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## Journal of Medical Virology

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# 137

### PUBLICATION TYPE

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01466615, 10969071

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1977-2021

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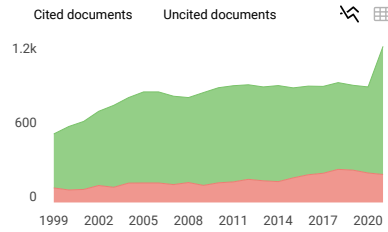
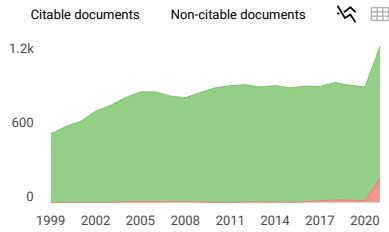
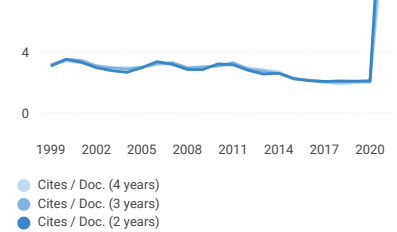
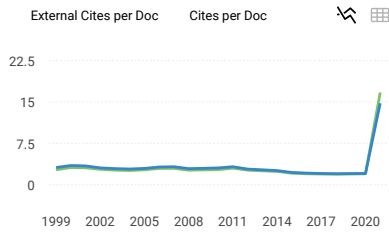
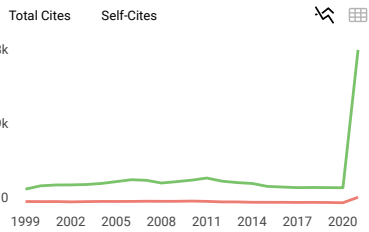
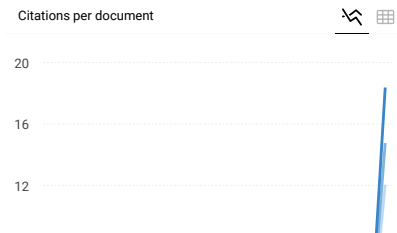
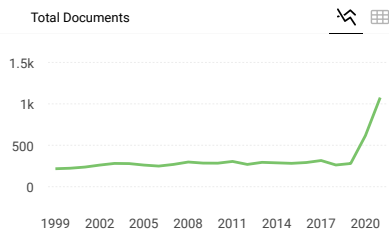
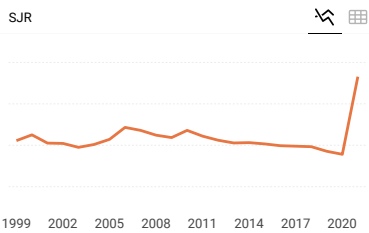
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Jie Pan, Songchun Yang, Xiaozhen Chen, Xuanlin Che, Wenrui Lin, Mingliang Chen, Xiang Chen, Guangtong Deng, Juan Su

e28598 | First Published: 24 February 2023



**Front Cover Caption:** The cover image is based on the Research Article *Two-year impact of COVID-19 pandemic on hospitalized patients with skin diseases in China* by Jie Pan et al., <https://doi.org/10.1002/jmv.28511>.

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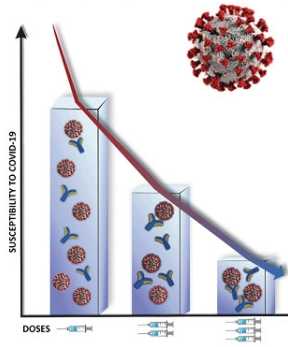
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## LETTER TO THE EDITOR

### [Nasal mucosa is much more susceptible than oral mucosa to infection of SARS-CoV-2 Omicron subvariants: Wearing nasal masks where facial masks cannot be used](#)

Zijie Lin, Lujia Sun, Liliang Li, Shibo Jiang

e28577 | First Published: 13 February 2023

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### [Does viral inoculum play a role in disease severity in COVID-19?](#)

Chenyu Sun MD, MSc, Vicky Yau, John Patrick Nanola Uy, Scott Lowe, Yanghua Tian PhD

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### [Limited enhancement of antibody and B-cell responses to prototype booster vaccination following SARS-CoV-2 Delta breakthrough infection](#)

Xun Wang, Xing He, Shujun Jiang, Zhangfan Fu, Shuai Jiang, Xiaoyu Zhao, Chaoyue Zhao, Yanning Li, Dianfan Li, Wenhong Zhang, Jingwen Ai, Yanliang Zhang, Chenqi Xu, Pengfei Wang

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### [A case of human buffalopox in Malappuram, India: The role of mpox surveillance in 2022](#)

Deepak Y. Patil, Sandhya George, Rima R. Sahay, Shubin Chenayil, Anita M. Shete, Sindhu C. Bhaskaramenon, Thekkumkara Surendran Anish, Rajlaxmi Jain, Fathima Abdul Nazeer, Reena John, Yash Joshi, R. Sivaprasad, Priyanka Waghmare, Shilpa Ray, Swapna Balakrishnan, Vaishnavi Kumari, Shubhangi Sathe, Pragya D. Yadav

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### [Detect and suppress future zoonotic-derived outbreaks: A lesson from the last two decades](#)

Nguyen K. Quan MD, Dang H. Thien, Nguyen T. Huy MD, PhD

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### [Early use of tecovirimat in a young man with severe mpox skin lesions: a case report](#)

Valentina Iannone, Arturo Ciccullo, Damiano Farinacci, Alberto Borghetti, Elena Visconti, Simona Marchetti, Maurizio Sanguinetti, Enrica Tamburrini, Simona Di Giambenedetto

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### [Distinguishing monkeypox from its mimickers](#)

Grant Sprow, Michelle Toker, Urmi Khanna, Benedict Wu

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### [A protocol of trial of ivermectin in COVID-19 treatment critically changed after its completion](#)

Kouji H. Harada, Arthit Phosri

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### [Monkeypox keratoconjunctivitis with associated Wessley immune ring in an immunocompetent patient](#)

Tafnes de Oliveira Quites, Leandro Ferreira Lopes Landeira, Thaísa Gomes Viana de Santana, Carolina Lamego Khouri, Monica Barcellos Arruda, Patrícia Alvarez da Silva Baptista, Shana Priscila Coutinho Barroso

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### [Concerns on Bebtelovimab \(LY-CoV1404\) used to neutralize Omicron subvariants](#)

Xuejun Wang, Yang Yang, Zhifei Song, Yiming Wang, Peng Yang, Xinyu Li, Fei Wang, Mingming Wang, Liting Shao, Shengqi Wang

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### [Monkeypox virus, herpes simplex virus, and cytomegalovirus skin coinfections](#)

Badr AbdullGaffar, Suad Abdulrahman

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### [SARS-COV-2 Omicron subvariant BF.7 is again triggering the Covid fear: What we need to know and what we should do?](#)

Adnan Akif, Mohiuddin Ahmed Bhuiyan, Md. Rabiul Islam

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### **Nirmatrelvir–ritonavir for the treatment of COVID-19 patients: A systematic review and meta-analysis**

Huzaifa A. Cheema, Uzair Jafar, Aruba Sohail, Abia Shahid, Syeda Sahra, Muhammad Ehsan, Farwa Athar, Jaffer Shah, Ranjit Sah

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### **Secondary complications and management strategies in human monkeypox: A case series**

Bahadar S. Srichawla, Maria A. García-Dominguez, Subtain Zia

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### **Effects of inactivated SARS-CoV-2 vaccination on male fertility: A retrospective cohort study**

Mingqiang Wang, Lingtong Huang

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### **Covid associated immune dysfunction (CAID) leading to increased pediatric hospitalizations**

Baran Erdik MD, MHPA

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## REVIEWS

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### **A systematic review and clinical atlas on mucocutaneous presentations of the current monkeypox outbreak: With a comprehensive approach to all dermatologic and nondermatologic aspects of the new and previous monkeypox outbreaks**

Homa Pourriyahi, Zeinab Aryanian, Zeinab Mohseni Afshar, Azadeh Goodarzi

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### **Role of noncoding RNAs with emphasis on long noncoding RNAs as cervical cancer biomarkers**

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### **Transmission of monkeypox/mpox virus: A narrative review of environmental, viral, host, and population factors in relation to the 2022 international outbreak**

Daniel Pan, Joshua Nazareth, Shirley Sze, Christopher A. Martin, Jonathan Decker, Eve Fletcher, T. Déirdre Hollingsworth, Michael R. Barer, Manish Pareek, Julian W. Tang

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### **Cross-reactivity of SARS-CoV-2 with other pathogens, especially dengue virus: A historical perspective**

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**mRNA vaccines: The future of prevention of viral infections?**

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### Multisystem inflammatory syndrome in adults: Characteristics, treatment, and outcomes

Chih-Cheng Lai, Chi-Kuei Hsu, Shun-Chung Hsueh, Muh-Yong Yen, Wen-Chien Ko, Po-Ren Hsueh

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### Coronavirus disease 2019 rebounds following nirmatrelvir/ritonavir treatment

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### Intravaginal delivery for CRISPR–Cas9 technology: For example, the treatment of HPV infection

Shuai Zhen, Hong Chen, Jiaojiao Lu, Xiling Yang, Xiaoqian Tuo, Shixue Chang, Yuhan Tian, Xu Li

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### Animal host range of mpox virus

Kangxin Li, Yupei Yuan, Lu Jiang, Yuwen Liu, Yihan Liu, Leiliang Zhang

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### It is time to improve the acceptance of COVID-19 vaccines among people with chronic diseases: A systematic review and meta-analysis

Yang Zhao, Juan Du, Zhen Li, Zhe Xu, Yaxin Wu, Wenshan Duan, Wenjing Wang, Tong Zhang, Junjie Xu, Hao Wu, Xiaojie Huang

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### Molecular evolution of the human monkeypox virus

Jonas Michel Wolf, Lucas Michel Wolf, Pamela Pereira Fagundes, Dalila Mabel Schmidt Tomm, Helena Petek, Aline Brenner, Juçara Gasparetto Maccari, Luiz Antonio Nasi

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## RESEARCH ARTICLES

### Predictors of severity in severe respiratory infection in children with COVID-19 respiratory infection in a developing country

Daniel Mauricio Beltran, Milena Villamil Osorio, Sara Liliana Goyeneche Fonseca, Sonia M. Restrepo-Gualteros, María José Rosero Garcia, Carlos E. Rodriguez-Martinez

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### Whole-genome single molecule real-time sequencing of SARS-CoV-2 Omicron

Florence Nicot, Pauline Trémeaux, Justine Latour, Romain Carcenac, Sofia Demmou, Nicolas Jeanne, Noémie Ranger, Clémentine De Smet, Stéphanie Raymond, Chloé Dimeglio, Jacques Izopet

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## **Nirmatrelvir-ritonavir therapy and COVID-19 vaccination improve clinical outcomes of SARS-CoV-2 Omicron variant infection**

Tangkai Qi, Yinpeng Jin, He Wang, Yixin Liao, Tiefu Liu, Enqiang Mao, Feng Li, Yinchuan Li, Xiaohong Fan, Yun Ling

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## **Monkeypox awareness and low vaccination hesitancy among men who have sex with men in China**

Yuwei Li, Xin Peng, Leiwen Fu, Bingyi Wang, Yinghui Sun, Yuanyi Chen, Yi-Fan Lin, Xinsheng Wu, Qi Liu, Yanxiao Gao, Weiran Zheng, Junye Bian, Zhen Lu, Xiaojun Meng, Hui Xue, Hui Li, Hongbo Jiang, Huachun Zou

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## **Safety and immunogenicity of a recombinant receptor-binding domain-based protein subunit vaccine (Noora vaccine™) against COVID-19 in adults: A randomized, double-blind, placebo-controlled, Phase 1 trial**

Jafar Salimian, Ali Ahmadi, Jafar Amani, Gholamreza Olad, Raheleh Halabian, Ali Saffaei, Masoud Arabfard, Mojtaba Nasiri, Shahram Nazarian, Hassan Abolghasemi, Gholamhossein Alishiri

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## **Analysis of the reliability of rapid diagnostic tests for varicella, including breakthrough cases**

