahajan et al. *Microbiome* (2022) 10:201
<https://doi.org/10.1186/s40168-022-01400-1>

Microbiome

RESEARCH

Open Access

Vaginal microbiome-host interactions modeled in a human vagina-on-a-chip



Gautam Mahajan^{1,2}, Erin Doherty¹, Tania To¹, Arlene Sutherland¹, Jennifer Grant¹, Abidemi Junaid¹, Aakanksha Gulati¹, Nina LoGrande¹, Zohreh Izadifar¹, Sanjay Sharma Timilsina¹, Viktor Horváth¹, Roberto Plebani^{1,3}, Michael France⁴, Indriati Hood-Pishchany⁵, Seth Rakoff-Nahoum⁵, Douglas S. Kwon^{6,7}, Girija Goyal¹, Rachele Prantil-Baun¹, Jacques Ravel⁴ and Donald E. Ingber^{1,8,9*}

← → ↻ 🌐 wyss.harvard.edu/news/a-breakthrough-in-bacterial-vaginosis-treatment-for-womens-health/

WYSS  INSTITUTE

Who We Are

Our Work

Collaborations

A breakthrough in bacterial vaginosis treatment for women's health

November 28, 2022

Human Organ Chip allows researchers to study effects of microbiome on vaginal health



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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9701078/pdf/40168_2022_Article_1400.pdf

<https://wyss.harvard.edu/news/a-breakthrough-in-bacterial-vaginosis-treatment-for-womens-health/>



A digital microfluidic analyzer stands behind a disposable lab-on-a-chip cartridge (forefront), where blood samples are collected to screen for the presence of rare diseases.

[nhlbi.nih.gov/news/2021/future-medicine-lab-chip-devices-starting-make-impact](https://www.nhlbi.nih.gov/news/2021/future-medicine-lab-chip-devices-starting-make-impact)

Researchers supported by the NHLBI are playing a key role in the development of this technology — and for good reason. The chips not only are capable of quickly diagnosing diseases, but they can also do so at a lower cost, faster speed, and with higher accuracy than their bulkier counterparts, researchers say. Some may be coming to a hospital or medicine cabinet near you.

“Watching discoveries move from the lab to the clinic is incredibly exciting,” said Stephanie M. Davis, Ph.D., NHLBI’s Small Business Program Coordinator. “The NHLBI Small Business Program is thrilled to see lab-on-a-chip technologies finally move toward the marketplace.”



NIH Public Access

Author Manuscript

Annu Rev Biomed Eng. Author manuscript; available in PMC 2013 September 22.

Published in final edited form as:

Annu Rev Biomed Eng. 2005 ; 7: 77–103. doi:10.1146/annurev.bioeng.7.011205.135108.

BLOOD-ON-A-CHIP

Mehmet Toner and Daniel Irimia

BioMEMS Resource Center, Center for Engineering in Medicine and Surgical Services, Massachusetts General Hospital, Shriners Hospital for Children, and Harvard Medical School, Boston, Massachusetts 02114

Mehmet Toner: mtoner@hms.harvard.edu; Daniel Irimia: dirimia@hms.harvard.edu

Abstract

Accurate, fast, and affordable analysis of the cellular component of blood is of prime interest for medicine and research. Yet, most often sample preparation procedures for blood analysis involve handling steps prone to introducing artifacts, whereas analysis methods commonly require skilled technicians and well-equipped, expensive laboratories. Developing more gentle protocols and affordable instruments for specific blood analysis tasks is becoming possible through the recent progress in the area of microfluidics and lab-on-a-chip-type devices. Precise control over the cell microenvironment during separation procedures and the ability to scale down the analysis to very small volumes of blood are among the most attractive capabilities of the new approaches. Here we review some of the emerging principles for manipulating blood cells at microscale and promising high-throughput approaches to blood cell separation using microdevices. Examples of specific single-purpose devices are described together with integration strategies for blood cell separation and analysis modules.





Keywords

lab-on-a-chip; point-of-care diagnostic; cell separation; sample preparation; microfluidic

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Micro-mechanical blood clot testing using smartphones

Justin Chan ¹✉, Kelly Michaelsen ²✉, Joanne K. Estergreen³, Daniel E. Sabath ³ & Shyamnath Gollakota ¹✉

University of Washington researchers have developed a new blood-clotting test that uses only a single drop of blood and a smartphone with a plastic attachment that holds a tiny cup [shown here] beneath the phone's camera.

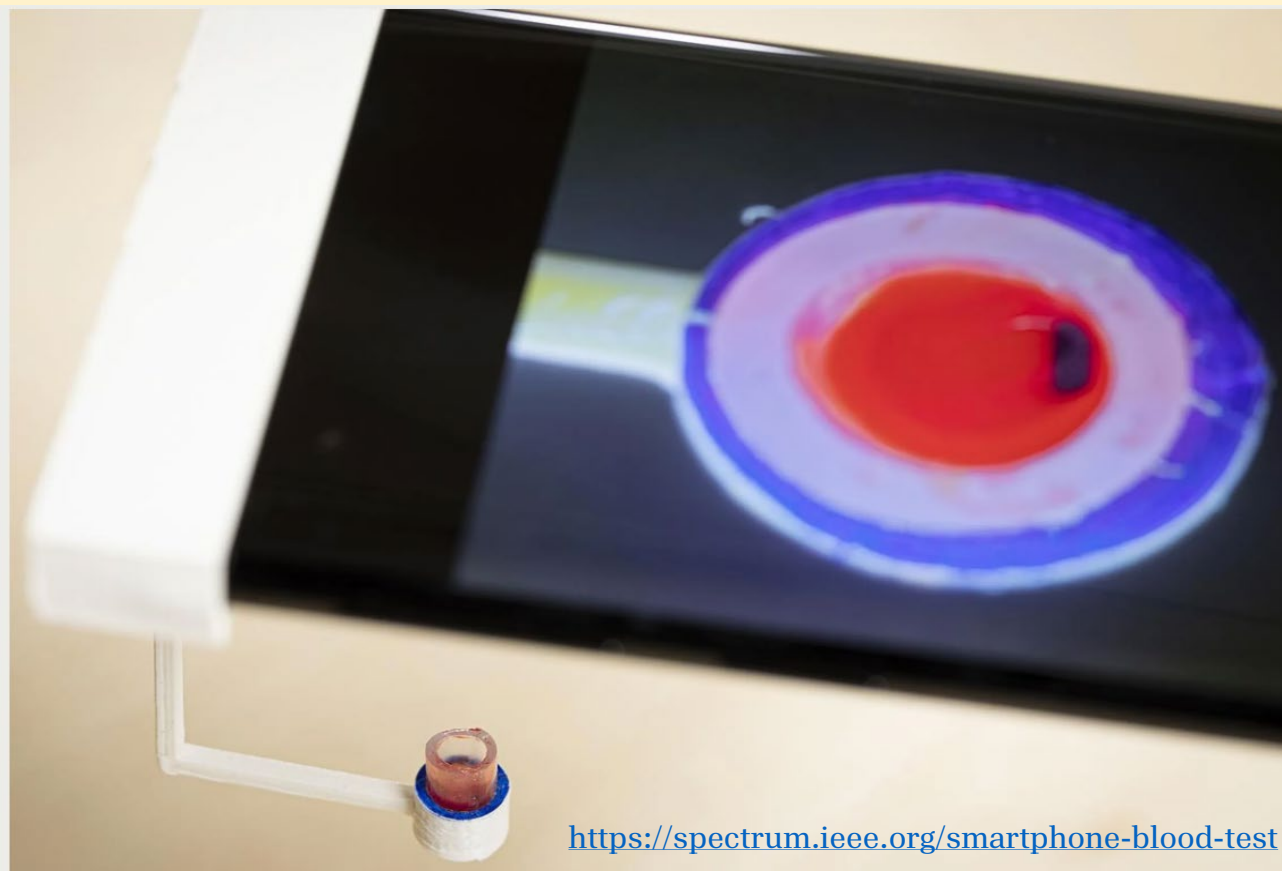
Blood Test Only Needs a Drop and a Smartphone for Results > The tech shows promise, although user-friendly “single drop of blood” platforms are still a few years away

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8837659/pdf/41467_2022_Article_28499.pdf

Chan J, Michaelsen K, Estergreen JK, Sabath DE, Gollakota S.

