

Prediction is very difficult, especially about the future.



Niels Bohr



HIV/AIDS



Morbidity and Mortality Weekly Report (MMWR)
Weekly | June 5, 1981 | 30(21);1-3

Pneumocystis Pneumonia --- Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candida mucosal infection.



Morbidity and Mortality Weekly Report (MMWR)
Weekly | December 10, 1982 | 31(48);625-9

Epidemiologic Notes and Reports Possible Transfusion-Associated Acquired Immune Deficiency Syndrome (AIDS) -- California

CDC has received a report of a 20-month old infant the from San Francisco area who developed unexplained cellular immunodeficiency and opportunistic infection. This occurred after multiple transfusions, including a transfusion of platelets derived from the blood of a male subsequently found to have the acquired immune deficiency syndrome (AIDS).

Two years from recognition of disease to identification of the causative agent.

Science. 1983 May 20;220(4559):868-71.

Isolation of T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS).

Barré-Sinoussi F, Chermann JC, Rey F, Nugeyre MR, Chamaret S, Gruest J, Dauguet C, Axler-Blin C, Vézinet-Brun F, Rouzioux C, Rozenbaum W, Montagnier L.

Science. 1984 May 4;224(4648):500-3.

Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS.

Gallo RC, Salahuddin SZ, Popovic M, Shearer GM, Kaplan M, Haynes BF, Palker TJ, Redfield R, Oleske J, Safai B, et al.



Borna

Five years



10 May 1985 | Vol 228, Issue 4700 | pp. 755-756 | DOI: 10.1126/science.3922055

R. ROTT, S. HERZOG, B. FLEISCHER, A. WINOKUR, J. AMSTERDAM, W. DYSON, AND H. KOPROWSKI

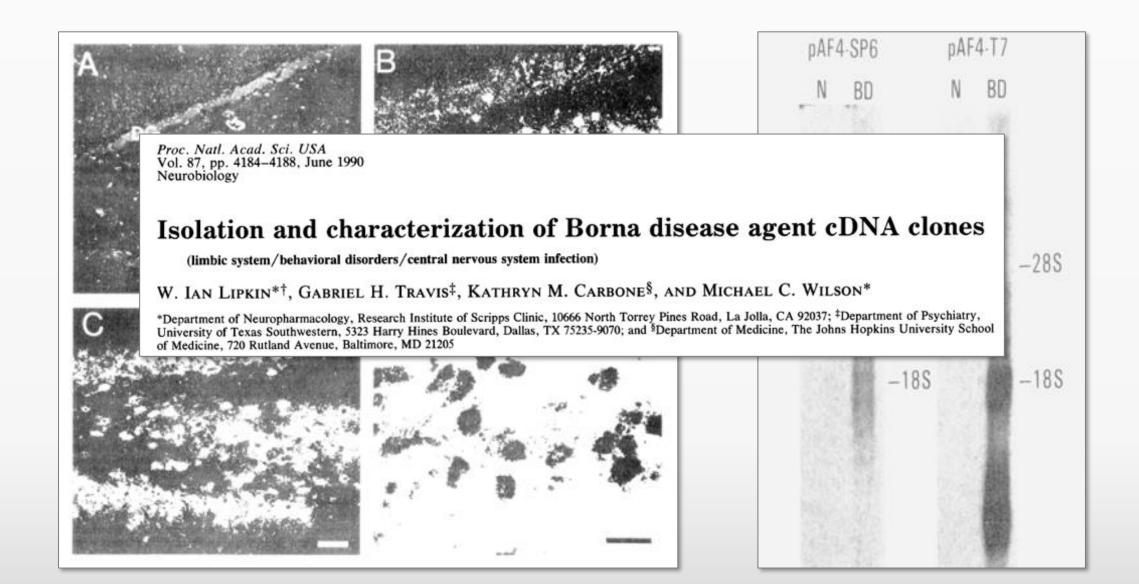
Detection of serum antibodies to Borna disease virus in patients with psychiatric disorders

Abstract

Borna disease virus causes a rare meningoencephalitis in horses and sheep and has been shown to produce behavioral effects in some species. The possibility that the Borna virus is associated with mental disorders in humans was evaluated by examining serum samples from 979 psychiatric patients and 200 normal volunteers for the presence of Borna virus-specific antibodies. Antibodies were detected by the indirect immunofluorescence focus assay. Antibodies to the virus were demonstrated in 16 of patients but none of the normal volunteers. The patients with the positive serum samples were characterized by having histories of affective disorders, particularly of a cyclical nature. Further studies are needed to define the possible involvement of Borna virus in human psychiatric disturbances.



Subtractive Cloning of BDV





Dandenong Virus

Two weeks



A New Arenavirus in a Cluster of Fatal Transplant-Associated Diseases

ORIGINAL ARTICLE | March 6, 2008 | DOI: 10.1056/NEJMoa073785

Palacios G, Druce J, Du L, Tran T, Birch C, Briese T, Conlan S, Quan PL, Hui J, Marshall J, Simons JF, Egholm M, Paddock CD, Shieh WJ, Goldsmith CS, Zaki SR, Catton M, Lipkin WI