Yuki Higashimoto, Fumihiko Hattori, Yoshiki Kawamura, Kei Kozawa, Aoi Hamano, Mizuki Kato, Sayaka Kato, Asuka Hosokawa, Yasuko Enya, Masaru Ihira, Tetsushi Yoshikawa

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## **Comparable humoral and cellular immunity against Omicron variant BA.4/5 of once-boosted BA.1/2 convalescents and twice-boosted COVID-19-naïve individuals**

Chang Kyung Kang, Min-Gang Kim, Seong-wook Park, Yong-Woo Kim, Chan Mi Lee, Pyoeng Gyun Choe, Wan Beom Park, Nam Joong Kim, Minji Kim, Soojin Lee, Ik Soo Kim, Chang-Han Lee, Hyun Mu Shin, Hang-Rae Kim, Myoung-don Oh

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## **Immunogenicity of novel DNA vaccines encoding receptor-binding domain (RBD) dimer-Fc fusing antigens derived from different SARS-CoV-2 variants of concern**

Ting Zhang, Zhirong Wang, Jiaojiao Yang, Xuemei Xu

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## **Tumor cell vaccine combined with Newcastle disease virus promote immunotherapy of lung cancer**

Hui Wang, Fulong Nan, Zhou Zeng, Xueming Zhang, Dingxin Ke, Shuyun Zhang, Xiaoqiong Zhou, Delei Niu, Tianyu Fan, Shasha Jiang, Xianjuan Zhang, Yunyang Wang, Bin Wang, Wanming Zhang

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## **Evaluation of the performance of a rapid antigen test (Roche) for COVID-19 diagnosis in an emergency setting in Sweden**

Anna Heydecke, Karolina Gullsby

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## **Discovery of Isojacareubin as a covalent inhibitor of SARS-CoV-2 main protease using structural and experimental approaches**

Abbas Khan, Wang Heng, Kashif Imran, Guanghao Zhu, Jun Ji, Yani Zhang, Xiaoqing Guan, Guangbo Ge, Dong-Qing Wei

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### **Inhibition of PIKFYVE kinase interferes ESCRT pathway to suppress RNA virus replication**

Zhen Luo, Yicong Liang, Mingfu Tian, Zhihui Ruan, Rui Su, Muhammad Adnan Shereen, Jialing Yin, Kailang Wu, Jun Guo, Qiwei Zhang, Yongkui Li, Jianguo Wu

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### **Head-to-head comparison of genotyping of human papillomavirus by real-time multiplex PCR assay using type-specific primers and SPF10-PCR-based line probe assay**

Jian Yin, Siying Peng, Changning Zhang, Xinyue Li, Fangfang Hu, Wen Chen, Youlin Qiao

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### **Analysis on the physiological changes of residents before and during the COVID-19 pandemic: A cross-sectional study**

Jinlong Chen, Xueying Cheng, Yue Xu, Tingting Shi, Chunran Zhu, Xu Wang

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### **Dysregulation of memory B cells and circulating T follicular helper cells is a predictor of poor immune recovery in HIV-infected patients on antiretroviral therapy**

Yan Liu, Zhen Li, Xiaofan Lu, Yi-Qun Kuang, Deshenyue Kong, Xin Zhang, Xiaodong Yang, Xiuwen Wang, Tingting Mu, Hu Wang, Yihang Zhang, Junyan Jin, Wei Xia, Hao Wu, Tong Zhang, Christiane Moog, Bin Su

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### **Monitoring of SARS-CoV-2 concentration and circulation of variants of concern in wastewater of Leuven, Belgium**

Annabel Rector, Mandy Bloemen, Marijn Thijssen, Leen Delang, Joren Raymenants, Jonathan Thibaut, Bram Pussig, Lore Fondu, Bert Aertgeerts, Marc Van Ranst, Chris Van Geet, Jef Arnout, Elke Wollants

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### **Oxidative stress—A key determinant of complications and negative outcome in hepatitis E virus infected pregnancies: A comprehensive account involving cases from northeast India**

Natasha Kashyap, Mafidul Islam, Harpreet Kaur, Diptika Tiwari, Anjuma Begum, Moumita Bose, Chandana Ray Das, Anjan Kumar Saikia, Pankaj Kalita, Purabi Deka Bose, Sujoy Bose

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### **Human cytomegalovirus infection perturbs neural progenitor cell fate via the expression of viral microRNAs**

Xuan Jiang, Siqing Liu, Ya-Ru Fu, Xi-Juan Liu, Xiao-Jun Li, Bo Yang, Hai-Fei Jiang, Zhang-Zhou Shen, Endalkachew Ashenafi Alemu, Pavel Vazquez, Yaping Tang, Mari Kaarbø, Michael A. McVoy, Simon Rayner, Min-Hua Luo

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### **Impact of nucleic acid extraction procedures on human papillomavirus (HPV) detection and genotyping**

Klaudia Naegele, Fabian H. Weissbach, Karoline Leuzinger, Rainer Gosert, Lukas Bubendorf, Hans H. Hirsch

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## High C-reactive protein to lymphocyte ratio predicts mortality outcomes of patients with severe fever with thrombocytopenia syndrome: A multicenter study in China

Fang Qian, Wei Zhou, Yuanni Liu, Ziruo Ge, Jianming Lai, Zhenghua Zhao, Yang Feng, Ling Lin, Yi Shen, Zhonglu Zhang, Wei Zhang, Tianli Fan, Yongxiang Zhao, Zhihai Chen

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## Dysbiosis of the stool DNA and RNA virome in Crohn's disease

Cheng Kong, Guang Liu, Matthew F. Kalady, Tao Jin, Yanlei Ma

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## HBsAg (-)/HBsAb (-)/HBeAg (-)/HBeAb (+)/HBcAb (+) predicts a high risk of hepatitis B reactivation in patients with B-cell lymphoma receiving rituximab based immunochemotherapy

Li-Ping Shui, Yan Zhu, Xiao-Qin Duan, Yu-Ting Chen, Li Yang, Xiao-Qiong Tang, Hong-Bin Zhang, Qing Xiao, Li Wang, Lin Liu, Xiao-Hua Luo

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## Investigating the effect of ribavirin treatment on genetic mutations in Crimean–Congo haemorrhagic fever virus (CCHFV) through next-generation sequencing

Jake D'Addiego, Nazif Elaldi, Nadina Wand, Karen Osman, Binnur Koksall Bagci, Emma Kennedy, Ayse Nur Pektas, Eilish Hart, Gillian Slack, Roger Hewson

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## Impact of alcohol consumption on coronavirus disease 2019 severity: A systematic review and meta-analysis

Baozhu Wei, Yang Liu, Hang Li, Yuanyuan Peng, Zhi Luo

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## Treatment with integrase inhibitors alters SARS-CoV-2 neutralization levels measured with HIV-based pseudotypes in people living with HIV

Erick De La Torre-Tarazona, Alba González-Robles, Almudena Cascajero, Paloma Jiménez, José María Miró, Sonsoles Sánchez-Palomino, José Alcamí, Maria José Buzón, Javier García-Pérez, the Hospital Clinic HIV Investigators

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## Disentangling the common genetic architecture and causality of rheumatoid arthritis and systemic lupus erythematosus with COVID-19 outcomes: Genome-wide cross trait analysis and bidirectional Mendelian randomization study

Minhao Yao, Xin Huang, Yunshan Guo, Jie V. Zhao, Zhonghua Liu

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## Receptor-binding domain-based SARS-CoV-2 vaccine adjuvanted with cyclic di-adenosine monophosphate enhances humoral and cellular immunity in mice

María José Germanó, Constanza Giai, Diego Esteban Cargnelutti, María Isabel Colombo, Sebastián Blanco, Brenda Konigheim, Lorena Spinsanti, Javier Aguilar, Sandra Gallego, Hugo Alberto Valdez, Juan Pablo Mackern-Oberti, Maria Victoria Sanchez

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## Monkeypox outbreak in Genoa, Italy: Clinical, laboratory, histopathologic features, management, and outcome of the infected patients

Giulia Ciccarese, Antonio Di Biagio, Bianca Bruzzone, Antonio Guadagno, Lucia Taramasso, Giorgio Oddenino, Giorgia Brucci, Laura Labate, Vanessa De Pace, Mario Mastrodonardo, Francesco Broccolo, Giacomo Robello, Francesco Drago, Matteo Bassetti, Aurora Parodi

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### ***IFNL3/4* polymorphisms as a two-edged sword: An association with COVID-19 outcome**

Sanja Matic, Dragan Milovanovic, Zeljko Mijailovic, Predrag Djurdjevic, Predrag Sazdanovic, Srdjan Stefanovic, Danijela Todorovic, Suzana Popovic, Katarina Vitosevic, Vladimir Vukicevic, Milena Vukic, Nenad Vukovic, Nevena Milivojevic, Marko Zivanovic, Vladimir Jakovljevic, Nenad Filipovic, Dejan Baskic, Natasa Djordjevic

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### **Twelve-month clinical, functional, and radiological outcomes in patients hospitalized for SARS-CoV-2 pneumonia**

Marco Bongiovanni, Giuseppe Barilaro, Francesco Bini

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### **A new glutamine synthetase index to evaluate hepatic lobular restoration in advanced fibrosis during anti-HBV therapy**

Shuyan Chen, Bingqiong Wang, Jialing Zhou, Xiaoning Wu, Tongtong Meng, Hui Liu, Tailing Wang, Xinyan Zhao, Shanshan Wu, Yuanyuan Kong, Xiaojuan Ou, Jidong Jia, Aileen Wee, Hong You, Yameng Sun

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### **Enhanced recombination among Omicron subvariants of SARS-CoV-2 contributes to viral immune escape**

Rishad Shiraz, Shashank Tripathi

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### **Persistent circulation of soluble and extracellular vesicle-linked Spike protein in individuals with postacute sequelae of COVID-19**

Vaughn Craddock, Aatish Mahajan, Leslie Spikes, Balaji Krishnamachary, Anil K. Ram, Ashok Kumar, Ling Chen, Prabhakar Chalise, Navneet K. Dhillon

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### **Factors affecting prolonged SARS-CoV-2 infection and development and validation of predictive nomograms**

Yifei Guo, Yue Guo, Yongmei Zhang, Fahong Li, Jie Yu, Yao Zhang, Zhongliang Shen, Richeng Mao, Haoxiang Zhu, Jiming Zhang

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### **Impact of air pollutants on influenza-like illness outpatient visits under COVID-19 pandemic in the subcenter of Beijing, China**

Xin-Yao Lian, Lu Xi, Zhong-Song Zhang, Li-Li Yang, Juan Du, Yan Cui, Hong-Jun Li, Wan-Xue Zhang, Chao Wang, Bei Liu, Yan-Na Yang, Fuqiang Cui, Qing-Bin Lu

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### **“Mitochondrial pathogenic mutations and metabolic alterations associated with COVID-19 disease severity”**

Diksha Kumari, Yamini Singh, Sayar Singh, Vikas Dogra, Ashish Kumar Srivastava, Swati Srivastava, Iti Garg, Mona Bargoutya, Javid Hussain, Lilly Ganju, Rajeev Varshney

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### **Nonpharmaceutical interventions reduce the incidence and mortality of COVID-19: A study based on the survey from the International COVID-19 Research Network (ICRN)**

Seung Hyun Park, Sung Hwi Hong, Kwanghyun Kim, Seung Won Lee, Dong Keon Yon, Sun Jae Jung, Ziad Abdeen, Ramy Abou Ghayda, Mohamed Lemine Cheikh Brahim Ahmed, Abdulwahed Al Serouri, Waleed Al-Herz, Humaid O. Al-Shamsi, Sheeza Ali, Kosar Ali, Oidov Baatarkhuu, Henning Bay Nielsen, Enrico Bernini-Carri, Anastasiia Bondarenko, Ayun Cassell, Akway Cham, Melvin L. K. Chua, Sufia Dadabhai, Tchin Darre, Hayk Davtyan, Elena Dragioti, Barbora East, Robert Jeffrey Edwards, Martina Ferioli, Tsvetoslav Georgiev, Lilian A. Ghandour, Harapan Harapan, Po-Ren Hsueh, Saad I. Mallah, Aamer Ikram, Shigeru Inoue, Louis Jacob,