Micro-mechanical blood clot testing using smartphones.

Nature Commun. 2022 Feb 11; 13(1):831. doi: 10.1038/s41467-022-28499-y. PMID: 35149711; PMCID: PMC8837659.



<https://spectrum.ieee.org/smartphone-blood-test>

Théo Willeman*, Justine Grunwald, Marc Manceau, Frédéric Lapierre, Lila Krebs-Drouot, Coralie Boudin, Virginie Scolan, H el ene Eysseric-Guerin, Fran oise Stanke-Labesque and Bruno Revol

Smartphone swabs as an emerging tool for toxicology testing: a proof-of-concept study in a nightclub

<https://doi.org/10.1515/cclm-2024-0242>

Received February 22, 2024; accepted March 27, 2024;
published online April 5, 2024


From the journal [Clinical Chemistry and Laboratory Medicine \(CCLM\)](#)

<https://doi.org/10.1515/cclm-2024-0242>

OPEN

 Check for updates

Per- and polyfluoroalkyl substances (PFAS) and thyroid hormone measurements in dried blood spots and neonatal characteristics: a pilot study

Ana K. Rosen Vollmar¹, Elizabeth Z. Lin¹, Sara L. Nason², Katerina Santiago³, Caroline H. Johnson¹, Xiaomei Ma³, Krystal J. Godri Pollitt¹ and Nicole C. Deziel ¹✉

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Is a PFAS smartphone sensor in the works?

BACKGROUND: Pediatric thyroid diseases have been increasing in recent years. Environmental risk factors such as exposures to chemical contaminants may play a role but are largely unexplored. Archived neonatal dried blood spots (DBS) offer an innovative approach to investigate environmental exposures and effects.

OBJECTIVE: In this pilot study, we applied a new method for quantifying per- and polyfluoroalkyl substances (PFAS) to 18 archived DBS from babies born in California from 1985–2018 and acquired thyroid hormone measurements from newborn screening tests. Leveraging these novel data, we evaluated (1) changes in the concentrations of eight PFAS over time and (2) the relationship between PFAS concentrations, thyroid hormone concentrations, and neonatal characteristics to inform future research.

METHODS: PFAS concentrations in DBS were measured using ultra-high-performance liquid chromatography-mass spectrometry. Summary statistics and non-parametric Wilcoxon rank-sum and Kruskal–Wallis tests were used to evaluate temporal changes in PFAS concentrations and relationships between PFAS concentrations, thyroid hormone concentrations, and neonatal characteristics.

RESULTS: The concentration and detection frequencies of several PFAS (PFOA, PFOS, and PFOSA) declined over the assessment period. We observed that the timing of specimen collection in hours after birth was related to thyroid hormone but not PFAS concentrations, and that thyroid hormones were related to some PFAS concentrations (PFOA and PFOS).

IMPACT STATEMENT: This pilot study examines the relationship between concentrations of eight per- and polyfluoroalkyl substances (PFAS), thyroid hormone levels, and neonatal characteristics in newborn dried blood spots (DBS) collected over a period of 33 years. To our knowledge, 6 of the 22 PFAS we attempted to measure have not been quantified previously in neonatal DBS, and this is the first study to examine both PFAS and thyroid hormone concentrations using DBS. This research demonstrates the feasibility of using newborn DBS for quantifying PFAS exposures in population-based studies, highlights methodological considerations in the use of thyroid hormone data for future studies using newborn DBS, and indicates potential relationships between PFAS concentrations and thyroid hormones for follow-up in future research.

Keywords: PFAS; Per- and polyfluoroalkyl substances; Dried blood spot; Thyroid hormone; Newborn; Environmental exposure

Journal of Exposure Science & Environmental Epidemiology (2023) 33:737–747; <https://doi.org/10.1038/s41370-023-00603-4>

<https://www.niehs.nih.gov/health/topics/agents/pfc>

Business strategy of low usage fees lowers the barrier to market entry.

Don't think market of millions. Think about creating markets for the

NEXT BILLION USERS with mobile phones!

◆ Think cable TV

Remember **PAY PER VIEW ?**

◆ Think plain old telephone system (POTS)

Remember **PAY PER CALL ?**

◆ Think purchasing power parity (PPP) of the next billion users

Remember PAPPU (**PAY A PENNY PER USE**)

PAY PER USE • Analytics-Lab-on-a-Chip-on-a-Flash Drive

BLOOD BANK TEST SENSOR

EBV Sensor

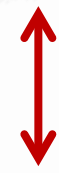
Glucose Sensor

Cholesterol Sensor

SARS-CoV-2 Sensor



There's an app for that



Hot swappable, modular, smart



NK Labs
ARA Prototype

Digital Health: Analytics-Lab-on-a-Chip-on-a-FlashDrive

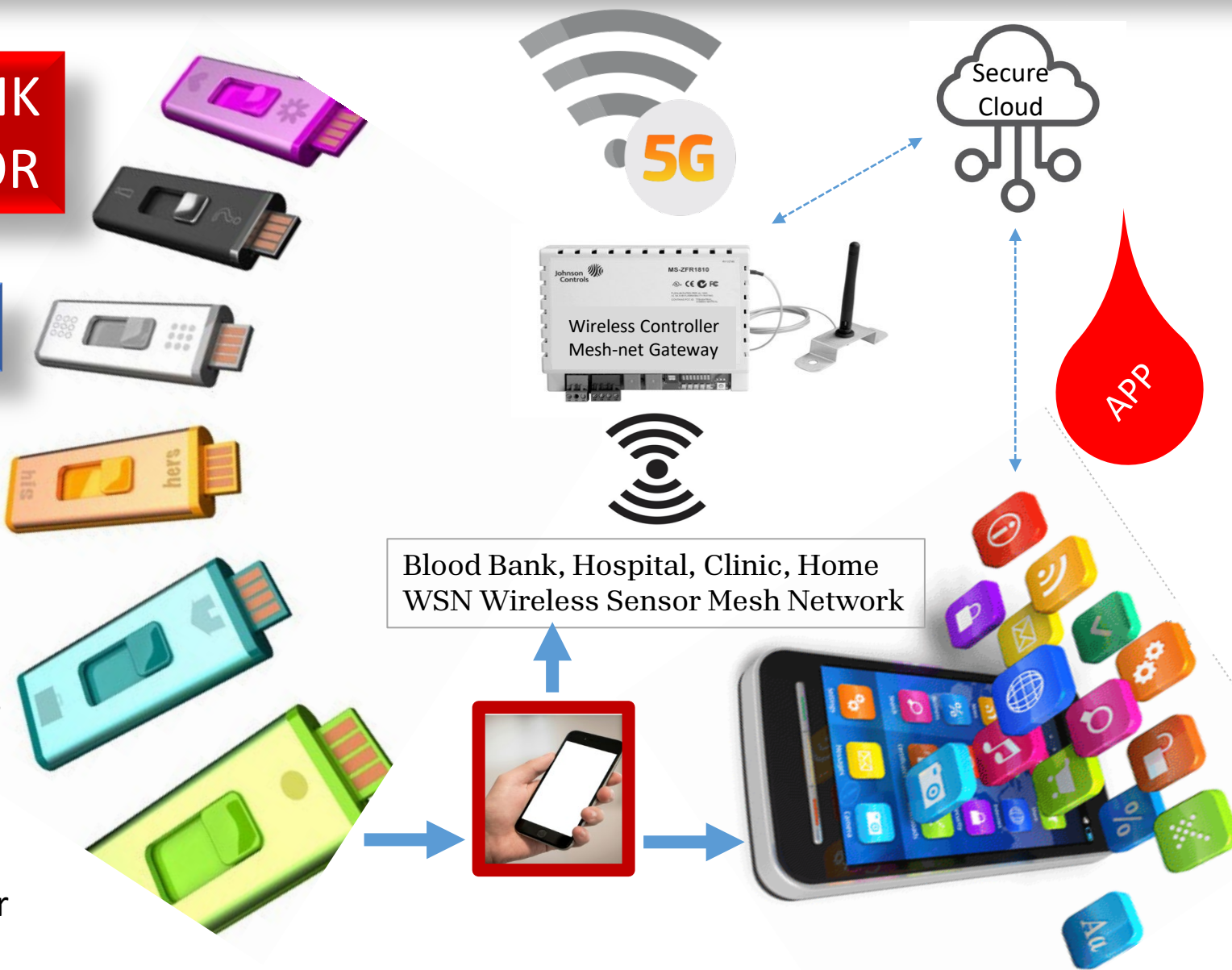
**BLOOD BANK
TEST SENSOR**

EBV Sensor

Glucose Sensor

Cholesterol Sensor

SARS-CoV-2 Sensor





Nanotechnology for Hematology, Blood Transfusion, and Artificial Blood

Micro and Nano Technologies

2022, Pages 265-283



Chapter 12 - Lab-on-a-chip for analysis of blood

[Hayder A. Abdulbari](#)