Austin Health, Victoria CDC

Columbia

Victorian Infectious Disease Reference Laboratory 454 Life Sciences

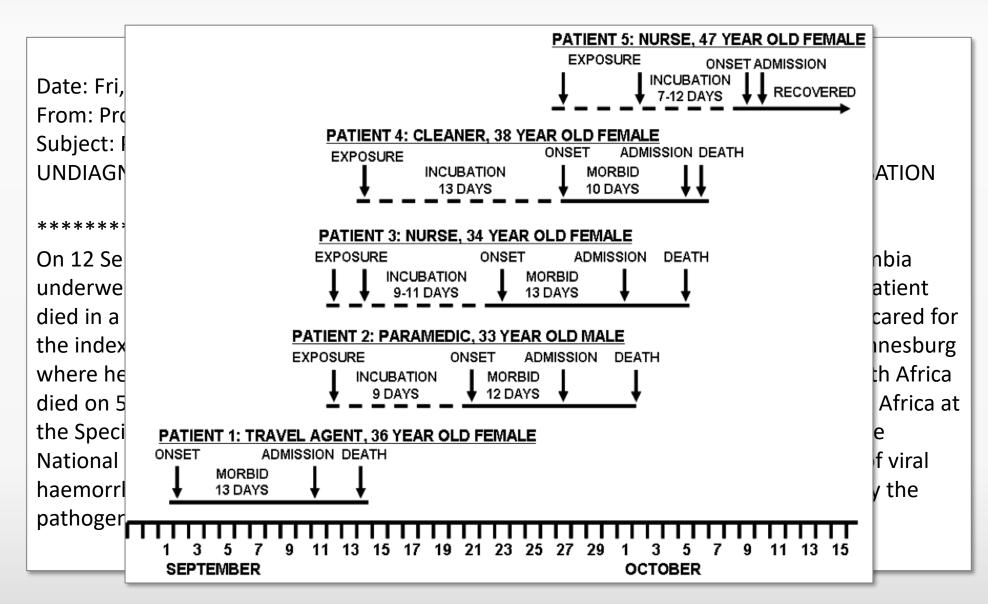


Gustavo Palacios



LuJo

One week

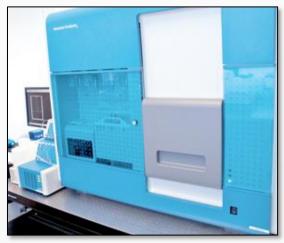




Evolution of High-Throughput Sequencing



Roche 454



Illumina



Ion Torrent



Illumina HiSeq X Ten



Oxford Nanopore MinION



Prioritization?

>2,000 Viruses Discovered/Characterized at CII Alone

Humans

Adenoviruses (1 species)

Astroviruses (4 species)

Bocaviruses (4 species)

Cosaviruses (4 species)

Enteroviruses (9 EVA, 15EVB, 8EVC,

1EVD (EV68),1 untyped)

Dengue Virus

LuJo Virus

Orthobunyaviruses

Parvoviruses (3 species)

Phlebovirus (7 species)

Rotaviruses (1 species)

Rhabdobirus (2 species)

Rhinovirus A, C

Polyomaviruses

Other Mammals

Bat Adenoviruses

Bat Astroviruses

Bat Bocaviruses

Bat Coronaviruses (35+ species)

Bat Hepaciviruses and Pegiviruses

Bat Filovirus (distant relation to

Ebola and Marburg)

Bat Herpesviruses

Bat Paramyxoviruses

Bat Parvoviruses

Bat Polyomaviruses

Canine Hepacivirus

Canine Kobuvirus

Cattle Orbivirus (6 species)

Cattle Orthomyxovirus (2 species)

Cetacean Influenza Virus

Cetacean Polyomavirus

Gorilla Parvovirus

Gorilla Metapneumovirus

Hedgehog Rhabdovirus

Horse Pegiviruses

Minke Whale Astrovirus

Porcine Astrovirus

Porcine Circovirus

Porcine Picobirnavirus

Rodent Hepaciviruses and Pegiviruses

Sea Lion Reovirus

Avians

Avian Bornavirus (2 genotypes) Avian Farmington Virus Turkey Hepatitis Virus (4 genotypes)





Insects

Mosquito Rhabdovirus (8 species)

Mosquito Orbivirus

Mosquito Alphavirus

Mosquito Nidovirus

Mite Rhabdovirus

Insect Phlebovirus (19 species)

Insect Negevirus

Metagenomic studies of Apis mellifera

Fish/Reptiles/Other

Piscine reovirus (Salmon)

Clam retrovirus

Snake nidovirus

Tilapia Lake virus



Faster, Cheaper, Easier

Sequence-Capture Based Diagnosis and Discovery: VirCapSeq-VERT





H1N1 INFLUENZA is one of many viruses snared by a single new test.

Trawling for Viruses

A new method identifies every virus in a given sample with near-perfect accuracy

When doctors want to identify the virus behind an infection, they usually turn to the polymerase chain reaction (PCR) a method for "amplifying" scattered bits of DNA into a sample large enough to study. To use PCR, however, a physician must know what kind of virus to look for, and that involves guesswork.