Slobodan M. Janković, Umesh Jayarajah, Milos Jesenak, Pramath Kakodkar, Nathan Kapata, Yohannes Kebede, Yousef Khader, Meron Kifle, David Koh, Višnja Kokić Maleš, Katarzyna Kotfis, Ai Koyanagi, James-Paul Kretchy, Sulaiman Lakoh, Jinhee Lee, Jun Young Lee, Maria da Luz Lima Mendonça, Lowell Ling, Jorge Llibre-Guerra, Masaki Machida, Richard Makurumidze, Ziad A. Memish, Ivan Mendoza, Sergey Moiseev, Thomas Nadasdy, Chen Nahshon, Silvio A. Namendys-Silva, Blaise Nguendo Yongs, Amalea Dulcene Nicolasora, Zhamilya Nugmanova, Hans Oh, Atte Oksanen, Oluwatomi Owopetu, Zeynep Ozge Ozguler, Konstantinos Parperis, Gonzalo Emanuel Perez, Krit Pongpirul, Marius Rademaker, Nemanja Radojevic, Anna Roca, Alfonso J. Rodriguez-Morales, Enver Rosh, Khwaja Mir Islam Saeed, Ranjit Sah, Boris Sakakushev, Dina E. Sallam, Brijesh Sathian, Patrick Schober, P. Shaik Syed Ali, Zoran Simonović, Tanu Singhal, Natia Skhvitaridze, Marco Solmi, Kannan Subbaram, Kalthoum Tizaoui, John Thato Tlhakanelo, Julio Torales, Junior Smith Torres-Roman, Dimitrios Tsartsalis, Jadamba Tsolmon, Duarte Nuno Vieira, Sandro G. Viveiros Rosa, Guy Wanghi, Uwe Wollina, Ren-He Xu, Lin Yang, Kashif Zia, Muharem Zildzic, Jae Il Shin, Lee Smith

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### Emerging Omicron subvariants evade neutralizing immunity elicited by vaccine or BA.1/BA.2 infection

Zehui Chen, Jiaming Li, Jing Zheng, Yifei Jin, Yidun Zhang, Fei Tang, Jingjing Li, Hongliang Cheng, Lina Jiang, Huixin Wen, Chao Hong, Xiaohong Zeng, Shijie Huang, Bing Lu, Li Li, Zhongyi Wang

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### Appearance of extrapyramidal symptoms in adolescent psychiatry patients during COVID-19 infection

Aysegul Tonyali, Gul Karacetin, Celal Yesilkaya, Feyza Nur Tas Arik, Binay Kayan Ocakoglu

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### Association of *ESR1* gene polymorphisms with the susceptibility to Hepatitis B virus infection and the clinical outcomes

Jiaxin Xie, Yibo Ding, Xiaopan Li, Rui Pu, Wenbin Liu, Peng Li, Jianhua Yin

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### Cocirculation of A(H3N2) and B/Victoria increased morbidity in hospitalized patients in the 2019–2020 A(H1N1)pdm09 predominant influenza season in Israel

Menucha Jurkowicz, Itai Nemet, Nofar Atari, Ilana S. Fratty, Limor Kliker, Hilda Sherbany, Nathan Keller, Eugene Leibovitz, Ella Mendelson, Michal Mandelboim, Michal Stein

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### Delayed cutaneous hypersensitivity reactions following the use of infliximab or adalimumab in patients with coronavirus disease 2019

Jing Wang, Xuedong Yin, Linlin Yu, Weiwei Cheng, Ling Wang, Bin Zhao, Zhiling Li, Xiaoping Jing

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### The case fatality rate of COVID-19 during the Delta and the Omicron epidemic phase: A meta-analysis

Kisong Kim, Kyuyeon Cho, Junmin Song, Masoud Rahmati, Ai Koyanagi, Seung Won Lee, Dong Keon Yon, Jae Il Shin, Lee Smith

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### Developmental outcomes in children born to women with possible subclinical rubella exposures during pregnancy

Jill Hutton

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### Pharmaco-virological algorithm to target risk of drug resistance among a population of HIV-infected key populations in Togo

Valentine M. Ferré, Alexandra M. Bitty-Anderson, Gilles Peytavin, Minh P. Lê, Claver A. Dagnra, Romain Coppée, Fifonsi A. Gbeasor-Komlanvi, Diane Descamps, Charlotte Charpentier, Didier K. Ekouevi

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### **Torque teno virus (TTV): A gentle spy virus of immune status, predictive marker of seroconversion to COVID-19 vaccine in kidney and lung transplant recipients**

Piergiorgio Roberto, Lilia Cinti, Anna Napoli, Daniele Paesani, Rodolfo J. Riveros Cabral, Fabrizio Maggi, Manuela Garofalo, Renzo Pretagostini, Anastasia Centofanti, Carolina Carillo, Federico Venuta, Aurelia Gaeta, Guido Antonelli

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### **Surveillance for SARS-CoV-2 and its variants in wastewater of tertiary care hospitals correlates with increasing case burden and outbreaks**

Nicole Acosta, Maria A. Bautista, Barbara J. Waddell, Kristine Du, Janine McC Calder, Puja Pradhan, Navid Sedaghat, Chloe Papparis, Alexander Buchner Beaudet, Jianwei Chen, Jennifer Van Doorn, Kevin Xiang, Leslie Chan, Laura Vivas, Kashtin Low, Xuewen Lu, Jangwoo Lee, Paul Westlund, Thierry Chekouo, Xiaotian Dai, Jason Cabaj, Srijak Bhatnagar, Norma Ruecker, Gopal Achari, Rhonda G. Clark, Craig Pearce, Joe J. Harrison, Jon Meddings, Jenine Leal, Jennifer Ellison, Bayan Missaghi, Jamil N. Kanji, Oscar Larios, Elissa Rennert-May, Joseph Kim, Steve E. Hruday, Bonita E. Lee, Xiaoli Pang, Kevin Frankowski, John Conly, Casey R. J. Hubert, Michael D. Parkins

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### **Persistent effects of COVID-19 in patients hospitalized during the first wave of the pandemic: The impact of persistent fatigue on quality of life in a cross-sectional study**

Joseph P. Skinner, Lauren V. Moran

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### **Molecular characterization of rotavirus infections in children less than 5 years of age with acute gastroenteritis in Tehran, Iran, 2021–2022: Emergence of uncommon G9P[4] and G9P[8] rotavirus strains**

Atefeh Kachooei, Ahmad Tava Koli, Sara Minaeian, Mahdieh Hosseini, Somayeh Jalilvand, Tayebeh Latifi, Arash Arashkia, Angila Ataei-Pirkooh, Zabihollah Shoja

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### **Ultrastructural analysis of monkeypox virus replication in Vero cells**

Amanda Stéphanie Arantes Witt, Giliane de Souza Trindade, Fernanda Gil de Souza, Mateus Sá Magalhães Serafim, Alana Vitor Barbosa da Costa, Marcos Vinícius Ferreira Silva, Felipe Campos de Melo Iani, Rodrigo Araújo Lima Rodrigues, Erna Geessien Kroon, Jônatas Santos Abrahão

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### **ELISPOT assays with pp65 peptides or whole HCMV antigen are reliable predictors of immune control of HCMV infection in seropositive kidney transplant recipients**

Federica Zavaglio, Francesca Rivela, Irene Cassaniti, Francesca Arena, Elisa Gabanti, Anna L. Asti, Daniele Lilleri, Teresa Rampino, Fausto Baldanti, Marilena Gregorini

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### **Immune-dysregulation in subacute sclerosing panencephalitis: An exploratory case–control study**

Vijayaragavan Vijayarvarman, Hardeep S. Malhotra, Imran Rizvi, Neeraj Kumar, Shweta Pandey, Mili Jain, Wahid Ali, Vinay Suresh, Ravindra K. Garg, Amita Jain, Rajesh Verma, Praveen Sharma, Ravi Uniyal

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## Evolution and emergence of primate-specific interferon regulatory factor 9

Sam Drury, Grace Claussen, Allison Zetterman, Hideaki Moriyama, Etsuko N. Moriyama, Luwen Zhang

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## Identification of two proposed novel human rhinovirus types: Bpat107 and Cpat58

Qiang Zhang, Zhibo Xie, Baicheng Xia, Yage Wang, Wenbo Xu, Yan Zhang

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## Inhibition of influenza A virus replication by a marine derived quinolone alkaloid targeting virus nucleoprotein

Yang Zhang, Wei-Feng Xu, Yunjia Yu, Qun Zhang, Lianghao Huang, Cui Hao, Chang-Lun Shao, Wei Wang

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## Two-year impact of COVID-19 pandemic on hospitalized patients with skin diseases in China

Jie Pan, Songchun Yang, Xiaozhen Chen, Xuanlin Che, Wenrui Lin, Mingliang Chen, Xiang Chen, Guangtong Deng, Juan Su

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## SERTAD3 induces proteasomal degradation of ZIKV capsid protein and represents a therapeutic target

Nina Sun, Rong-Rong Zhang, Guang-Yuan Song, Qiaomei Cai, Saba R. Aliyari, Karin Nielsen-Saines, Jae U. Jung, Heng Yang, Genhong Cheng, Cheng-Feng Qin

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## A hepatitis B virus core antigen-based virus-like particle vaccine expressing SARS-CoV-2 B and T cell epitopes induces epitope-specific humoral and cell-mediated immune responses but confers limited protection against SARS-CoV-2 infection

Anna M. Hassebroek, Harini Sooryanarain, Connie L. Heffron, Seth A. Hawks, Tanya LeRoith, Thomas E. Cecere, William B. Stone, Debra Walter, Hassan M. Mahsoub, Bo Wang, Debin Tian, Hannah M. Ivester, Irving C. Allen, Albert J. Auguste, Nisha K. Duggal, Chenming Zhang, Xiang-Jin Meng

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## Higher clearance rates of multiple HPV infections may explain their lower risk of HSIL: A retrospective study in Wenzhou, China

Xinyu Ni, Jiaming Hu, Yin Huang, Jinxin Tao, Hua Zhu

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## Contribution of genotypes in Prothrombin and Factor V Leiden to COVID-19 and disease severity in patients at high risk for hereditary thrombophilia

Aslıhan Kiraz, Ozlem Sezer, Adem Alemdar, Sezin Canbek, Nilgun Duman, Atıl Bisgin, Tulin Cora, Hatice İlgin Ruhi, Mahmut Cerkez Ergoren, Bilgen Bilge Geçkinli, Sebnem Ozemri Sag, Hilmi Erdem Gözden, Ozlem Oz, Zuhal Mert Altıntaş, Sinem Yalcıntepe, Adem Keskin, Ayşegül Yabacı Tak, Şeyma Aktaş Paskal, Uğur Fahri Yürekli, Mercan Demirtas, Emine Unal Evren, Abdullah Hanta, Müşerref Başdemirci, Kaya Suer, Burhan Balta, Nadir Kocak, Halil Gürhan Karabulut, Havva Cobanogulları, Esra Arslan Ateş, Sevcan Tuğ Bozdoğan, Damla Eker, Sadiye Ekinci, Süleyman Nergiz, Timur Tuncalı, Serap Yagbasan, Ceren Alavanda, Nuket Yurur Kutlay, Hakan Evren, Murat Erdoğan, Sule Altiner, Tamer Sanlidag, Gizem Akıncı Gonen, Arzu Vicdan, Nazan Eras, Hatice Koçak Eker, Özgür Balasar, Gulden Tuncel, Munis Dunder, Hakan Gurkan, Sehime Gulsun Temel

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## Needle-free injection system delivery of ZyCoV-D DNA vaccine demonstrated improved immunogenicity and protective efficacy in rhesus macaques against SARS-CoV-2

Pragya D. Yadav, Sanjay Kumar, Kshitij Agarwal, Mukul Jain, Dilip R. Patil, Kapil Maithal, Basavaraj Mathapati, Suresh Giri, Sreelekshmy Mohandas, Anita Shete, Gajanan Sapkal, Deepak Y. Patil, Ayan Dey, Harish Chandra, Gururaj Deshpande, Nivedita Gupta, Priya Abraham, Himanshu Kaushal, Rima R. Sahay, Anuradha

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### **Analysis of long noncoding RNAs and messenger RNAs expression profiles in the hearts of mice with acute viral myocarditis**