[Show more](#) ▾

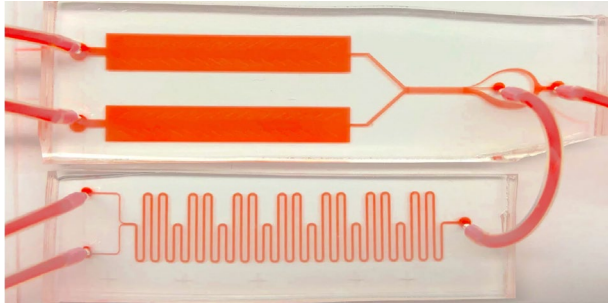
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<https://doi.org/10.1016/B978-0-12-823971-1.00013-1>

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Abstract

With the growing popularity of microfluidics devices, medical science is also progressing its way through fast and efficient microfabricated diagnosis devices. Blood testing and analysis are primary and necessary steps in medical diagnosis; hence smart and fast microdiagnostic devices are considered essential. Blood is the most vital fluid, containing all the essential minerals and vitamins, and it can be a carrier for other biological pathogens such as a bacterium, virus, or other microorganism, making it the perfect subject for analysis for an accurate diagnosis. This chapter introduces and discusses microfluidics technology's influence on the diagnosis of blood diseases. The chapter starts with a comprehensive introduction of the rapid development of microfluidics technology and its applications followed by sections that detail the microfluidics science fundamentals, lab-on-chip, and [microfabrication](#) techniques. It then explains specifically the influence of microfluidics technology in the development of different blood testing techniques and methods with a more comprehensive focus on its applications in sexually transmitted diseases.



A prototype of the RT-ELISA, essentially an entire lab within a chip with tiny pipes and valves no wider than a human hair | Photo by Caitlin Maikawa

For even the most routine of medical checkups, a blood test is often the first order of business.

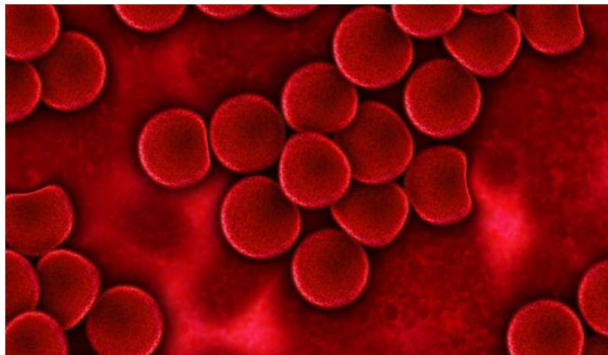
<https://medicalxpress.com/news/2024-01-biomarker-quality-blood-donations.html>

JANUARY 31, 2024

✓ Editors' notes

Researchers identify new biomarker in quality of blood donations

by Kelsea Pieters, CU Anschutz Medical Campus



engineering.stanford.edu/magazine/article/new-lab-chip-turns-blood-test-snapshots-continuous-movies

Stanford University

Stanford | ENGINEERING

Computation & Data, Electronics & Networking, Health

A new lab-on-a-chip turns blood test snapshots into continuous movies

The device can sense levels of virtually any protein or molecule in the blood, and could be transformative for disease detection, patient monitoring and biomedical research.

Poudineh M, Maikawa CL, Ma EY, Pan J, Mamerow D, Hang Y, Baker SW, Beirami A, Yoshikawa A, Eisenstein M, Kim S, Vučković J, Appel EA, Soh HT. (2021) **A fluorescence sandwich immunoassay for the real-time continuous detection of glucose and insulin in live animals.** Nat Biomed Eng. 2021 Jan; 5(1):53-63. doi: 10.1038/s41551-020-00661-1. Epub 2020 December 21. PMID: 33349659; PMCID: PMC7856282.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7856282/pdf/nihms-1646031.pdf>

To: Shoumen Pa Datta



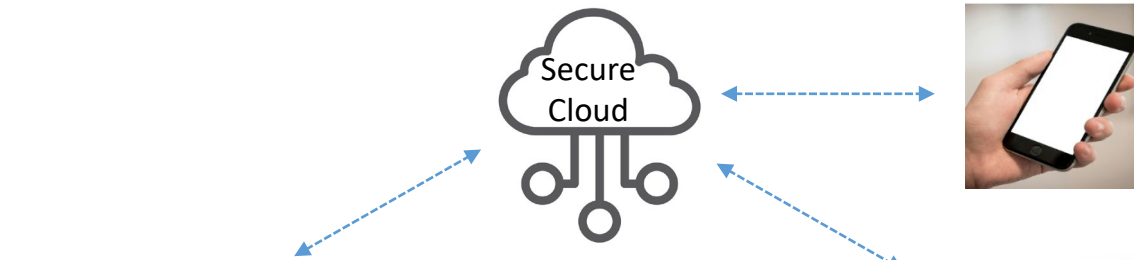
Sun 4/7/2024 3:58 PM

Are you asking if blood banks can do this? If so, the answer is yes.

I'd like to talk to you about the possibility and problems.

Former CEO of a Blood Bank

Digital Health Hematology Services (DHHS)



Blood Bank Digital



Local Wireless Sensor Mesh Network



Wireless Sensors

Data-Informed Decision Support (DIDS) Systems
Distributed Secure Near Real-time Mobile Digital Health Services

Datta, 2018 / Datta, 2023

Data-Informed Decision Support (DIDS) Systems Distributed Near♦ Real-time Mobile Detection Services

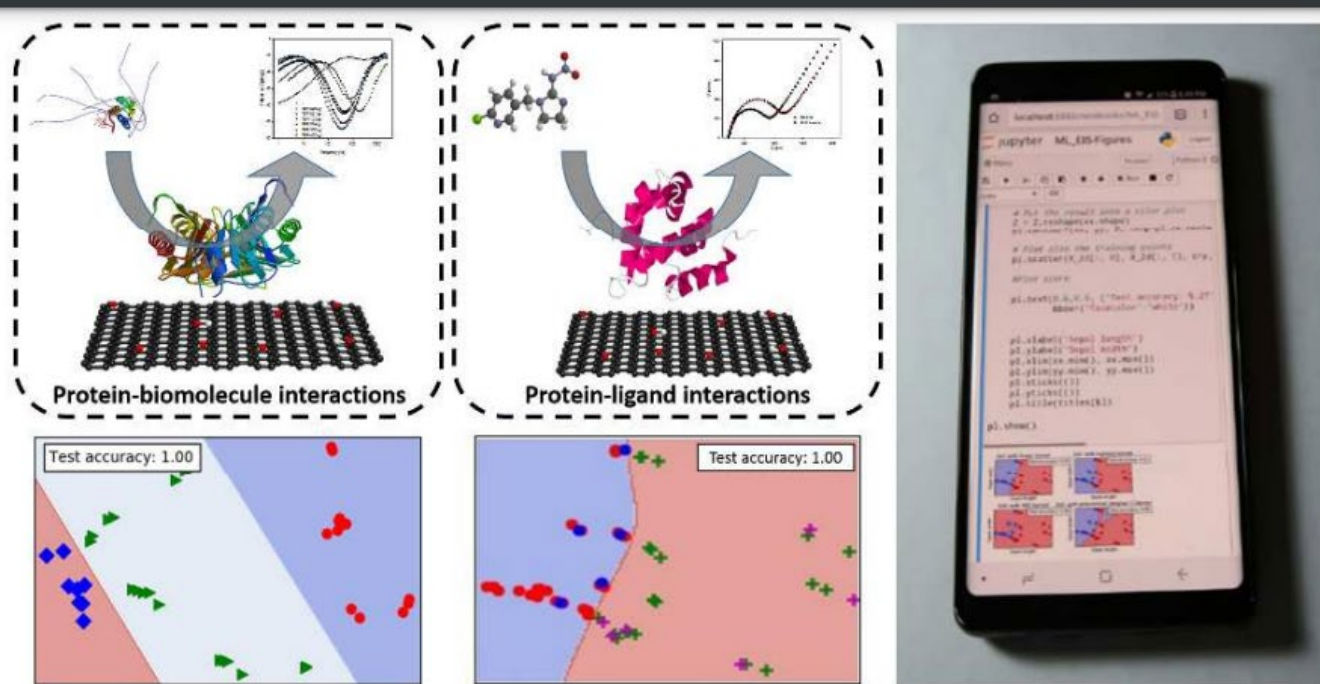
Rong Y , Padron AV , Hagerty KJ , Nelson N , Chi S , Keyhani NO , Katz J , **Datta** SPA , Gomes C , McLamore ES (2018) ***Post hoc support vector machine learning for impedimetric biosensors based on weak protein-ligand interactions.*** *Analyst*. 2018 April 30;143(9):2066-75 doi: 10.1039/c8an00065d