This past September a team of Columbia University researchers described a new method that could eliminate that guesswork. The technique, which has the unfortunate name of "virome capture sequencing platform for vertebrate viruses," or VirCapSeq VERT, can find every virus in a given drop of saliva, tissue or spinal fluid with near-perfect accuracy. The method makes it possible to simultaneously analyze 21 samples in less than 48 hours at an estimated cost of just \$200 per sample. It can also detect novel or mutated viruses, so long as they are at least 40 percent identical to known ones. "When someone goes into an emergency room and winds up having all kinds of tests run, it costs thousands of dollars," says W. Ian Lipkin, John Snow Professor of Epidemiology at Columbia University's Mailman School of Public Health. "This method is very inexpensive and allows us to personalize medi-

that will improve life, transform computing and maybe even save the planet

VEARS OF SCIENTIFIC AMERICAN

To develop the technique, Lipkin and his colleagues first created adatabase of more

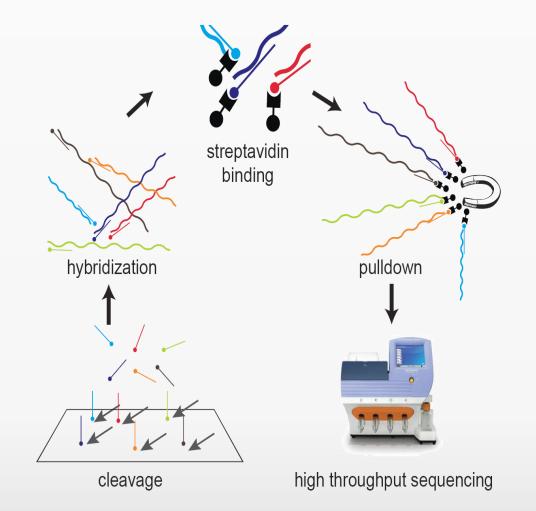
cine by telling you exactly what you have." To develop the technique, Lipkin and his colleagues first created a database of more than 1,000 vertebrate viruses. Then they synthesized genetic probes to match every strain of every virus—two million of them, each a strand of DNA 25 to 50 nanometers long. When a probe encounters a matching virus, it binds to it. To extract those viruses, laboratory workers add magnetic beads measuring one to three microns in diameter to the mix; a chemical linker binds the beads to the genetic probes and the viruses they

have captured. Researchers then insert a tube containing the mixture into a magnet stand, which pulls the probes to the tube's walls. After researchers isolate and wash the probe-bead-virus combos, they genetically sequence the viruse, eliminating the risk of false positives. Liphín and his colleagues are now looking to team up with a commercial provider that can distribute the technology to hospitals and clinics around the world. They are also planning on adding probes for all known infectious bacteria and fungil.

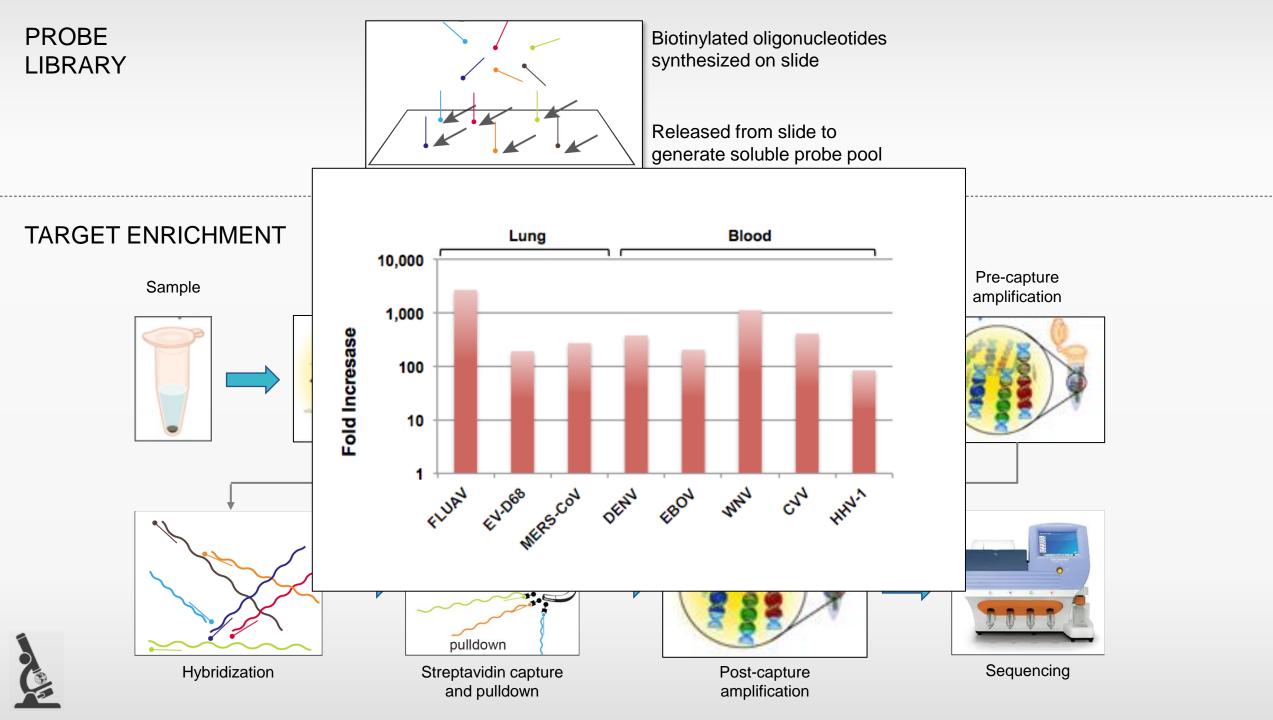
-R.N.