Yimin Xue, Jun Ke, Jiuyun Zhang, Mingguang Chen, Lijuan Zeng, Qiaolian Fan, Chunfu Zheng, Feng Chen

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### **Complete genome analyses of G12P[8] rotavirus strains from hospitalized children in Surabaya, Indonesia, 2017–2018**

Laura Navika Yamani, Takako Utsumi, Yen Hai Doan, Yoshiki Fujii, Zayyin Dinana, Rury Mega Wahyuni, Emily Gunawan, Soegeng Soegijanto, [Alpha Fardah Athiyah](#), Subijanto Marto Sudarmo, Reza Gunadi Ranuh, Andy Darma, Soetjipto, Juniastuti, Rheza Gandhi Bawono, Chieko Matsui, Lin Deng, Takayuki Abe, Hiroyuki Shimizu, Koji Ishii, Kazuhiko Katayama, Maria Inge Lusida, Ikuo Shoji

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### **Machine learning-driven blood transcriptome-based discovery of SARS-CoV-2 specific severity biomarkers**

Pandikannan Krishnamoorthy, Athira S Raj, Himanshu Kumar

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### **Efficacy of serum apelin and galectin-3 as potential predictors of mortality in severe COVID-19 patients**

Nurcan Kırıcı Berber, Ayşegül Altıntop Geçkil, Nazife Özge Altan, Tuğba Raika Kiran, Önder Otlu, Mehmet Erdem, Erdal İn

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### **Inhibiting cardiac autophagy suppresses Zika virus replication**

Xin Ma, Yinnong Jia, Jing Yuan, Qiu-Ju Tang, Wen-Cong Gao, Guang-Feng Zhou, Ren-Hua Yang, Wei Pang, Chang-Bo Zheng

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### **How does SARS-CoV-2 infection impact on immunity, procession and treatment of pan cancers**

Nan Xiong, Qiangming Sun

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### **A decrease in the incidence of encephalitis in South Korea during the COVID-19 pandemic: A nationwide study between 2010 and 2021**

Se Hee Kim, Jee Yeon Baek, Minkyung Han, Myeongjee Lee, Sung Min Lim, Ji Young Lee, Ji-Man Kang, Inkyung Jung, Hoon-Chul Kang, Jong Gyun Ahn

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### **Colchicine and risk of hospitalization due to COVID-19: A population-based study**

María Sáenz-Aldea, Ángel Salgado-Barreira, Margarita Taracido Trunk, María Piñeiro-Lamas, María T. Herdeiro, Manuel Portela-Romero, Marc Saez, Adolfo Figueiras

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### **Development and validation of a deep learning model to diagnose COVID-19 using time-series heart rate values before the onset of symptoms**

Heewon Chung, Hoon Ko, Hooseok Lee, Dong Keon Yon, Won Hee Lee, Tae-Seong Kim, Kyung Won Kim, Jinseok Lee

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## Memory impairment among recovered COVID-19 patients: The prevalence and risk factors, a retrospective cohort study

Muayad A. Merza, Hind B. Almufty, Heewa A. Younis, Suzan O. Rasool, Shinah A. Mohammed

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## Integrative systems immunology uncovers molecular networks of the cell cycle that stratify COVID-19 severity

Caroline Aliane de Souza Prado, Dennyson Leandro M. Fonseca, Youvika Singh, Igor Salerno Filgueiras, Gabriela Crispim Baiocchi, Desirée Rodrigues Praça, Alexandre H. C. Marques, Raquel Costa Silva Dantas-Komatsu, Júlia N. Usuda, Paula Paccielli Freire, Ranieri Coelho Salgado, Sarah Maria da Silva Napoleao, Rodrigo Nalio Ramos, Vanderson Rocha, Guangyan Zhou, Rusan Catar, Guido Moll, Niels Olsen Saraiva Camara, Gustavo Cabral de Miranda, Vera Lúcia Garcia Calich, Lasse M. Giil, Neha Mishra, Florian Tran, Andre Ducati Luchessi, Helder I. Nakaya, Hans D. Ochs, Igor Jurisica, Lena F. Schimke, Otavio Cabral-Marques

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## Upregulation of PD-L1 by SARS-CoV-2 promotes immune evasion

Hsiang-Chi Huang, Shih-Han Wang, Guo-Chen Fang, Wen-Cheng Chou, Chun-Che Liao, Cheng-Pu Sun, Jia-Tsrong Jan, Hsiu-Hua Ma, Hui-Ying Ko, Yi-An Ko, Ming-Tsai Chiang, Jian-Jong Liang, Chun-Tse Kuo, Te-An Lee, Diego Morales-Scheihing, Chen-Yang Shen, Shih-Yu Chen, Louise D. McCullough, Lu Cui, Gerlinde Wernig, Mi-Hua Tao, Yi-Ling Lin, Yao-Ming Chang, Shu-Ping Wang, Yun-Ju Lai, Chia-Wei Li

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e28481 | First Published: 07 January 2023

[Abstract](#) | [Full text](#) | [PDF](#) | [References](#) | [Request permissions](#)

## Genetic analysis and biological characterization of H10N3 influenza A viruses isolated in China from 2014 to 2021

Yuancheng Zhang, Jianzhong Shi, Pengfei Cui, Yaping Zhang, Yuan Chen, Yujie Hou, Liling Liu, Yongping Jiang, Yuntao Guan, Hualan Chen, Huihui Kong, Guohua Deng

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### Importance

Avian influenza virus, which frequently jumps to humans and causes severe illness and death, poses a continuing threat to public health. Understanding the genesis and characteristics of avian influenza viruses will help prevent future human influenza pandemics. In this study, we provide evidence that the human-infecting H10N3 viruses are reassortants with internal genes from chicken H9N2 viruses and surface genes from duck viruses, suggesting a critical role for ducks in the generation of viruses with human-infecting potential. Our findings demonstrate that some H10N3 viruses exhibit higher affinity for human-type receptors than for avian-type receptors, and some can transmit via direct contact and/or respiratory droplets in the guinea pig model, suggesting the potential risk posed by H10N3 viruses.

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## Low prevalence of influenza viruses and predominance of A(H3N2) virus with respect to SARS-CoV-2 during the 2021–2022 season in Bulgaria

Neli Korsun, Ivelina Trifonova, Veselin Dobrinov, Iveta Madzharova, Iliyana Grigorova, Iva Christova

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[Abstract](#) | [Full text](#) | [PDF](#) | [References](#) | [Request permissions](#)

## Baricitinib or imatinib in hospitalized COVID-19 patients: Results from COVINIB, an exploratory randomized clinical trial

Alejandro Morales-Ortega, Ana Isabel Farfán-Sedano, Juan Víctor San Martín-López, Almudena Escribá-Bárcena, Beatriz Jaenes-Barrios, Elena Madroñal-Cerezo, Cristina Llarena-Barroso, Nieves Mesa-Plaza, Begoña Frutos-Pérez, José Manuel Ruiz-Giardín, Miguel Ángel Duarte-Millán, Sara Isabel Piedrabuena-García, Lorena Carpintero-García, Eduardo Canalejo-Castrillero, Belén Mora-Hernández, Carlos Javier García-Parra, Héctor Agustín Magro-García, Alicia Algaba-García, Belén Hernández-Muniesa, Berta Nasarre-López, Ana Ontañón-Nasarre, María Jesús Domínguez-García, Dulce Gómez-Santos, Santiago Prieto-Menchero, Jaime García de Tena, Fernando Bermejo, Mario García-Gil, Sonia Gonzalo-Pascua, David Bernal-Bello, the COVINIB Study Group investigators

e28495 | First Published: 13 January 2023

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## Isolation and characterization of mammalian orthoreovirus from bats in the United States

Liping Wang, Baoliang Zheng, Zhenyu Shen, Nirmalendu Deb Nath, Yonghai Li, Timothy Walsh, Yan Li, William J. Mitchell, Dongchang He, Jinhwa Lee, Susan Moore, Suxiang Tong, Shuping Zhang, Wenjun Ma

e28492 | First Published: 12 January 2023

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## Rapid detection of monkeypox virus by multiple cross displacement amplification combined with nanoparticle-based biosensor platform

Juan Zhou, Fei Xiao, Jin Fu, Nan Jia, Xiaolan Huang, Chunrong Sun, Chunyan Liu, Hui Huan, Yi Wang

e28479 | First Published: 07 January 2023

[Abstract](#) | [Full text](#) | [PDF](#) | [References](#) | [Request permissions](#)

## Single-cell transcriptomics dissects epithelial heterogeneity in HPV<sup>+</sup> cervical adenocarcinoma

Cong Wang, Lei Li, Fuhao Wang, Xia Li, Jujie Sun, Xiaohui Li, Tianyu Lei, Qingyu Huang, Guangyu Zhang, Hongqing Wang, Dapeng Li, Jue Jia, Chunyan Li, Feng Geng, Jinbo Yue, Chao Liu

e28480 | First Published: 07 January 2023

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## Characterization of cross-reactive monoclonal antibodies against SARS-CoV-1 and SARS-CoV-2: Implication for rational design and development of pan-sarbecovirus vaccines and neutralizing antibodies

Shibo Li, Jianbo Wu, Weiyu Jiang, Haiyan He, Yunjiao Zhou, Wei Wu, Yidan Gao, Minxiang Xie, Anqi Xia, Jiaying He, Qianqian Zhang, Yuru Han, Nan Wang, Guangqi Zhu, Qiuqing Wang, Zheen Zhang, Christian T. Mayer, Kang Wang, Xiangxi Wang, Junqing Wang, Zhenguo Chen, Shibo Jiang, Lei Sun, Rong Xia, Qiao Wang

e28440 | First Published: 27 December 2022

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## Real-world effectiveness of sotrovimab and remdesivir for early treatment of high-risk hospitalized COVID-19 patients: A propensity score adjusted retrospective cohort study

Lin Pin Koh, Siang Li Chua, Shawn Vasoo, Matthias Paul Han Sim Toh, Jeremy Nicholas Cutter, Puay Hoon Nah, Yee-Sin Leo, Jun Xin Tay, Barnaby Edward Young, David C. Lye, Sean W. X. Ong

e28460 | First Published: 05 January 2023

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## ACE2 PET to reveal the dynamic patterns of ACE2 recovery in an infection model with pseudocorona virus

Xiao Li, Wei Yin, Ao Li, Danni Li, Xiaolong Gao, Ruizhi Wang, Bin Cui, Shuang Qiu, Rou Li, Lina Jia, Changjing Zuo, Lan Zhang, Ming Li

e28470 | First Published: 06 January 2023

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## Establishment of a diverse head and neck squamous cancer cell bank using conditional reprogramming culture methods

Daniel Li, Carlos Thomas, Nitisha Shrivastava, Adam Gersten, Nicholas Gadsden, Nicolas Schlecht, Nicole Kawachi, Bradley A. Schiff, Richard V. Smith, Gregory Rosenblatt, Stelby Augustine, Evripidis Gavathiotis, Robert Burk, Michael B. Prystowsky, Chandan Guha, Vikas Mehta, Thomas J. Ow

e28388 | First Published: 08 December 2022

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## Omicron infection increases IgG binding to spike protein of predecessor variants

Gokulnath Mahalingam, Yogapriya Periyasami, Porkizhi Arjunan, Rajesh K. Subaschandrabose, Tamil V. Mathivanan, Roshlin S. Mathew, Ramya K. T. Devi, Prasanna S. Premkumar, Jayaprakash Muliylil, Alok Srivastava, Mahesh Moorthy, Srujan Marepally

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### **Head-to-head comparison of genotyping of human papillomavirus by GP5+/6+-PCR-based reverse dot blot hybridization assay and SPF10-PCR-based line probe assay**

Jian Yin, Siying Peng, Xinyue Li, Changning Zhang, Fangfang Hu, Wen Chen, Youlin Qiao

e28435 | First Published: 26 December 2022

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### **Efficacy and safety of nirmatrelvir/ritonavir (Paxlovid) for COVID-19: A rapid review and meta-analysis**

Behnam Amani, Bahman Amani

e28441 | First Published: 28 December 2022

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### **The pattern of cytokines expression and dynamic changes of renal function at 6 months in patients with Omicron COVID-19**