Near♦ Real-time depends on material science (sensor engineering), biochemical & physical chemistry** of molecular interactions (binding kinetics, affinity, equilibrium), timing in software systems (Δt) and network engineering infrastructure with respect to telecommunications (latency, bandwidth and jitter).

** McLamore, Eric S. and **Datta, Shoumen P.A.** (2023) ***A Connected World: System-Level Support through Biosensors*** *Annual Review of Analytical Chemistry* (Palo Alto, CA) 2023 June 14; 16(1):285-309. doi: 10.1146/annurev-anchem-100322-040914. Epub 2023 April 5. PMID: 37018797.

<https://doi.org/10.1146/annurev-anchem-100322-040914>

MIT Library <https://dspace.mit.edu/handle/1721.1/123983>



Proof of Concept: Data-Informed Decision Support (DIDS)

Figure 1. An open source support vector machine learning algorithm was developed for analyzing impedimetric biosensor data. Interactions. We tested the tool for analyzing weak/transient interactions including protein-DNA, protein-protein, and protein-small molecule. The cloud-based tool can be used for point of need applications with a mobile phone or tablet.

Rong Y , Padron AV , Hagerty KJ , Nelson N , Chi S , Keyhani NO , Katz J , **Datta** SPA , Gomes C , McLamore ES . ***Post hoc support vector machine learning for impedimetric biosensors based on weak protein-ligand interactions.***

Analyst. 2018 Apr 30;143(9):2066-75 doi: 10.1039/c8an00065d PMID: 29629449.

<https://pubs.rsc.org/en/content/getauthorversionpdf/c8an00065d>



HHS Public Access

Author manuscript

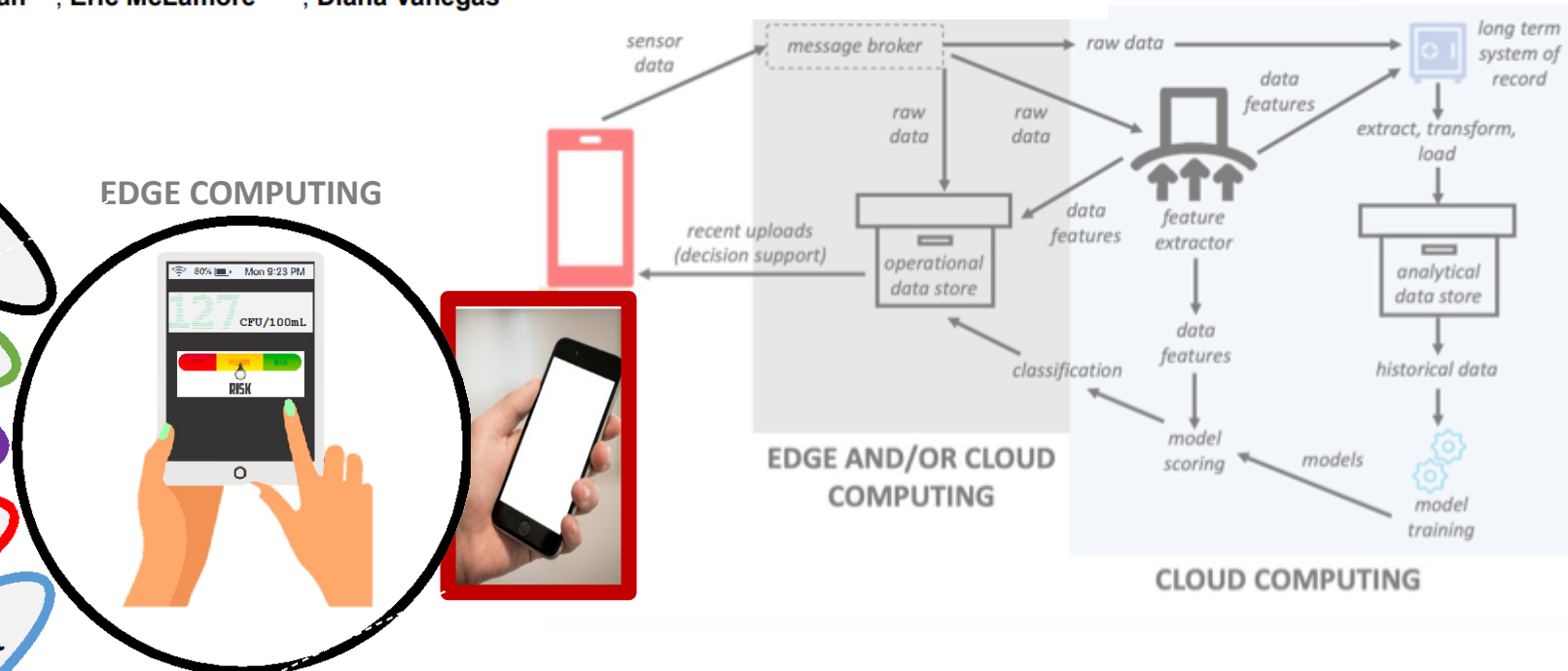
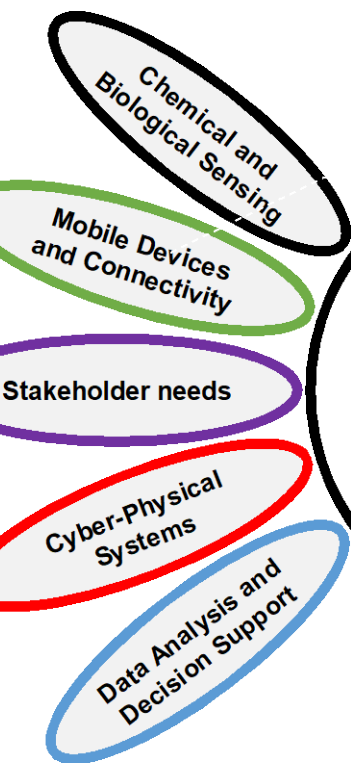
Front Sens (Lausanne). Author manuscript; available in PMC 2022 August 18.

Published in final edited form as:

Front Sens (Lausanne). 2022 ; 3: . doi:10.3389/fsens.2022.917380.