34 Scientific American, December 2015

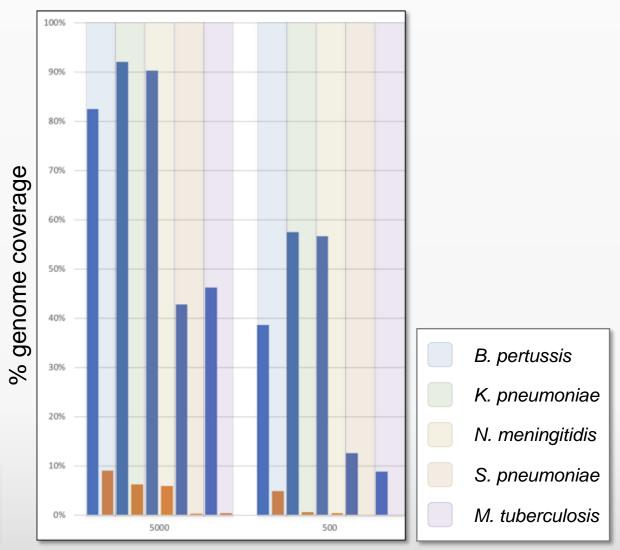
© 2015 Scientific American

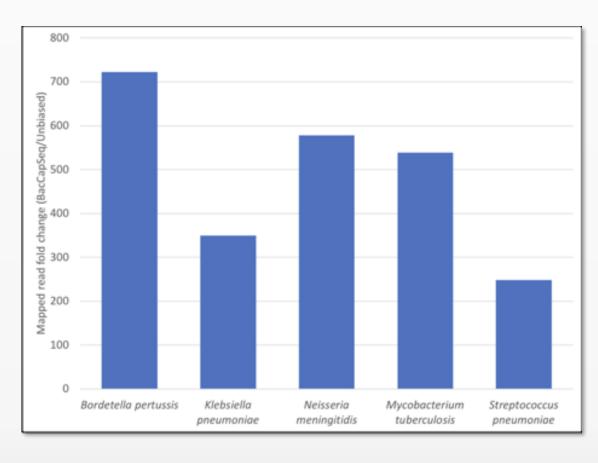






BacCapSeq Bacterial pathogens, antimicrobial resistance







Innovation is Enabling Improvements in Timeliness and Sensitivity in Sequencing

Instrument	# of Samples	# of Reads	Read Length	Runtime
Illumina NextSeq 1000/2000	100	1.2 billion	150 nt	11h
Illumina NextSeq 500	40	400 million	150 nt	12h
Illumina MiSeq	3	25 million	300 nt	5h
Illumina MiniSeq	3	25 million	150 nt	4h
Illumina iSeq	1	4 million	150 nt	9.5h
Oxford Nanopore MinION	1	5 million	1000 nt	8h

Workflow	Unbiased	Capture
Extraction	1h	1h
Library preparation	6h	6h
Hybridization	n/a	1h
Sequencing on MiniSeq	4h	4h
Bioinformatics analysis	8h	2h
Total turn around time	19h	14h
Sensitivity	1x	100-1000x

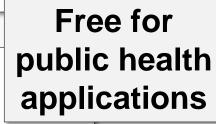




Abstract: The present invention provides novel methods, systems, tools, and kits for the simultaneous detection, identification and/or characterization of all viruses known or suspected to infect vertebrates. The methods, systems, tools, and kits described herein are based upon the virome capture sequencing platform ("VirCapSeq-VERT"), a novel platform developed by the inventors. The invention also provides methods and kits for designing and constructing of the virome capture sequencing platform.

Filed: September 19, 2016

Publication Date: September 20, 2018 Document Identifier: US 20180265935 A1





Department of Health

KATHY HOCHUL Governor

MARY T. BASSETT, M.D., M.P.H. Commissioner

KRISTIN M. PROUD

Acting Executive Deputy Commissioner

January 26, 2022

Mahesh M. Mansukhani, M.D. Columbia University Laboratory of Personalized Genomic Medicine 630 West 168th St Rm 11-453 PFI: 7313 New York, NY 10032

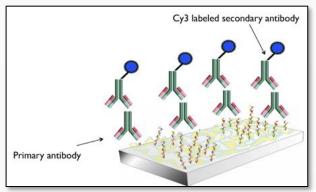
Project ID: 85920

Dear Dr. Mansukhani:

Thank you for submitting portions of your standard operating procedure manual and validation data needed to evaluate your next generation sequencing-based method for Columbia VirCapSeq-VERT in plasma specimens. After carefully evaluating all the information provided, the Clinical Laboratory Reference System's reviewers have found your validation data for this testing acceptable. You may offer this testing under your current permit in the category of Virology.



Indirect Methods for Microbe Discovery and Implication High-Throughput Serology Using Peptide Microarrays



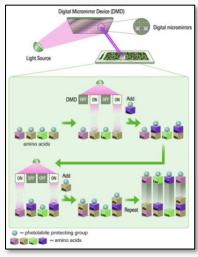
3M feature density 24M features needed to tile the vertebrate virus proteome



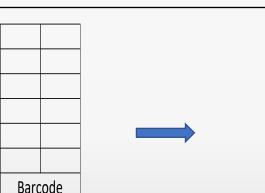
Data Production

Overlap

images



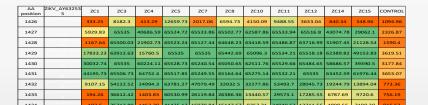
Synthesis in situ



Virtual image of each array, peptides are printed randomly on each sub array, and co-ordinates known for each peptide.