Lanbo Teng, Xinyuan Song, Miaomiao Zhang, Yingying Han, Ge Chang, Wenxiu Chang, Zhongyang Shen

e28477 | First Published: 07 January 2023

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### **A novel, ultrafast, ultrasensitive diagnosis platform for the detection of SARS-CoV-2 using restriction endonuclease-mediated reverse transcription multiple cross displacement amplification**

Junfei Huang, Xinggui Yang, Lijuan Ren, Weijia Jiang, Yan Huang, Ying Liu, Chunting Liu, Xu Chen, Shijun Li

e28444 | First Published: 29 December 2022

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### **The salivary and nasopharyngeal microbiomes are associated with SARS-CoV-2 infection and disease severity**

Josh G. Kim, Ai Zhang, Adriana M. Rauseo, Charles W. Goss, Philip A. Mudd, Jane A. O'Halloran, Leyao Wang

e28445 | First Published: 30 December 2022

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### **Dynamics of nosocomial SARS-CoV-2 transmissions: Facing the challenge of variants of concern in a Brazilian reference hospital**

Andressa Taíz Hoffmann, Mariana Soares da Silva, Juliana Schons Gularte, Alessandro Comaru Pasqualotto, José Luiz Proença Módena, Alana Witt Hansen, Claudio Marcel Berdún Stadnik, Teresa Cristina Teixeira Sukienik, Meriane Demoliner, Fágner Henrique Heldt, Micheli Filippi, Vyctoria Malayhka de Abreu Góes Pereira, Cristiani Gomes de Marques, Ionara Ines Kohler, Daniela Muller De Quevedo, Fernando Rosado Spilki

e28446 | First Published: 29 December 2022

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### **Surveillance, isolation and genomic characterization of *Pteropine orthoreovirus* of probable bat origin among patients with acute respiratory infection in Malaysia**

Kok Keng Tee, Po Qhuan Chan, Alson Mun-Khin Loh, Sarbhan Singh, Chee How Teo, Thevambiga Iyadorai, Jack Bee Chook, Kim Tien Ng, Yutaka Takebe, Kok Gan Chan, I-Ching Sam, Kenny Voon

e28520 | First Published: 24 January 2023

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### **Impact of nonalcoholic fatty liver disease status change on antiviral efficacy of nucleos(t)ide analogues in HBeAg-positive chronic hepatitis B**

Yanhua Tang, Rong Fan, Zhixian Lan, Qing Xie, Jiping Zhang, Xieer Liang, Hao Wang, Deming Tan, Jun Cheng, Shijun Chen, Qin Ning, Xuefan Bai, Min Xu, Xinyue Chen, Junqi Niu, Junping Shi, Hong Ren, Zhiliang Gao, Maorong Wang, Xiaoguang Dou, Jinlin Hou, Jian Sun

e28501 | First Published: 19 January 2023

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## Weekly symptom profiles of nonhospitalized individuals infected with SARS-CoV-2 during the Omicron outbreak in Hong Kong: A retrospective observational study from a telemedicine center

Jingyuan Luo, Jialing Zhang, Hiu To Tang, Hoi Ki Wong, Yanfang Ma, Duoli Xie, Bo Peng, Aiping Lyu, Chun Hoi Cheung, Zhaoxiang Bian

e28447 | First Published: 30 December 2022

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## Microglia innate immune response contributes to the antiviral defense and blood–CSF barrier function in human choroid plexus organoids during HSV-1 infection

Haowen Qiao, Yuanpu Chiu, Xinyan Liang, Shangzhou Xia, Mariam Ayrapetyan, Siqi Liu, Cuiling He, Ruocen Song, Jianxiong Zeng, Xiangxue Deng, Weiming Yuan, Zhen Zhao

e28472 | First Published: 06 January 2023

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## A vaccine delivery system promotes strong immune responses against SARS-CoV-2 variants

Zhiwei Lei, Leqing Zhu, Pan Pan, Zhihui Ruan, Yu Gu, Xichun Xia, Shengli Wang, Weiwei Ge, Yangrong Yao, Fazeng Luo, Heng Xiao, Jun Guo, Qiang Ding, Zhinan Yin, Yongkui Li, Zhen Luo, Qiwei Zhang, Xin Chen, Jianguo Wu

e28475 | First Published: 06 January 2023

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## Disparities in survival outcomes among Black patients with HPV-associated oropharyngeal cancer

Sujith Baliga, Darrion Mitchell, Vedat O. Yildiz, Emile Gogineni, David J. Konieczkowski, John Grecula, Dukagjin M. Blakaj, Xuefeng Liu, Mauricio E. Gamez

e28448 | First Published: 30 December 2022

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## Prophylactic tenofovir alafenamide for hepatitis B virus reactivation and reactivation-related hepatitis

Goki Suda, Masaru Baba, Yoshiya Yamamoto, Takuya Sho, Koji Ogawa, Megumi Kimura, Shunichi Hosoda, Sonoe Yoshida, Akinori Kubo, Qingjie Fu, Zijian Yang, Yoshimasa Tokuchi, Takashi Kitagataya, Osamu Maehara, Shunsuke Ohnishi, Ren Yamada, Masatsugu Ohara, Naoki Kawagishi, Mitsuteru Natsuzaka, Masato Nakai, Kenichi Morikawa, Ken Furuya, Kazuharu Suzuki, Takaaki Izumi, Takashi Meguro, Katsumi Terashita, Jun Ito, Tomoe Kobayashi, Izumi Tsunematsu, Naoya Sakamoto

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### Lay Summary

Hepatitis B virus (HBV) reactivation during antitumor or immunosuppressive therapy could be fatal. Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir with high efficacy and safety for hepatitis B infection. Nonetheless, there exist no prospective studies on the efficacy of TAF prophylaxis for the prevention of HBV reactivation. This prospective multicenter study is the first to show the high efficacy of TAF prophylaxis for the prevention of HBV reactivation.

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## RSV-CLASS —Clinical Assessment Severity Score: An easy-to-use clinical disease severity score for respiratory syncytial virus infection in hospitalized children

Julia Gsenger, Thomas Bruckner, Clara Marlene Ihling, Rebecca Marie Rehbein, Sarah Valerie Schnee, Johannes Hoos, Britta Manuel, Johannes Pfeil, Paul Schnitzler, Julia Tabatabai

e28541 | First Published: 02 February 2023

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## Usefulness of dried blood spot samples for monitoring hepatitis C treatment outcome and reinfection among people who inject drugs in a test-and-treat program

Anna Not, Verónica Saludes, Mont Gálvez, Anna Miralpeix, Antoni E. Bordoy, Noemí González, Sara González-Gómez, Laura Muntané, Juliana Reyes-Urueña, Xavier Majó, Joan Colom, Xavier Fornas, Sabela Lens, Elisa Martró

e28544 | First Published: 02 February 2023

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## Cross-sectional analysis reveals autoantibody signatures associated with COVID-19 severity

Gabriela C. Baiocchi, Aristo Vojdani, Avi Z. Rosenberg, Elroy Vojdani, Gilad Halpert, Yuri Ostrinski, Israel Zyskind, Igor S. Filgueiras, Lena F. Schimke, Alexandre H. C. Marques, Lasse M. Giil, Yael B. Lavi, Jonathan I. Silverberg, Jason Zimmerman, Dana A. Hill, Amanda Thornton, Myungjin Kim, Roberta De Vito, Dennyson L. M. Fonseca, Desireé R. Praça, Paula P. Freire, Niels O. S. Camara, Vera L. G. Calich, Carmen Scheibenbogen, Harald Heidecke, Miriam T. Lattin, Hans D. Ochs, Gabriela Riemekasten, Howard Amital, Yehuda Shoenfeld, Otavio Cabral-Marques

e28538 | First Published: February 2023

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## Local immune dysregulation and subsequent inflammatory response contribute to pulmonary edema caused by *Enterovirus* infection in mice

Tiantian Sun, Dong Li, Xinchun Dai, Caiyun Meng, Yi Li, Cheng Cheng, Wangquan Ji, Peiyu Zhu, Shuaiyin Chen, Haiyan Yang, Yuefei Jin, Weiguo Zhang, Guangcai Duan

e28454 | First Published: 04 January 2023

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## Association between trans fatty acids and COVID-19: A multivariate Mendelian randomization study

Xuxu Liu, Zhiwei Du, Jing Wang, Qiang Wang, Yi Zheng, Le Niu, Chenjun Hao, Dongbo Xue, Yingmei Zhang

e28455 | First Published: 04 January 2023

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## An integrated strategy to identify COVID-19 causal genes and characteristics represented by LRRC37A2

Zijun Zhu, Xinyu Chen, Chao Wang, Sainan Zhang, Rui Yu, Yubin Xie, Shuofeng Yuan, Liang Cheng, Lei Shi, Xue Zhang

e28585 | First Published: 16 February 2023

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## The effect of synbiotic adjunct therapy on clinical and paraclinical outcomes in hospitalized COVID-19 patients: A randomized placebo-controlled trial

Mahsa Vaezi, Sahar Ravanshad, Mina Akbari Rad, Hossein Zarrinfar, Mona Kabiri

e28463 | First Published: 05 January 2023

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## SHORT COMMUNICATIONS

### First report of coinfection and whole-genome sequencing of norovirus and sapovirus in an acute gastroenteritis patient from Pakistan

Massab Umair, Zaira Rehman, Syed Adnan Haider, Muhammad Usman, Muhammad Suleman Rana, Aamer Ikram, Muhammad Salman

e28458 | First Published: 04 January 2023

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### Risk stratification for cervical precancer and cancer by DH3-HPV partial genotyping and cytology in women attending cervical screening: A retrospective cohort study

Yunfeng Fu, Ying Li, Xiao Li, Xinyu Wang, Weiguo Lü

e28482 | First Published: 07 January 2023

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### Infection by SARS-CoV-2 with alternate frequencies of mRNA vaccine boosting

Jeffrey P. Townsend, Hayley B. Hassler, Alex Dornburg

e28461 | First Published: 05 January 2023

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### SARS-CoV-2 infection of kidney tissues from severe COVID-19 patients

e28566 | First Published: 09 February 2023

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### Whole-genome sequencing of hMPXV1 in five Italian cases confirms the occurrence of the predominant epidemic lineage

Diego Forni, Chiara Moltrasio, Manuela Sironi, Alessandra Mozzi, Eleonora Quattri, Luigia Venegoni, Marzia Zamprogno, Andrea Citterio, Mario Clerici, Angelo Valerio Marzano, Rachele Cagliani

e28493 | First Published: 12 January 2023

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### Significant neutralizing escapes of Omicron and its sublineages in SARS-CoV-2-infected individuals vaccinated with inactivated vaccines

Fan Shen, Cui-Xian Yang, Ying Lu, Mi Zhang, Ren-Rong Tian, Xing-Qi Dong, An-Qi Li, Yong-Tang Zheng, Wei Pang

e28516 | First Published: 21 January 2023

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### Clustered cases of human adenovirus types 4, 7, and 14 infections in US Department of Defense Beneficiaries during the 2018–2019 season

Adam R. Pollio, Anthony C. Fries, Yu Yang, Jerry J. Hughes, Christian K. Fung, Matthew A. Conte, Robert A. Kuschner, Natalie D. Collins, Elizabeth A. Macias, Jun Hang

e28571 | First Published: 10 February 2023

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## ERRATUM

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### Erratum

e28515 | First Published: 31 January 2023

**ⓘ This article corrects the following: >**

#### Comparison of secondary attack rate and viable virus shedding between patients with SARS-CoV-2 Delta and Omicron variants: A prospective cohort study

Sung-Woon Kang, Ji Yeun Kim, Heedo Park, So Yun Lim, Jeonghun Kim, Euijin Chang, Seongman Bae, Jiwon Jung, Min Jae Kim, Yong Pil Chong, Sang-Oh Lee, Sang-Ho Choi, Yang Soo Kim, Man-Seong Park, Sung-Han Kim

Volume 95, Issue 1, Journal of Medical Virology | First Published online: December 10, 2022

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## CORRIGENDUM

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### Corrigendum

e28581 | First Published: 22 February 2023

**ⓘ This article corrects the following: >**

#### Mpox diagnostics: Review of current and emerging technologies

Chuan Kok Lim, Jason Roberts, Michael Moso, Kwee Chin Liew, Mona L. Taouk, Eloise Williams, Thomas Tran, Eike Steinig, Leon Caly, Deborah Ann Williamson