Development of a Biosensor Based on Angiotensin-Converting Enzyme II for Severe Acute Respiratory Syndrome Coronavirus 2 Detection in Human Saliva

Geisianny Moreira^{1,2}, Lisseth Casso-Hartmann¹, **Shoumen Palit Austin Datta**^{3,4}, Delphine Dean^{5,6}, Eric McLamore^{1,2,7}, Diana Vanegas^{1,2,*}



McLamore ES, Palit Austin **Datta** S, Morgan V, Cavallaro N, Kiker G, Jenkins DM, Rong Y, Gomes C, Claussen J, Vanegas D, Alocilja EC. **SNAPS: Sensor Analytics Point Solutions for Detection & Decision Support Systems**. Sensors (Basel). 2019 November 13; 19(22):4935. doi: 10.3390/s19224935. PMID: 31766116 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6891700/pdf/sensors-19-04935.pdf>



Helping hematologists conquer blood diseases worldwide

About ASH ASH Foundation

RESEARCH

EDUCATION

ADVOCACY

CAREERS

MEETINGS

PUBLICATIONS

ANNUAL MEETING PRESS PROGRAM



Very Good
Good
Poor
Double hit
Frontline Treatment
Anthracycline/Rituximab-based regimen
Non-Anthracycline based regimen
Relapsed/Refractory to frontline therapy
Median number

AMERICAN SOCIETY OF HEMATOLOGY / NEWSROOM / PRESS RELEASES / STUDIES HIGHLIGHT IMPACTS OF APPLYING NEW TECHNOLOGIES IN EVERYDAY CARE

Studies Highlight Impacts of Applying New Technologies in Everyday Care

CITATION

PUBLISHED ON:

DEC 09 2023

Digital Health Hematology Services (DHHS)

not if, but when

Blood Bank Digital

Digital Health : The new BMI ??

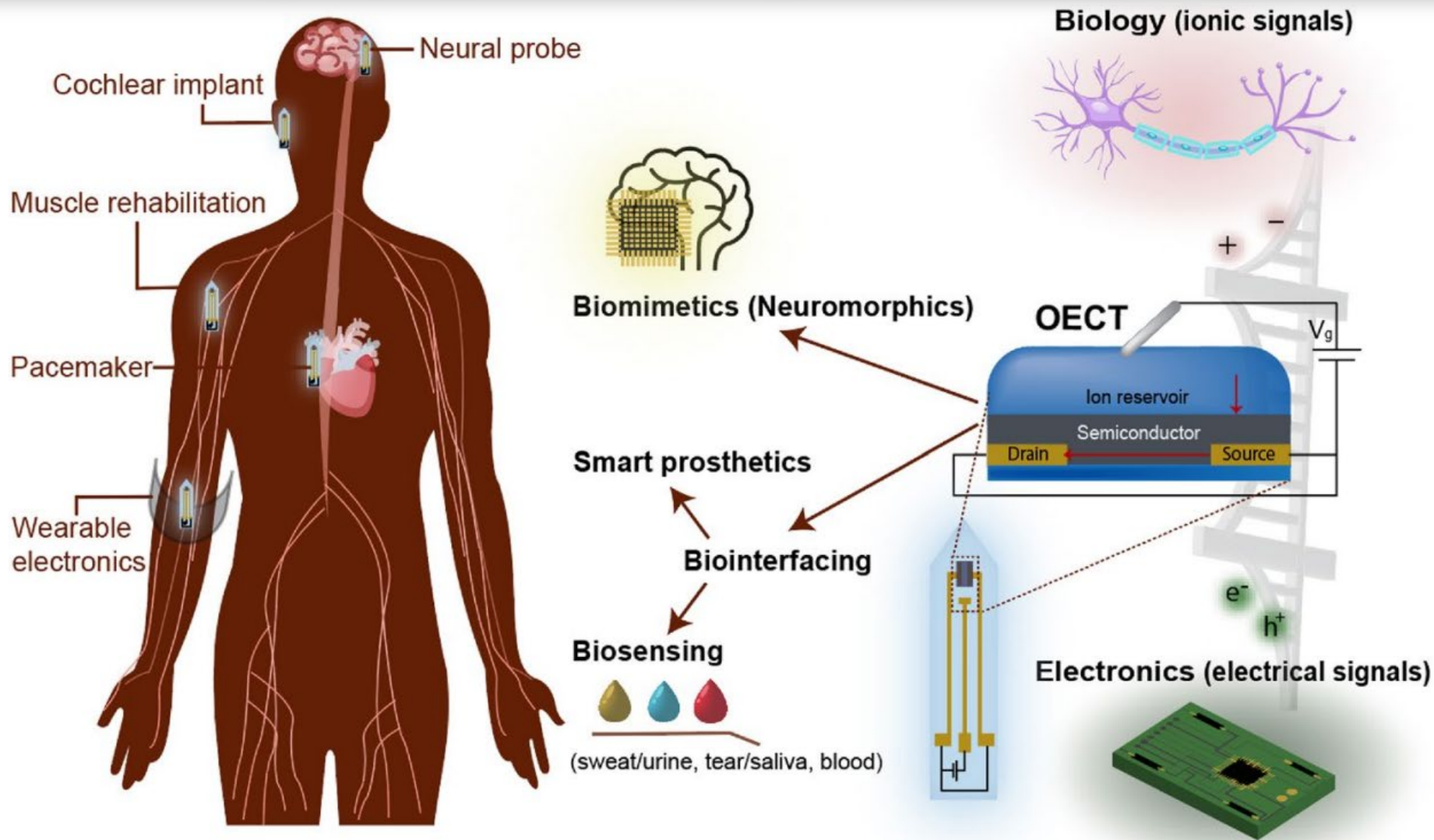
Body-Machine Interface (BMI)

not if, but when

Digital Healthcare ?

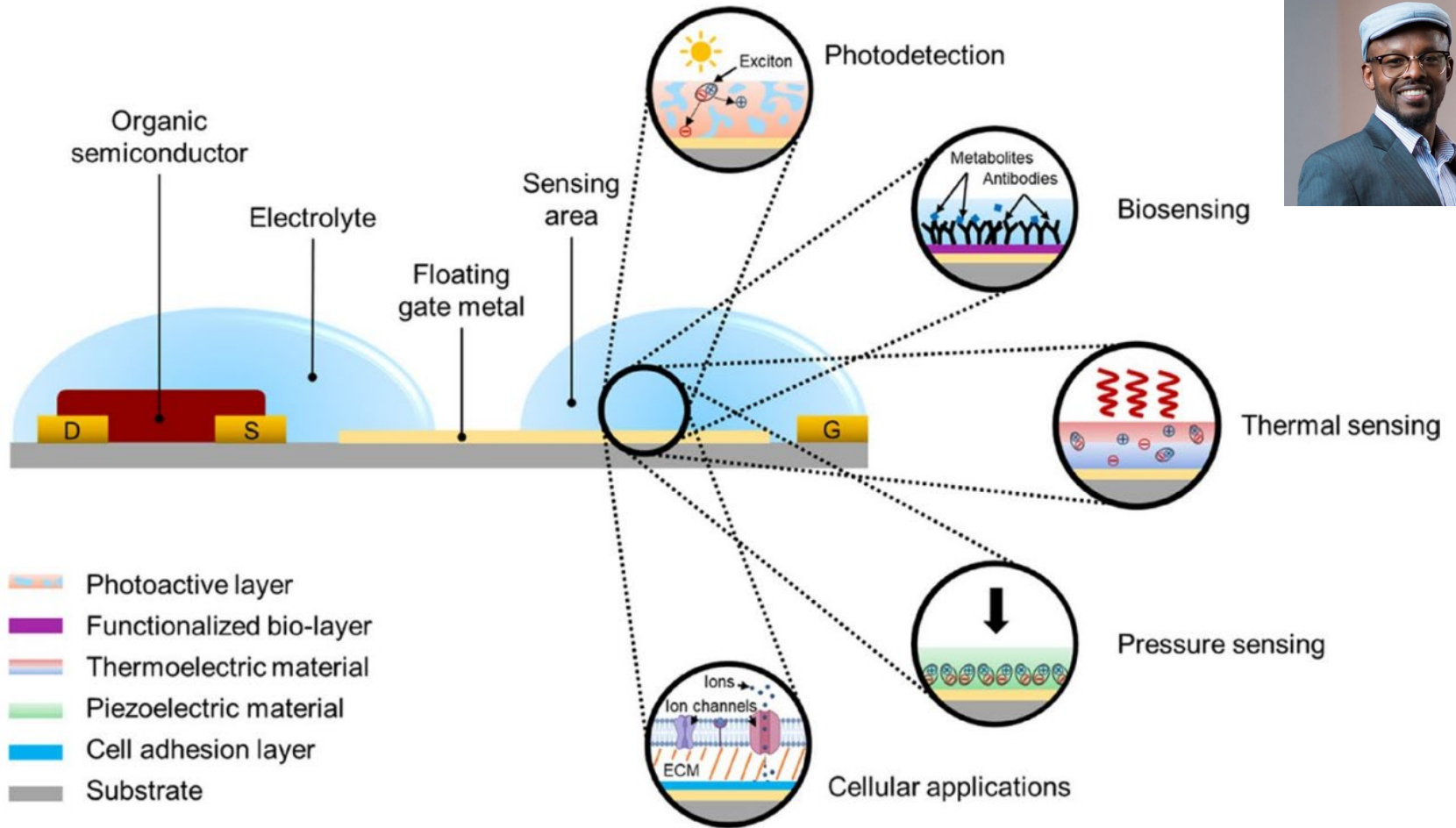
Body-Machine Interface (in a material world)