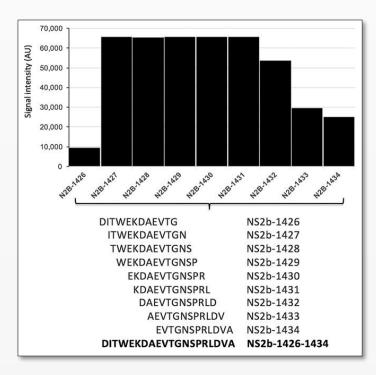
Scanned array image after secondary IgG and IgM Ab binding (Fluorescent signals)



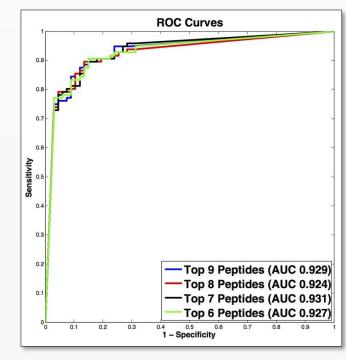
Fluorescent signals converted to arbitrary units (data) and transferred to heat maps



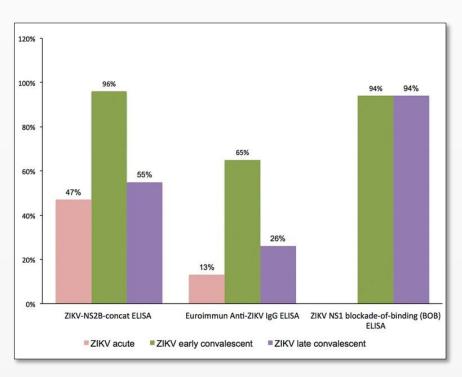
Diagnosis of Zika Virus Infection by Peptide Array and Enzyme-Linked Immunosorbent Assay



Identification of an immunoreactive 20-amino-acid ZIKV NS2B peptide



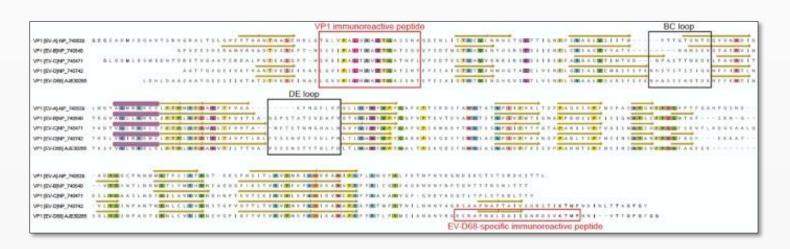
Average receiver operating characteristic (ROC) curves over 1,000 runs using the 9 overlapping peptides identified (comprising 20-aa ZIKV NS2B peptide), with an average area under the curve (AUC) of 0.931



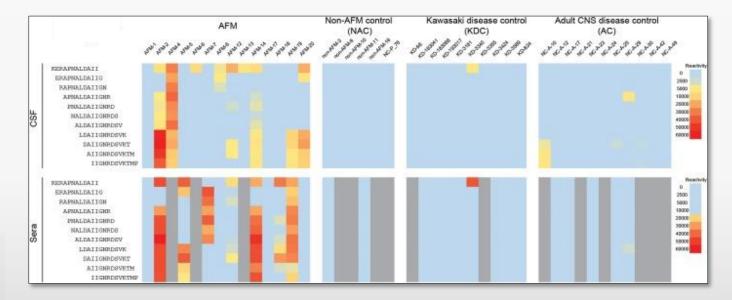
ZIKV-NS2B-concat ELISA sensitivity comparison with Euroimmun anti-ZIKV IgG ELISA and ZIKV-ELISA



Antibodies to Enterovirus D68 in Cerebrospinal Fluid of Patients with Acute Flaccid Myelitis



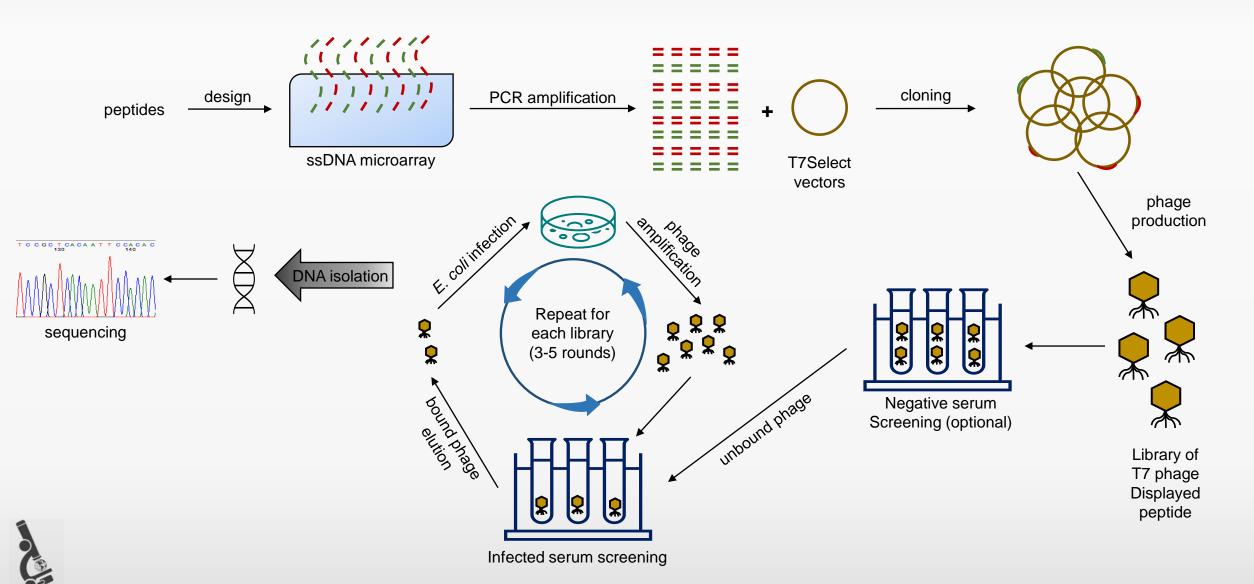
Identification of an immunoreactive peptide sequence region in VP1 protein of reference sequence entries for EV-A, EV-B, EV-C, and EV-D