Volume 95, Issue 1, Journal of Medical Virology | First Published online: January 3, 2023

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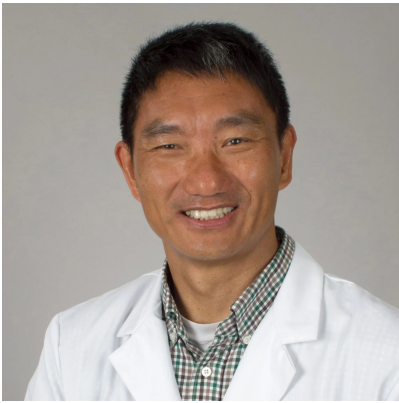
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### Shou-Jiang Gao

#### Editor-in-Chief

Dr. Gao received his Ph.D. in Microbiology and Health from the University of Bordeaux, Bordeaux (1993), France, and Postdoctoral training in Parasitology with Dr. John Burand in the University of Massachusetts at Amherst (1993-1994) and in Tumor Virology with Drs. Yuan Chang and Patrick Moore in Columbia University (1994-1997). He was a faculty member at the University of Texas Health

Science Center at San Antonio (1997-2001: Assistant Professor; 2002-2006: Associate Professor; 2007-2011: Professor; 2009-2011: HEB Endowed Chair for Cancer Research), then at the University of Southern California (2011-20018: Professor). He is currently a Professor in the Department of Microbiology and Molecular Genetics, University of Pittsburgh School of Medicine, and the Director of Cancer Virology Program of the University of Pittsburgh Medical Center (UPMC) Hillman Cancer Center and the Pittsburgh Foundation Endowed Chair for Cancer Therapy. Dr. Gao is an Elected Fellow of the American Academy of Microbiology (2014-). Dr. Gao is an expert in viral oncogenesis. His laboratory studies the oncogenic mechanisms of tumor viruses with current focus on Kaposi's sarcoma-associated herpesvirus (KSHV), which is associated with several AIDS-related malignancies including Kaposi's sarcoma, primary effusion lymphoma and a subset of multicentric Cattleman's disease. The research areas include mechanism of viral oncogenesis, metabolic reprogramming, cancer inflammation, cancer angiogenesis, epigenetic and epitranscriptomic reprogramming, functions of viral microRNAs, mechanism of persistent infection and reactivation, viral entry, trafficking and signaling, microbiome in cancer and infection, identification of therapeutic targets, development of therapeutic agents, and KSHV epidemiology.

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# Complete genome analyses of G12P[8] rotavirus strains from hospitalized children in Surabaya, Indonesia, 2017–2018

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## Abstract

Rotavirus A (RVA) is a major viral cause of acute gastroenteritis (AGE) worldwide. G12 RVA strains have emerged globally since 2007. There has been no report of the whole genome sequences of G12 RVAs in Indonesia. We performed the complete genome analysis by the next-generation sequencing of five G12 strains from hospitalized children with AGE in Surabaya from 2017 to 2018. All five G12 strains were Wa-like strains (G12-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1) and were clustered into lineage-III of VP7 gene phylogenetic tree. STM430 sample was observed as a mixed-infection between G12 and G1 strains: G12/G1-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1. A phylogenetic tree analysis revealed that all five Indonesian G12 strains (SOEP379, STM371, STM413, STM430, and STM433) were genetically close to each other in all 11 genome segments with 98.0%–100% nucleotide identities, except VP3 and NSP4 of STM430, suggesting that these strains have originated from a similar ancestral G12 RVA. The VP3 and NSP4 genome segments of STM430-G12P[8] were separated phylogenetically from those of the other four G12 strains,

probably due to intra-genotype reassortment between the G12 and G1 Wa-like strains. The change from G12P[6] lineage-II in 2007 to G12P[8] lineage-III 2017–2018 suggests the evolution and diversity of G12 RVAs in Indonesia over the past approximately 10 years.

#### KEYWORDS

complete genome, G12 strains, Indonesia, NGS, Rotavirus

## 1 | INTRODUCTION

Rotavirus A (RVA) is a major viral cause of acute gastroenteritis (AGE) worldwide, and RVAs continue to be the leading cause of diarrhea-related mortality among children <5 years of age which is estimated to be approximately 20% of the affected population. Low-income countries with no RVA vaccination programs are particularly affected by the RVA diarrhea.<sup>1,2</sup> The World Health Organization has been recommending the use of RVA vaccines in all national immunization programs since 2009. To date, 114 countries have introduced RVA vaccines.<sup>3</sup> Systematic review reports revealed vaccine effectiveness with reductions of  $\geq 32\%$  in diarrhea-associated morbidity and mortality in all countries. Although the introduction of vaccines has reduced the number of RVA-associated deaths, the effectiveness of licensed vaccines in low-income countries at 30%–40% lower than the effectiveness in high-income countries, is suboptimal<sup>4,5</sup> and showed that RVA gastroenteritis still results in >200 000 deaths annually.<sup>6</sup> These phenomenon remains incompletely understood.<sup>7,8</sup> In Asia, only a few countries have introduced the vaccine nationally or sub-nationally.<sup>9</sup> Indonesia has not yet implemented a RVA vaccine as a universal immunization program, but two RVA vaccines, Rotarix® (GSK) and RotaTeq® (Merck & Co.) have been commercially available in the private market in Indonesia since 2011. In Indonesia, diarrhea is the leading cause of child mortality, and approximately 38%–67% of hospitalized children in Indonesia have diarrhea due to RVA infection.<sup>10,11</sup> Indonesia is one of the countries with the greatest number of RVA deaths as a proportion of all global RVA deaths in children under 5 in 2017.<sup>12</sup>

RVA is a nonenveloped virus consisting of 11 gene segments of double-stranded RNA encoding six structural proteins (VP1, VP2, VP3, VP4, VP6, and VP7 genes) and five or six nonstructural proteins (NSP1, NSP2, NSP3, NSP4, and NSP5/NSP6).<sup>13</sup> The RVA genotypes are determined based on the nucleotide sequence identity in the open reading frame of each gene and are designated using a letter and a number. Two genes encoding VP7 (a glycoprotein) and VP4 (a protease-sensitive protein) are referred to as G and P types, respectively, and both proteins play crucial roles in recognition and neutralization by the immune system. To date, RVAs have been classified into 42G and 58P genotypes by the RVA Classification Working Group (<https://rega.kuleuven.be/cev/viralmetagenomics/virus-classification/rcwg>). Molecular epidemiological studies have identified the widespread circulation of various genotypes of RVAs,

showing that five G-genotypes, i.e., G1–G4 and G9 and three P-genotypes, i.e., P[4], P[6], and P[8] are commonly associated with human infection.<sup>14,15</sup>

G12 rotaviruses have received little attention until recently. Since 1998, a decade after their first detection in the Philippines, G12 strains have been detected in Asia, Europe, South America, and North America, suggesting their possible emergence worldwide.<sup>16</sup> G12 genotype was the sixth major human G-genotype.<sup>16,17</sup> There have been reports of outbreaks in parts of West Africa such as Nigeria with G12 RVA strains<sup>18,19</sup> and some other countries identified G12 RVA as a prevalent genotype.<sup>16,17</sup> The vast majority of G12 strains have been isolated in Asia and more specifically in Southeast Asia.<sup>16</sup> G12 RVA has a very large genetic diversity caused mainly by genetic reassortments.<sup>16,18</sup>

The geographical region may contribute to the variation of G12 strains isolated around the world. Four different combinations of the G12 genotype and a P-genotype have been detected: G12P[4], G12P[6], G12P[8], and G12P[9].<sup>16,17</sup> Thus far, G12 strains were clustered into three lineages: I, II, and III. The first G12 strain, L26 (G12P[4]), isolated from a diarrheic child in the Philippines in 1987, was classified into lineage-I. More than 10 years after the isolation of strain L26, the G12P[9] strain named T152 was isolated in Thailand and was clustered into lineage-II. Many G12 strains isolated in the 2000s were clustered into lineage-III.<sup>16</sup>

In Indonesia, the first detection of a G12 strain, G12P[6], was obtained from a 14-day-old febrile infant with diarrhea, vomiting, moderate dehydration and malnutrition who was brought to Sumber Waras Hospital in West Jakarta in December, 2007. The strain isolated from this patient's stool was genotyped by semi-nested reverse transcription-polymerase chain reaction (RT-PCR) targeting the VP7 and VP4 genes, which are two of the 11 segments in the RVA genome.<sup>20</sup> There has been no other reports about G12 RVA strains in Indonesia, and the whole genome sequence of G12 strains in Indonesia has not been reported.

A whole genome-based genotyping method using the analysis of all 11 gene segments has been used for RVA epidemiology, with classification into genogroups based on the overall genomic RNA homology. Three genogroups of human RVA have been defined: Wa-like, DS-1-like, and AU-1-like. Of these three constellations, the Wa-like strains are the most predominant followed by the DS-1-like strains, and the AU-1-like strains are the least numerous strains in humans globally.<sup>21</sup> It is urgently necessary to fully sequence and

characterize G12 RVA strains, as this information will contribute to our understanding of the evolutionary pattern and the diversity of emerging G12 strains. In this study, we performed a whole genome analysis of five G12 RVA strains detected in Indonesia in 2017–2018 by using the next-generation sequencing (NGS) technique.

## 2 | MATERIALS AND METHODS

### 2.1 | Specimens

During the RVA surveillance in 2017–2018 among hospitalized children with AGE in Surabaya, Indonesia, 67 RVA-positive stool samples were detected by an immunochromatography assay and RT-PCR. We used these RVA-positive samples for the whole genome analyses by NGS. The most commonly observed RVA genotypes were G1 and G3, and 62 of the 67 samples were excluded from this study; G12 RVA strains were detected in only five samples, all of which were included in the present investigation.

We thus analyzed the whole genome sequences of G12 RVA strains isolated from five stool specimens of  $\leq 5$ -year-old children with AGE treated as inpatients at Dr. Soetomo hospital and Soerya hospital in Surabaya, East Java, Indonesia in 2017–2018. SOEP379 was isolated from an inpatient child treated at Soerya hospital, and STM371, STM413, STM430, and STM433 were isolated from children treated at Dr. Soetomo hospital. AGE was defined as the occurrence of three times looser than normal stools during a 24-h period. This study was approved by the Research Ethics Board of both hospitals, Universitas Airlangga (ethics approval number 2054/UN3.14/LT/2015) in Indonesia and Kobe University (ethics approval number 1857) in Japan. Written informed consent was obtained from the children's parents or guardians.

### 2.2 | Isolation of RNA virus and RT-PCR genotyping

Stool specimens were 10-fold diluted with phosphate-buffered saline (PBS; pH 7.4) and clarified by centrifugation at 10 000g for 10 min. Aliquots of all of the samples were then stored at  $-80^{\circ}\text{C}$  before use. Viral RNA was extracted using Trizol LS Reagent (Life Technologies). In brief, 80  $\mu\text{l}$  of the aliquot of a stool suspension in PBS was mixed with 240  $\mu\text{l}$  of Trizol LS reagent and incubated for 5 min at room temperature. Then, 320  $\mu\text{l}$  of 100% ethanol was added to the mixture. The mixture was placed into a Zymo-Spin IIC column (Zymo Research) and was centrifugated at 12 000g for 1 min, and washed with the prewash buffer and the wash buffer following the manufacturer's instructions. The viral RNAs were eluted with DNase/RNase-free water and used for RT-PCR genotyping and the whole genome analysis by NGS.