<https://dmse.mit.edu/faculty/aristide-gumyusenge>



Roh, H., Cunin, C., Samal, S. *et al.* **Towards organic electronics that learn at the body-machine interface: A materials journey.** *MRS Communications* 12, 565–577 (2022). <https://doi.org/10.1557/s43579-022-00269-3>

Is this the soul of BMI (body-machine interface) ? Bio-sensing using organic electrochemical transistors



What is the question? Only good questions will unlock the potential of convergence.

CONVERGE ?

Population genetics (local, global)
from **metabolomic data** acquired
from blood bank (blood donors)
and blood (cord) bank samples

with

BMI (body-machine interface) data

Cellular senescence is a stress response that elicits a permanent cell cycle arrest and triggers phenotypic changes, e.g., production of a bioactive secretome, referred to as the senescence-associated secretory phenotype (**SASP**). Acute senescence induction protects against cancer and limits fibrosis, but lingering senescent cells drive age-related disorders. Targeting senescent cells to delay aging and limit dysfunction, known as “senotherapy,” could be a fool’s errand. Yet, drugs that selectively kill senescent cells, termed “senolytics” are gaining momentum. SASP-centered molecules are targets for senescence-associated diseases. Should we target these molecules, too?

What type of metabolome ?

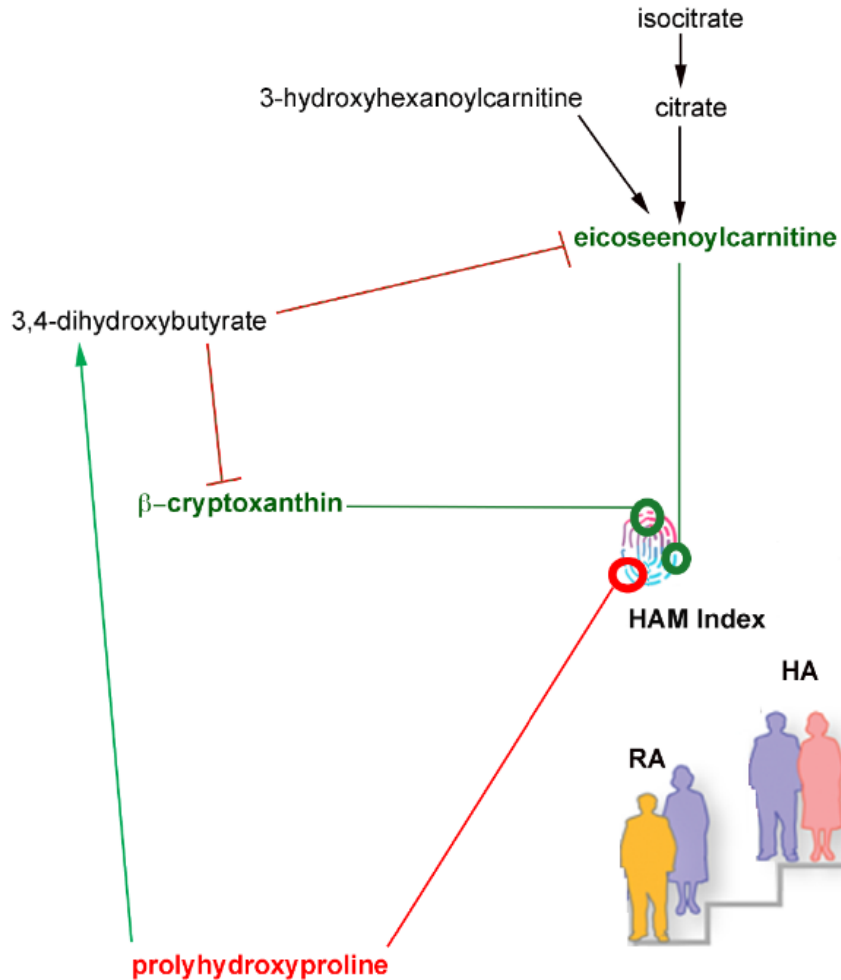
Clues for target molecules ?

Molecular fingerprint from senescence-associated secretome phenotype (SASP**) / inflammation markers**

Birch J, Gil J. (2020) **Senescence and the SASP: many therapeutic avenues.** Genes Dev. 2020 Dec 1; 34(23-24):1565-1576. doi: 10.1101/gad.343129.120. PMID: 33262144 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7706700/pdf/1565.pdf>

HAMSANATHAN ET AL.

www.ncbi.nlm.nih.gov/pmc/articles/PMC11019119/pdf/ACEL-23-e14104.pdf



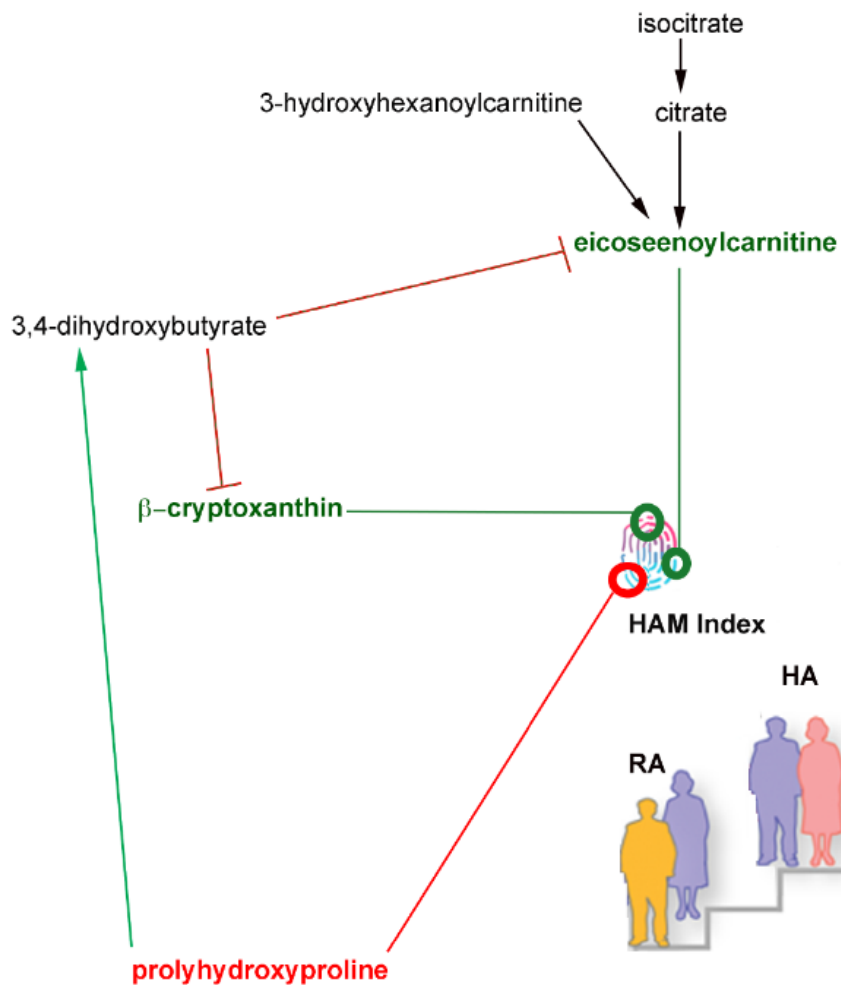
CAUSAL (??) METABOLITES FOR BIOLOGICAL AGING ?