Immunoreactivity against an EV-D68specific 22-aa VP1 capsid peptide in patients with AFM, non-AFM controls (NAC), Kawasaki disease controls (KDC), and adult CNS disease controls (AC).



Multiplex Serology Using Phage Display



Concordance Between Peptide Array and Granular Phage Display

Opportunities to Discriminate Between Infections With Related Viruses and Find Evidence of Reactivation

Peptide Array
Phage Display

Herpesvirus Reactivation in ME/CFS

Virus	Protein	CASE1	CASE2	CASE3	CASE4	CASE5	CASE6	CASE7	CASE8
HHV4	BZLF1								
HHV4	C M protease								
HSV1	E- Protein								
HHV-6A	Helicase								
HHV3	Large Tegument Protein								
HHV3	UL32								

Convalescent COVID-19

Virus	Protein	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6
	NP						
	GP						
Coronavirus							



Er



Vijay Bondre, National Institute of Virology, Pune





डा. सौम्या स्वामीनाथन

एमडी, एकएएससी, एकएनएससी, एकएएमएस सचिव, भारत सरकार स्वास्थ्य अनुसंघान विभाग स्वास्थ्य एवं परिवार कल्याण मंत्रालय

महानिदेशक, आई सी एम आर Dr. Soumya Swaminathan MD. FASc, FNASc, FAMS

Secretary to the Government of India

Department of Health Research Ministry of Health & Family Welfare

Director-General, ICMR



भारतीय आयुर्विज्ञान अनुसंधान परिषद

स्वास्थ्य अनुसंधान विभाग स्वास्थ्य एवं परिवार कल्याण मंत्रालय वी. रामलिंगस्वामी भवन, अंसारी नगर नई दिल्ली-110 029 (भारत)

Indian Council of Medical Research

Department of Health Research Ministry of Health & Family Welfare V. Ramalingaswami Bhawan, Ansari Nagar New Delhi-110 029 (INDIA)

No. Secy.(DHR) & DG,ICMR/ 2017 Dated, the 17th August, 2017



I am writing to invite you to visit the ICMR Hqrs in New Delhi and the NIV field Unit at Gorakhpur, Uttar Pradesh to assist with the investigation of encephalitis outbreak.

As you are aware, AES has been claiming the lives of children in Eastern Uttar Pradesh for many years and the etiology remains unknown in 50% of the cases. Your inputs to improve the diagnosis using advanced sequencing techniques for pathogen discovery will be very useful. I look forward to meeting you in India next week.

With regards,

Yours sincerely,

Myseur X

(Soumya Swaminathan)

Prof. W. Ian Lipkin, MD
John Snow Professor of Epidemiology and
Director
Center for Infection and Immunity
Mailman School of Public Health
Professor of Pathology and Neurology
College of Physicians & Surgeons
Columbia University
722 West 168th Street, 17th Floor

New York, NY 10032

sh

Ran Out in an Indian Hospital

dren From Dying?

stantimes

ths: Oppn demands ogi Adityanath, health

esh' CM Yogi Adityanath's silence in the aftermath of the children's deaths in College that has left the state stunned.





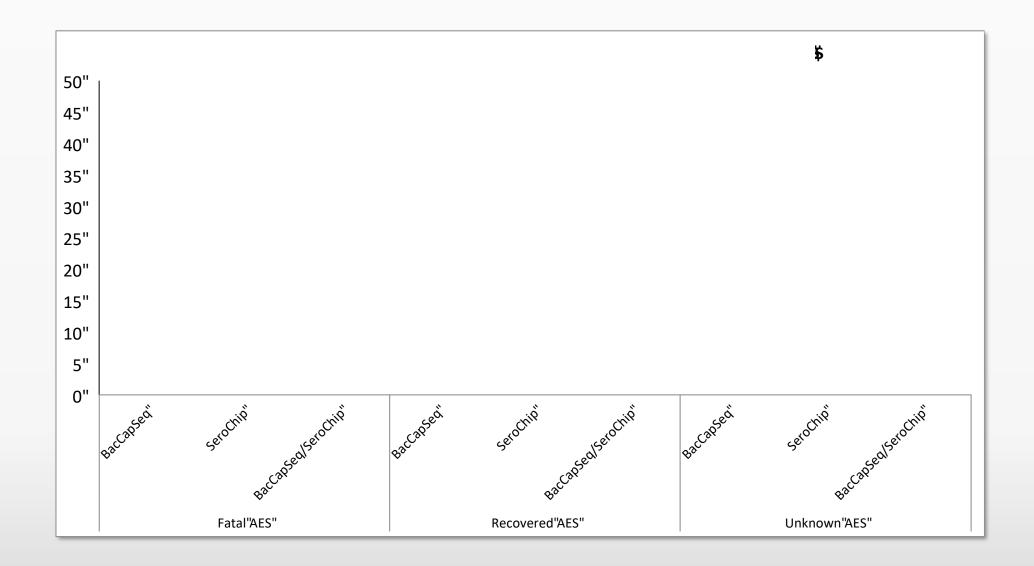


Agents Detected by VirCapSeq-VERT and BacCapSeq in Cerebrospinal Fluid (CSF) of Children with Acute Encephalitis Syndrome (AES)