Viral extracted were subjected to genotyping in the VP7 (G typing) and VP4 genes (P typing) by multiplex RT-PCR. The VP7 and VP4 primer sets used had been previously described.<sup>22</sup> In particular, the VP7 primer set allowed us to correctly identify equine-like G3

among the other epidemic strains (G1, G2, typical human G3, G4, G8, G9, and G12).<sup>23</sup> The RNA samples were initially incubated at  $65^{\circ}\text{C}$  for 5 min with the first PCR primers. Subsequently, reverse transcription reaction was performed at  $45^{\circ}\text{C}$  for 10 min and at  $94^{\circ}\text{C}$  for 2 min, followed by 40 cycles of amplification (at  $98^{\circ}\text{C}$  for 10 s, at  $50^{\circ}\text{C}$  for 15 s, and at  $68^{\circ}\text{C}$  for 40 s), with a final extension at  $68^{\circ}\text{C}$  for 3 min. A total of 1  $\mu\text{l}$  of diluted (50-fold) first PCR products was then used for a second PCR. The initial denaturation step was conducted at  $98^{\circ}\text{C}$  for 10 min, followed by 20 cycles of amplification (at  $98^{\circ}\text{C}$  for 10 s, at  $50^{\circ}\text{C}$  for 15 s, and at  $68^{\circ}\text{C}$  for 60 s), with a final extension at  $68^{\circ}\text{C}$  for 3 min. Both negative and positive controls were included in each experiment. Then, RT-PCR products were run in the agarose gel electrophoresis and D1000 ScreenTape assay on 4150 TapeStation (Agilent Technologies) was performed to visualize the size of PCR products.

### 2.3 | Complementary DNA (cDNA) library building and Illumina Miseq sequencing for NGS analysis

The preparation of the cDNA library and the Illumina Miseq sequencing were performed as previously described.<sup>24,25</sup> Briefly, a 200-bp fragment library ligated with bar-coded adapters was constructed for individual strains using an NEBNext Ultra RNA library Prep Kit for Illumina ver. 1.2 (New England Biolabs) according to the manufacturer's instructions. Library purification was performed using Agencourt AMPure XP magnetic beads (Beckman Coulter). The quality of the purified DNA libraries was assessed on a MultiNa MCE-202 bioanalyzer (Shimadzu Corporation). Nucleotide sequencing was performed on an Illumina Miseq sequencer (Illumina) using the Miseq Reagent Kit ver. 2 (Illumina) to generate 151 paired-end reads.

### 2.4 | Nucleotide analysis and determination of RVA genotypes detected by NGS analysis

The sequence data were analyzed and assembled in the CLC Genomics Workbench Software ver. 7.0.3 (CLC Bio). A de novo assembly was carried out for all samples and the resulting contigs were identified using the Nucleotide Basic Local Alignment Search Tool (NCBI BLAST). The mixed infection between RVAs was defined as when two or more sequences were present in the same genome segment and they were of the same or different genotypes. The different titers of RVA genomic RNA extracted from the stool specimen will reflect the number of copies in the library, and therefore, the number of reads obtained for the genes of each strain. Thus, genome constellation of each RVA strain in mixed infection sample was defined as all sequences for 11 genome segments have a similar rate between total read count and length of obtained sequences.

The genotype of each of 11 gene segments of G12P[8] strains were determined using the online database Virus pathogen Database and Analysis Resource (ViPR).<sup>23</sup> The sequence results were deposited in the DDBJ/GenBank database with accession numbers LC581220 to LC581275.



## 2.5 | Phylogenetic tree analyses

Sequence comparisons were carried out with the references retrieved from GenBank. Alignment between the study and reference strains was performed using a Multiple Sequence Comparison by Log Expectation alignment.<sup>26</sup> Phylogenetic trees were constructed in MEGA version 10.0 software using Maximum likelihood method.<sup>27</sup> The best substitution models were selected based on the corrected Akaike information criterion value as implemented in MEGA10. Models used in this study were Tamura 3-parameter (T92)+G+I (VP7, NSP3, NSP4, and NSP5), (T92)+G+I (NSP2), Tamura-Nei (TN93)+G+I (VP1 and VP3), General Time Reversible (GTR)+G+I (VP4, VP2, and NSP1). The reliability of the branching order was estimated from 1000 bootstrap replicates. Lineages of G12 RVA strains were assigned according to the literature.<sup>16,28</sup>

## 3 | RESULTS

### 3.1 | Genotype constellation of Indonesian G12 strains

Five G12 RVA strains isolated from stool samples of pediatric patients with AGE were used: SOEP379, STM371, STM413, STM430, and STM433. The patients were 6–24 months old (average 12.6 months old), consisting of two boys and three girls. The clinical

symptoms of the patients were diarrhea (5/5, 100%), watery diarrhea (1/5, 20%), vomiting (2/5, 40%), fever (2/5, 40%), abdominal pain (1/5, 20%), some dehydration (3/5, 60%), and severe dehydration (1/5, 20%). We analyzed the whole genome of all five strains by NGS. The open reading frames of the 11 genome segments of SOEP379, STM371, STM413, STM430, and STM433 strains were successfully determined using the Illumina MiSeq technology. The genotype constellation of all five strains revealed to be G12-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1, i.e., typical Wa-like strains. Of these, STM430 sample was observed as mixed-infection sample between G12 and G1 strains with two genome constellations: G12-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1 and G11-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1. No reassortment event with inter-genogroups or inter-species of RVA strains was detected (Table 1).

### 3.2 | Phylogenetic tree analysis

The analysis demonstrated that all of the Indonesian G12 strains have a close relationship with each other, as depicted by the single clade in the phylogenetic tree of VP7 gene (Figure 1). They were clustered into lineage-III. The VP7 gene of these strains were closely associated with the VP7 gene of strain RVA/Human-wt/USA/2013774166/2013/G12P8 and shared 99.14%–99.24% nucleotide identity (Table 2). In the phylogenetic tree of VP7 genes, we also identified the mixed-genotype strain with RVA G1 (STM430-G1P[8]), which

**TABLE 1** RVA genotype constellations of five human G12 RVA study strains compared to the published human G12 RVA strains

G12 strain	Year	Genogroup	VP7 (Lineage)	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5	Reference
L26	1987	DS-1-like	G12 (I)	P[4]	I2	R2	C2	M1/M2	A2	N1	T2	E2	H1	Previous study <sup>16</sup>
T152	1998	AU-1-like	G12 (II)	P[9]	I3	R3	C3	M3	A12	N3	T3	E3	H6	
RV161-00	2000–2002	DS-1-like	G12 (III)	P[6]	I2	R2	C2	M2	A2	N2	T2	E1	H2	
RV176-00	2000–2002	DS-1-like	G12 (III)	P[6]	I2	R2	C2	M2	A2	N2	T2	E6	H2	
N26-02	2000–2002	DS-1-like	G12 (III)	P[6]	I2	R2	C2	M2	A2	N1	T2	E6	H2	
Dhaka25-02	2002–2005	Wa-like	G12 (III)	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1	
Dhaka12-03	2002–2005	Wa-like	G12 (III)	P[6]	I1	R1	C1	M1	A1	N1	T1	E1	H1	
Mattlab13-03	2002–2005	Wa-like	G12 (III)	P[6]	I1	R1	C1	M1	A1	N1	T2	E1	H1	
SOEP379-18	2017–2018	Wa-like	G12 (III)	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1	
STM371-17	2017–2018	Wa-like	G12 (III)	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1	
STM413-17	2017–2018	Wa-like	G12 (III)	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1	Present study
STM433-17	2017–2018	Wa-like	G12 (III)	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1	
STM430-17	2017–2018	Wa-like	G1/G12 (III)	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1	

Note: The Wa-, DS-1-, and AU-1-like genogroups were assigned to human strains if at least seven gene segments belonged to the Wa-, DS-1-, and AU-1-like genotype, respectively. Colors were added to visualize patterns or gene constellations. Green: Wa-like, red: DS-1-like, and yellow: AU-like gene segments. Gray: Subtype 4A, and blue: RVA gene from animals. \*Green is Wa-like strain. \*Red is DS-1-like strain. \*Yellow is AU-1-like strain. \*Gray is an ST3-like strain. \*Blue is a RVA gene from an animal.

Abbreviation: Rotavirus A.

was clustered together with RVA/Human-wt/IDN/STM457/2018/G1P[8] from Indonesia and near RVA/Human-wt/IND/RV1326/2013/G1 from India (Figure 1).

The VP4 genes of all five G12 strains were genotyped as P[8] (Figure 2). On the phylogenetic tree, all Indonesian G12 strains clustered closely to RVA/Human-wt/BGD/Bang-065/2008/G9P8 in VP4 gene and shared 99.08%–99.35% nucleotide identity (Table 2). STM430-G1 strain was also genotyped as P[8] but grouped as a different branch from the other G12 strains; it was found to be closely related to two strains of G1P[8] isolated from Indonesia, RVA/Human-wt/IDN/STM453/2018/G1P[8]. In addition, type P[8] of strain STM430-G1 is also phylogenetically close to RVA/Human-wt/JPN/Tokyo17-21/2017/G3P8 (Figure 2). The genetic backbone of all samples was Wa-like strain (Table 1 and Figure 2). The results of the phylogenetic analysis of the VP6, VP1–VP3, and NSP1–NSP5 genes of the five study strains are illustrated in Figures S1–S9.

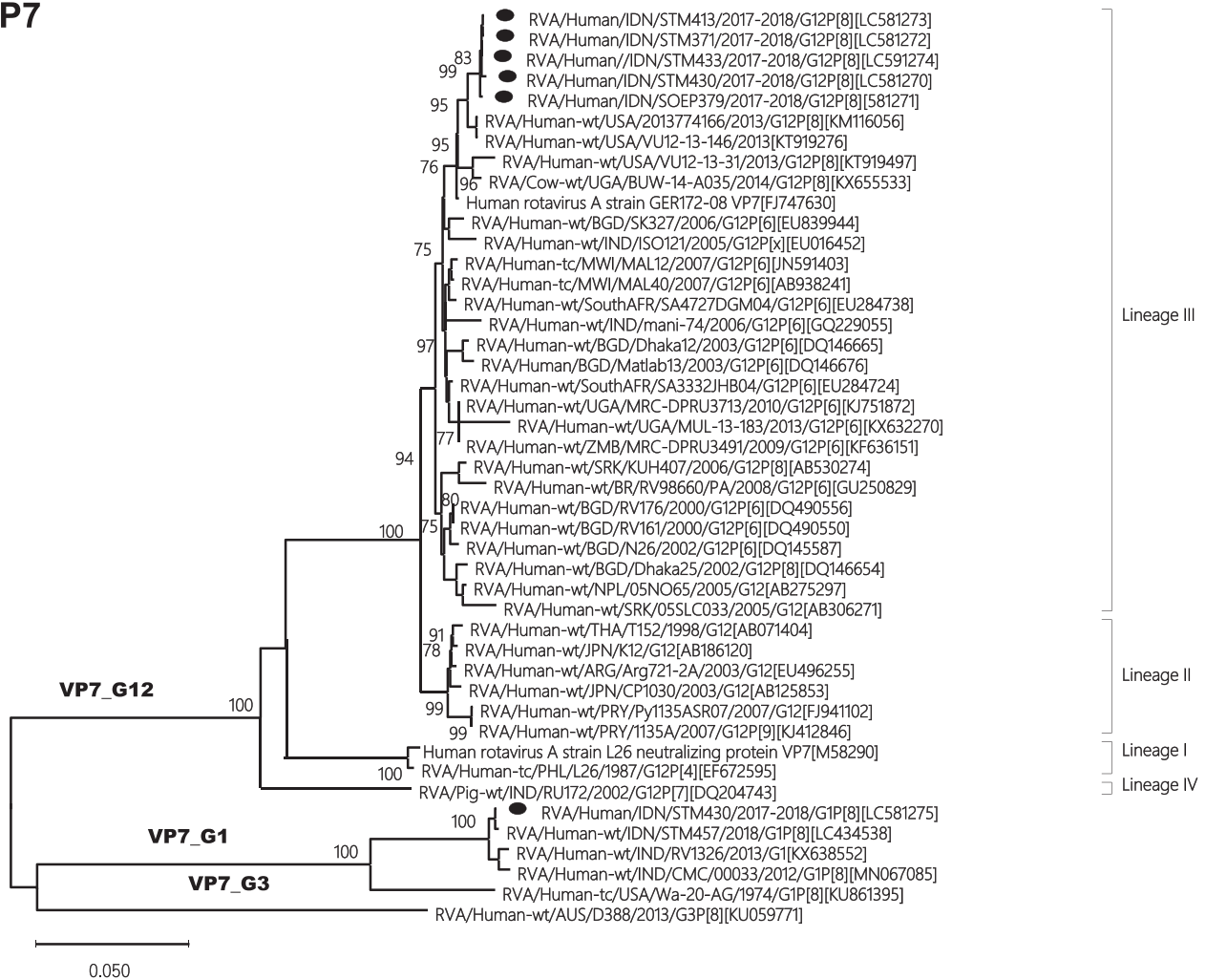
Five Indonesian G12 strains were closely related to each other in all 11 genome segments with 98.0%–100% nucleotide identities,

except VP3, and NPS4 gene of STM430-G12 strain (Figures 1 and 2, Figures S1–S9). The VP3 and NSP4 genes of STM430-G12 strain were separated into a different clade from the four other G12 study strains and clustered with other Indonesian strains RVA G1P[8] (RVA/Human-wt/IDN/STM387/2017/G1P8; RVA/Human-wt/IDN/STM453/2018/G1P8 or RVA/Human-wt/IDN/STM457/2018/G1P8) as described in the phylogenetic tree.