Eicosenoylcarnitine and β -cryptoxanthin were positively causal to the healthy aging metabolic (HAM) index (HAMI) whereas prolyhydroxyproline had a negative impact on HAMI. Other metabolites, for example, 3,4 dihydroxybutyrate were seen to negatively impact β -cryptoxanthin and eicosenoylcarnitine. Prolyhydroxyproline was identified to positively influence 3,4 dihydroxybutyrate, suggesting cross talk between these group of metabolites (implicated in HAM and biological aging).

Could these molecules also serve as targets for testing donor blood samples?

HAMSANATHAN ET AL.

www.ncbi.nlm.nih.gov/pmc/articles/PMC11019119/pdf/ACEL-23-e14104.pdf



CAUSAL (??) METABOLITES FOR BIOLOGICAL AGING ?

Could these molecules also serve as targets for testing donor blood samples?

Can we envision a longitudinal epidemiological study where we test for these metabolites in stored blood samples from repeat blood donors in blood banks, locally and globally?

Will such analyses provide time series metabolomic data on the dynamics of these metabolites?

Can such data reveal target molecules for future cellular and molecular therapies?

It bears to be reiterated

CONVERGE

Population genetics (local, global)
from **metabolomic data** acquired
from blood bank (blood donors)
and blood (cord) bank samples

with

BMI (body-machine interface) data

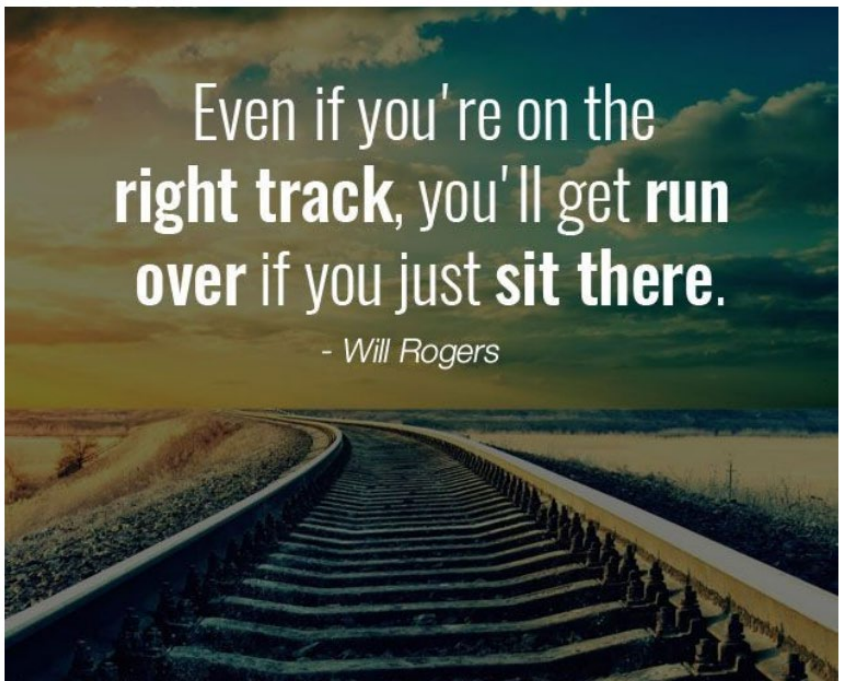
Invention? Innovation??

connecting “spaces unrelated” to catalyze discovery

“FOCUS ON
PURPOSE,
NOT YOUR
TITLE.”

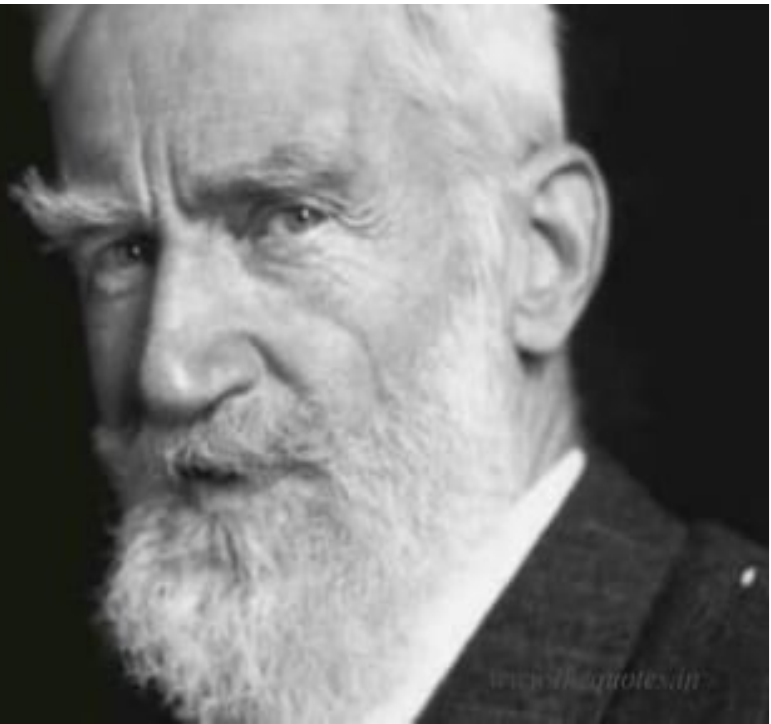
—“Worry less about what you want to be and think more about what you want to do.” Focus on purpose, for example, helping save lives and you’ll always have an impact, even if it is a drop in the ocean of need.





Even if you're on the
right track, you'll get **run
over** if you just **sit there**.

- *Will Rogers*



Some men see things as they are
and ask why. Others dream things
that never were and ask why not.

George Bernard Shaw

Data. Think Differently. Research for greater good.



Rather than socio-spatial data mapping for murder, hate, why not find data for cures?

DON'T MAKE THIS MISTAKE WITH DATA

PLEASE DON'T LET

AI

CORRUPT AND RUIN YOUR DATA ANALYTICS

<https://people.csail.mit.edu/brooks>



The Seven Deadly Sins of AI Predictions

Mistaken extrapolations, limited imagination, and other common mistakes that distract us from thinking more productively about the future.

By Rodney Brooks



October 6, 2017

Rodney Brooks is the Panasonic Professor of Robotics (emeritus) at MIT. He is a robotics entrepreneur. Dr. Brooks is the former Director (1997 - 2007) of the MIT Artificial Intelligence Laboratory and then the MIT Computer Science & Artificial Intelligence Laboratory ([CSAIL](#)). He received a Ph.D. in Computer Science from Stanford University in 1981. He held research positions at Carnegie Mellon University and MIT, and a faculty position at Stanford before joining the faculty of MIT in 1984. From June 2014 until May 2020 he was a member of the Visiting Committee on Advanced Technology, [VCAT](#), at the National Institute of Standards and Technology, [NIST](#). Since June 2015 he has been an external member of GE's Robotics Advisory Council. From January 2016 until mid 2019 he was Deputy Chairman of the Advisory Board of Toyota Research Institute. From February 2019 until January 2021 he was "Luminary" at Bell Labs. Dr. Brooks is a Member of the National Academy of Engineering (NAE), a Founding Fellow of the Association for the Advancement of Artificial Intelligence (AAAI), a Fellow of the American Academy of Arts & Sciences (AAAS), a Fellow of the American Association for the Advancement of Science (the other AAAS), a Fellow of the Association for Computing Machinery (ACM), a Fellow of the Institute of Electrical and Electronics Engineers (IEEE), a Member of the Australian Academy of Science (AAS) and a Fellow of the Australian Academy of Technological Sciences and Engineering (ATSE).