	Fatal (n=223)	Discharged (n=283)	ed (n=283) OR 95% CI		p-value	
Human Herpesvirus 1	13 (5.8)	6 (2.1)	3.392	1.292	9.810	0.013
Human Herpesvirus 3	0 (0.0)	1 (0.4)	0.003	0.003	9.530	0.612
Human Herpesvirus 6	0 (0.0)	1 (0.4)	0.004	0.004	10.966	.723
Human Herpesvirus 7	0 (0.0)	1 (0.4)	0.006	0.006	17.262	0.949
Human Parvovirus 4	8 (3.6)	10 (3.5)	0.389	0.389	2.694	0.942
Human Parvovirus B19	3 (1.3)	2 (0.7)	0.626	0.626	21.181	0.152
Human Immunodeficiency Virus	10 (4.5)	11 (3.9)	0.454	0.454	2.777	0.790
GB Virus C/Human Pegivirus	11 (4.9)	15 (5.3)	0.749	0.749	4.118	0.189
Human Papillomavirus	6 (2.7)	10 (3.5)	0.362	0.362	3.028	0.884
Torque Teno Virus	8 (3.6)	10 (3.5)	0.450	0.450	3.189	0.695
Human Coxsackievirus	1 (0.4)	3 (1.1)	0.077	0.077	5.217	0.839
Hepatitis A Virus	4 (1.8)	1 (0.4)	0.844	0.844	53.399	0.077
Human Adenovirus	3 (1.3)	2 (0.7)	0.564	0.564	18.681	0.192
Mumps Virus Genotype C	5 (2.2)	6 (2.1)	0.310	0.310	3.427	0.937
Merkel Cell Polyoma	3 (13)	7 (2.5)	0.200	0.200	3.016	0.812
Gemycircularvirus	1 (0.4)	7 (.25)	0.038	0.038	1.776	0.235
Rhinovirus	0 (0.0)	1 (0.4)	0.001	0.001	3.938	0.293
Densovirus/Ambidensovirus	0 (0.0)	3 (1.1)	0.002	0.002	3.364	0.386
Norovirus	1 (0.4)	0 (0.0)	0.123	0.132	373.129	0.548
Human Picobirnavirus	1 (0.4)	0 (0.0)	0.134	0.134	379.345	0.540
Japanese Encephalitis Virus	3 (1.3)	1 (0.4)	0.446	0.446	31.185	0.271
Measles Virus/Genotype D8	1 (0.4)	0 (0.0)	0.153	0.153	432.749	0.483
Enterovirus/Echovirus	0 (.0)	3 (1.1)	0.001	0.001	1.733	0.942
Nilaparvata Lugens Reovirus	76 (34.1)	115 (40.6)	0.474	0.474	1.006	0.054
Orientia tsutsugamushi	24 (10.8)	31 (11.0)	0.419	0.419	1.354	0.349
Rickettsiae	13 (5.8)	24 (8.5)	0.416	0.416	1.758	0.701



Viral and Bacterial Capture Sequencing and Unbiased Serology AES CSF Samples Positive for Orientia tsugtsugamushi





Global Alliance for Preventing Pandemics

Capacity Building

Mali Cohort June 2022



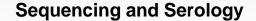






CII Collaborations (2001-)

Argentina, Australia, Brazil, Canada, Cambodia, China, Croatia, Democratic Republic of Congo, Ecuador, Germany, India, Indonesia, Israel, Kenya, Liberia, Mali, Mexico, Mongolia, New Zealand, Nicaragua, Nigeria, Norway, Peru, Russia, Saudi Arabia, Senegal, Sierra Leone, Singapore, Spain, Sweden, South Africa, Taiwan, Tanzania, The Gambia, Uganda, Zambia, Zimbabwe



- Supplies (volume purchasing)
- Computational tools and databases



DOI: 10.1172/JCI150646

A randomized double-blind controlled trial of convalescent plasma in adults with severe COVID-19 Max R. O'Donnell, ..., Andrew Eisenberger, Walter I. Lipkin



DOI:10.1101/2021.08.11.21261915

Molecular and serological investigation of the 2021 COVID-19 case surge in Mongolian vaccines Dashdorj NJ, ..., Lipkin WI, Mishra M

EMERGING INFECTIOUS DISEASES

DOI: 10.3201/eid2712.211818

SARS-CoV-2 sequence analysis of respiratory samples collected from hospitalized patients during the Liberia case surge in June, 2021 Bode Shobayo, ..., W. lan Lipkin, Nischay Mishra





Food Security: Piscine Reovirus

Bloomberg

Eduardo Thomson | October 11, 2011

Chile's Multiexport Heads to 17-Month Low on Fish Virus Concern

Multiexport Foods SA (MULTIFOO), the only salmon farmer on Chile's benchmark Ipsa index, headed for a 17 month low on concern a virus may effect production. Multiexport retreated 4.9% to 115.09 pesos at 4:30 pm Santiago time, the lowest price a closing basis since May 2010. The Ipsa rose 1.9%. Diario Financiero reported that regulators detected traces of "heart and skeletal inflammation," or HSMI, a virus among local farms.