Don't subject your data to hallucinations

twitter.com/rodneymarbrooks/status/1794814225015325154


← Post


 **Rodney Brooks** 
@rodneymarbrooks


The talk about hallucinations in LLMs has gotten it all wrong. The true hallucinations are by company execs who think it is OK to release to general users products that are based on LLMs that confabulate wildly, as all LLMs do. Time will show a high price paid by society.

3:33 PM · May 26, 2024 · 29K Views

27 85 301 54

 Post your reply Reply

 **Gilgamesh Akkadian** @WYSnotWYG · 22s
arxiv.org/abs/2402.03927
arxiv.org/pdf/2402.03927

 **Leak, Cheat, Repeat: Data Contamination and Evaluation Malpractices in Closed-Source LLMs**

Simone Balloccu Patřicia Schmidtová Mateusz Lango Ondřej Dušek
Charles University, Faculty of Mathematics and Physics
Institute of Formal and Applied Linguistics
Prague, Czech Republic
{balloccu, schmidtova, lango, odusek}@ufal.mff.cuni.cz

Who is Rodney Brooks? ● <https://people.csail.mit.edu/brooks>

What to do with ideas & uncorrupted data from research outcomes?

Here's one option, perhaps ...

When it comes to building startups in Boston, success begets success

And from HubSpot to Klaviyo, it's had its share of successful exits

Ron Miller @ron_miller / 1:07 PM EDT • April 6, 2024

Comment



How To Lead Change for Good

Collaborate Globally

Create Partnerships

Foster Key Alliances

Aspire to Inspire

Be Exemplary

Credibility

Dignity

Ethics

Teach

Learn

STEM

R&D

kasanoff.com/blog/2017/3/22/the-incredible-power-of-not-taking-credit

The Incredible Power of Not Taking Credit

February 22, 2019 · Leadership, Career



Image by alex mertzanis/Flickr

Nothing limits your ability to achieve great things more than your desire to take credit for what you have achieved. This paradox is at the center of most problems that companies face.

Happiness is key to success. Success is not the key to happiness.

STEM is a quite smart and fetching (catchy) moniker for marketing due to its global semantic cognitive imprint (aka “buzz”), but in education, it ought to become

STEEMM

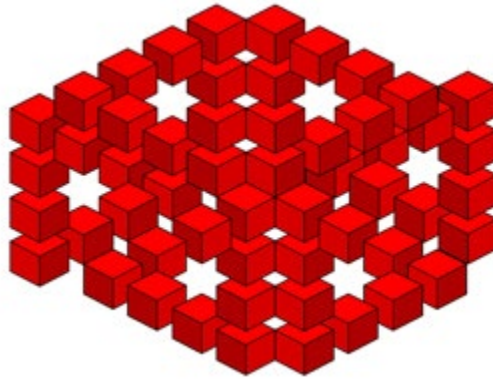
Science ◦ Technology ◦ Engineering ◦ Economics ◦ Medicine ◦ Mathematics

Utopians will be euphoric with STEEMMAHH with the addition of Music, Arts, Humanities and History, as well.

DHHS is a sub-section of “The Health of Nations - Part II”

“The Health of Nations” Parts 1, 2, & 3 are in the MIT Library

<https://dspace.mit.edu/handle/1721.1/153283>



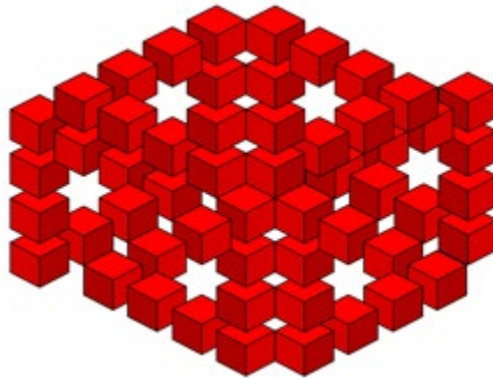
I have created nothing new

This document suggests ideas some of which are not original and not the outcome of the author’s research or creativity. The synthesis of existing facts and weaving them to propose new streams may be attributed to the author. The author has no claim or rights over the data, visuals and graphics used in this document. This presentation may be shared with anyone and disseminated or used for commercial or academic purposes by anybody, anywhere. If you have questions, contact shoumen@mit.edu ▪ sdatta8@mgh.harvard.edu
For information about the author go to <https://dspace.mit.edu/handle/1721.1/146158>

<https://dspace.mit.edu/handle/1721.1/107893>

Review “Healthcare” PDF for more cartoons

Forward looking statements and projections in this presentation are neither easy to accomplish nor instantaneous but are possible and credible.



Dr Shoumen Palit Austin Datta

MIT Auto-ID Labs, Senior Member, Affiliate, Department of Mechanical Engineering, Massachusetts Institute of Technology ▪ shoumen@mit.edu

Senior Scientist, MDPnP Lab Medical Device Interoperability, Massachusetts General Hospital, Harvard Medical School ▪ sdatta8@mgh.harvard.edu

NEW BLOOD

THERE WILL BE BLOOD

Is mimicking the cells that carry hemoglobin the key to a blood substitute?



Better than nature?

doi: 10.1126/science.za6bz9o

Decades of efforts have failed to develop a good substitute for oxygen-carrying red blood cells. A new candidate, ErythroMer, is still in preclinical testing but could be more durable and versatile than the real thing.



Red blood cells

SHELF LIFE

42 days

SIZE

7–8 μm

COMPATIBILITY

By blood type

ErythroMer

SHELF LIFE

2 years

SIZE

$\sim 0.2 \mu\text{m}$

COMPATIBILITY

Universal



A. FISHER/SCIENCE

For now, no human blood substitute is commercially available in the U.S. “There’s a real gap here where we don’t have access to blood for people bleeding to death outside of the hospital,” says Doctor, who co-founded and is chief science officer of KaloCyte, a company hoping to develop ErythroMer into a commercial product.

Universal Medium of Health, Healing, Humanity

<https://www.hhs.gov/givingequalsliving/>

Blood

<https://americasblood.org/about/leadership/>

~ 5 million Americans will need a blood transfusion each year. Someone needs blood every 2 seconds. 1 in 7 people entering a hospital need blood. ~ 22,000 liters of donated blood used each day, i.e., almost ~ 1,000 liters of blood transfused every hour, every day, every year, to save lives.

ACKNOWLEDGEMENTS

Anahita Dua, M.D., M.B.A., M.S.C., F.A.C.S., Vascular Surgeon, Associate Professor
Head of Vascular Surgery, Massachusetts General Hospital, Harvard Medical School

www.massgeneral.org/doctors/20714/anahita-dua

<https://vascular.org/news-advocacy/articles-press-releases/dr-anahita-dua-named-presidential-leadership-scholar>

Sheela Magge M.D., M.S.C.E., Professor of Pediatrics, Lawson Wilkins Endowed Chair of
Pediatric Endocrinology and Director, Division of Pediatric Endocrinology
Johns Hopkins University School of Medicine

<https://profiles.hopkinsmedicine.org/provider/Sheela+Magge/2700667>

<https://clinicalconnection.hopkinsmedicine.org/participant/sheela-natesh-magge-md-msce>

www.niddk.nih.gov/-/media/Files/News/Meetings/Magge_Bio_508.pdf

Julian Goldman, M.D., F.A.S.A. Massachusetts General Hospital, Harvard Medical School
Anesthesia, Critical Care and Pain Medicine, MGH Research Institute

Director, Biomedical Engineering, Mass General Brigham (MGB) <https://mdpnp.mgh.harvard.edu>

<https://researchers.mgh.harvard.edu/profile/14161732/Julian-Goldman>

Sanjay Sarma, Ph.D., Vice-President, Massachusetts Institute of Technology (MIT)

Fred and Daniel Fort Flowers (1941) Professor of Mechanical Engineering, MIT

President, CEO and Dean, Asia School of Business (MIT Sloan, Kuala Lumpur, Malaysia)

<https://meche.mit.edu/people/faculty/sesarma@mit.edu>

<https://asb.edu.my/about/leadership-team/sanjay-sarma/>

YOU

DON'T

HAVE

TO BE

PERFECT



YOU

JUST

HAVE

TO

START

Shoumen Palit Austin Datta

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&

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