Alexandra Morton

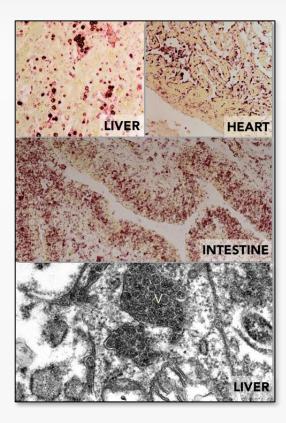
New Norwegian virus in supermarket farm salmon

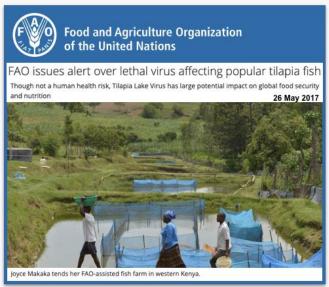
Sointula, BC (April 13, 2012) Test results report 44 out of 45 farm salmon purchased from the Superstore and T&T markets throughout Vancouver tested positive for a newly identified Norwegian virus. The piscine reovirus weakens the fish's heart causing Heart and Skeletal Muscle Inflammation (HSMI). HSMI is considered a "major challenge" in Norway infecting over 400 farms since it's symptoms first appeared in 1999. It has spread to the U.K.





Food Security: Tilapia Lake Virus







GLOBAL INFORMATION AND EARLY WARNING SYSTEM ON FOOD AND AGRICULTURE (GIEWS)

SPECIAL ALERT

No. 338

REGION: Global

DATE: 26 May 2017

Outbreaks of Tilapia lake virus (TiLV) threaten the livelihoods and food security of millions of people dependent on tilapia farming

Highlight

- Tilapia lake virus (TiLV) poses a great threat to the tilapia sector. Tilapias are farmed globally and are the second most important aquaculture species in terms of volumes produced, providing a key source of affordable animal protein, income to fishfarmers and fishers, and domestic and export earnings.
- TiLV has been confirmed in some countries in Asia, Africa and Latin America. It is likely that TiLV may have a wider distribution than is known today and its threat to tilapia farming at the global level is significant.
- While there is no public health concern for this pathogen, there is a significant risk of TiLV being translocated both inter- and intra-continentally through the movement of infected live tilapias in the absence of appropriate biosecurity measures.
- Tilapia producing countries need to be vigilant and take appropriate risk management measures (e.g. enhanced diagnostic testing of imported stocks and unexplained tilapia mortalities and reporting to biosecurity authorities, active surveillance, public information campaigns and contingency plans) to reduce the further spread and potential socio-economic impacts of this emerging disease.



United States – Israel Binational Agricultural Research and Development Fund קרן דו-לאומית למחקר ולפיתוח חקלאיים של ארצות הברית וישראל BARD - קמח

September 2020

Prof. lan Lipkin

Center for Infection and Immunity Mailman School of Public Health Columbia University

Dear Prof. Lipkin,

It is our deep pleasure to inform you that research conducted by you, together with Profs. Eran Bacharach from Tel Aviv University and Avi Eldar from the Kimron Veterinary Institute, on isolation and identification of the novel Tilapia Lake Virus, has been recognized for its outstanding scientific achievement and excellence. The research has been selected among the top 3most successful and impactful research projects in the environmental and social domains, amongst the 1,330 projects granted by the US-Israel Binational Research and Development fund over the entire 40 years of its existence. Please accept this formal letter of recognition with our warmest congratulations.

As you know, we have recently completed the BARD 40-year research impact assessment. The external review committee that oversaw the evaluation process was deeply impressed by your research approach leading to identification of the virus and establishing a first diagnostic tool, and the exceptional global implications following the elucidation of one of the primary disease concerns for tilapia farming worldwide. The findings were a stellar scientific breakthrough and have a tremendous impact on global food security, nutrition and farmers livelihoods.

The accomplishments driven from this research reflect the remarkable vision, dedication and persistence of the joint Israel-US team in pursuing and achieving ambitious scientific goals of tremendous value and the far-reaching implications for improved tilapia disease management and containment. In light of the above, we wish to recognize this research for its important social and environmental impact.

Furthermore, I would like to personally thank you for taking part in the survey and interviews. Your feedback was very much appreciated. The report is available online BARD 40-year review research impact evaluation report (Full case study featuring your research). I wish you and your colleagues much success in your further work, and, of course, wishing you all health during these times.



Prof. Yoram Kapulnik
Executive Director



Building a Global Immune System

We have the tools needed to expedite and democratize microbial surveillance and discovery

- Inexpensive, rapid, sensitive molecular methods for direct detection of microbial sequences
 local outbreak investigation and surveillance of humans and potential zoonotic sources for
 Pathogen X
- Multiplexed, granular methods for indirect detection and implication of infection through serology early evidence of cross species transmission of Pathogen X and insights into chronic diseases like ME/CFS and PASC
- Same tool kit can be used to broadly enhance biosecurity
 detect threats to the food supply and the emergence of antimicrobial resistance

Missing components

- Resources to build and sustain infrastructure for independent outbreak response and surveillance in low- and middle-income countries
- Commitment to sharing laboratory and clinical metadata
- International regulatory body that can facilitate clinical trials and approvals of diagnostics, drugs, and vaccines