The VP4, VP6, VP1–VP3, and NSP1–NSP3 genes of all these Indonesian G12 strains, except VP3 and NSP4 of STM430-G12, were clustered with the closest reference G12 strains outside Indonesia, including strains from Bangladesh, Hungary, United States, Thailand, and Slovakia (Figures 1 and 2, Figures S1–S9). Interestingly, NSP4 genes in all five study strains were closest to RVA/Cow-wt/UGA/BUW-14-A035/2014/G12P8 isolated from a cow (i.e., a strain transmitted from a human to a cow) in Uganda (Figure S8).

The nucleotide sequence identities for the 11 genes between samples and closest references analyzed by NCBI homology BLAST are shown in Table 2. Within samples, some study strains exhibited

## VP7



**FIGURE 1** Phylogenetic tree analysis of VP7 genes for G12 RVA strains detected in five samples collected in Surabaya, Indonesia. *Black inverted triangles and Bullets*: The RVA strains sequenced in this study. The reference strains obtained from the GenBank database are represented by the accession number, strain name, country, and year of isolation. Scale bar: 0.050 substitutions per nucleotide. RVA, Rotavirus A

**TABLE 2** Nucleotide sequence identity between G12 RVA genes obtained from Illumina MiSeq sequencing and the closest strains isolated from references based on NCBI homology BLAST

Gene	Accession no.	Genotype	Samples	Closest strain of NCBI homology (% nt identity)	Gene	Accession no.	Genotype	Samples	Closest strain of NCBI homology (% nt identity)
VP7	LC581270	G12P[8]	STM430	99.14% RVA/Human-wt/USA/	NSP1	LC721867	G12P[8]	STM430	99.45% Hungary human strain ERN5009 isolated 2012
	LC581271	SOEP379	SOEP379	2013774166/2013/G12P[8]		LC581221	SOEP379	99.38%	
	LC581272	STM371	STM371			LC581222	STM371	99.52%	
	LC581273	STM413	STM413			LC581223	STM413	99.59%	
	LC581274	STM433	STM433			LC581224	STM433	99.52%	
LC581275	G1P[8]	STM430	99.81% RVA/Human-wt/IDN/STM457/2018/G1P[8]	LC722500	G1P[8]	STM430	99.60% RVA/Human-wt/IDN/STM457/2018/G1P[8]		
VP4	LC721862	G12P[8]	STM430	99.22% RVA/Human-wt/BGD/Bang-	NSP2	LC721868	G12P[8]	STM430	98.80% RVA/Human-wt/USA/2013774165/2013/
	LC581261	SOEP379	SOEP379	065/2008/G9P[8]		LC581226	SOEP379	98.84% G12P[8]	
	LC581262	STM371	STM371			LC581227	STM371	98.88%	
	LC581263	STM413	STM413			LC581228	STM413	98.94%	
	LC721864	STM433	STM433			LC581229	STM433	98.94%	
LC722498	G1P[8]	STM430	99.83% RVA/Human-wt/IDN/STM457/2017/G3P[8]	LC722501	G1P[8]	STM430	100% RVA/Human-wt/IDN/STM387/2017/G1P8 and RVA/Human-wt/IDN/STM453/2017/G1P[8]		
VP6	LC721863	G12P[8]	STM430	99.76% RVA/human/SVK/2451/11	NSP3	LC721869	G12P[8]	STM430	98.93% RVA/Human-wt/THA/DBM2018-111/2018/
	LC581266	SOEP379	SOEP379			LC581231	SOEP379	98.77% G9P[8]	
	LC581267	STM371	STM371			LC581232	STM371	99.28%	
	LC581268	STM413	STM413			LC581233	STM413	98.88%	
	LC581269	STM433	STM433			LC581234	STM433	98.71%	
LC722499	G1P[8]	STM430	99.77% MN304727.1 RVA/Human-wt/NGR/2017	LC722502	G1P[8]	STM430	99.91% RVA/Human-wt/IDN/STM457/2017/G1P[8]		
VP1	LC721864	G12P[8]	STM430	99.25% RVA/Human-wt/USA/VU12-	NSP4	LC721870	G12P[8]	STM430	99.86% RVA/Human-wt/IDN/STM457/2018/G1P[8]
	LC581246	SOEP379	SOEP379	13-39/2013/G12P[8]		LC581236	(like G1)	99.46% RVA/Cow-wt/UGA/BUW-14-A035/2014/	
	LC581247	STM371	STM371			LC581237	SOEP379	99.47% G12P[8]	
	LC581248	STM413	STM413			LC581238	STM371	99.31%	
	LC581249	STM433	STM433			LC581239	STM413	99.18%	
LC722495	G1P[8]	STM430	99.88% RVA/Human-wt/IDN/STM453/2018/G1P[8]	LC722503	G1P[8]	STM430	99.44% RVA/Cow-wt/UGA/BUW-14-A035/2014/G12P8 (like G12)		
VP2	LC721865	G12P[8]	STM430	99.10% RVA/Human-wt/BGD/Bang-	NSP5	LC722504	G12P[8]	STM430	99.39% RVA/Human-tc/USA/DC5685-40-AG/1991/
	LC581251	SOEP379	SOEP379	015/2008/G12P[6]		LC581241	SOEP379	99.54% G1P[8]	
	LC581252	STM371	STM371			LC581242	STM371	99.52%	
	LC581253	STM413	STM413			LC581243	STM413	99.38%	
	LC581254	STM433	STM433			LC581244	STM433	99.54%	
LC722496	G1P[8]	STM430	99.89% RVA/Human-wt/IDN/STM453/2018/G1P8	LC721871	G1P[8]	STM430	100% RVA/Human-wt/IDN/STM457/2018/G1P[8]		

TABLE 2 (Continued)

Gene	Accession no.	Genotype	Samples	Closest strain of NCBI homology (% nt identity)	Gene	Accession no.	Genotype	Samples	Closest strain of NCBI homology (% nt identity)
VP3	LC721866	G12P[8]	STM430	99.81% RVA/Human-wt/IDN/STM387/					
	LC581256		(like G1)	98.44% 2018/G1P[8]					
	LC581257		SOEP379	98.33% RVA/Human-wt/USA/VU08-					
	LC581258		STM371	98.48% 09-6/2008/G12P[8]					
	LC581259		STM431	98.48%					
			STM433						
	LC722497	G1P[8]	STM430	97.59% RVA/Human-wt/USA/VU08-					
			(like G12)	09-6/2008/G12P[8]					

Abbreviation: RVA, Rotavirus A.

100% similarity in several genes; for example, STM413 and STM433 in VP7 gene, as well as STM371 and SOEP379 in NSP4 gene (data not shown). A homology analysis using NCBI BLAST showed no evidence of inter-species reassortment events in any of the gene segments. Nevertheless, some animal strains were included in the phylogenetic tree of several genes because they are highly related to those of human RVAs and have homology with the study strains, suggesting that human RVA strains were also potentially transmitted to an animal and vice versa. The RVA strains isolated from animals that were observed in the present phylogenetic tree were RVA/Cow-wt/UGA/BUW-14-A035/2014/G12P in VP6, VP7, NSP1, and NSP4 genes (Figure 1, Figures S1, S5, and S8), RVA strain Rat-wt/ITA/Rat14/2015/G3P3 in VP6 (Figure S1), Porcine RV NSP3 (NS34) messenger RNA (strain PRICE) in NSP3 (Figure S7), RVA/Cow/B85/MP/India/2008 in NSP4 (Figure S8), and RVA/Donkey-wt/ZAF/MRC-DPRU1967/XXXX/GXPX in NSP5 (Figure S9). Their nucleotide sequence similarity compared to the study strains were around 96.9%–99.6%.

### 3.3 | Confirmation of mixed infection in STM430 sample

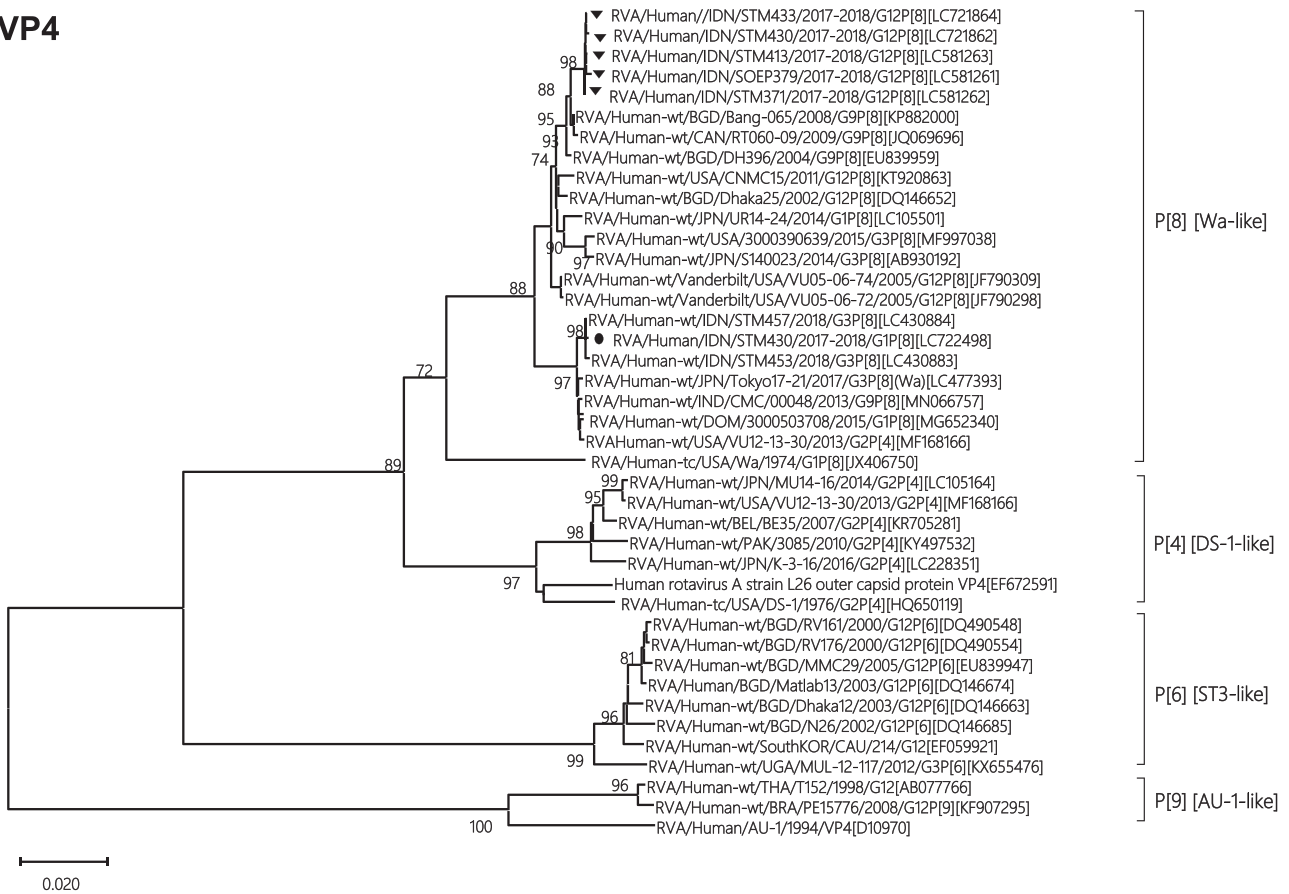
To confirm mixed infection for STM430 sample, the RNA was re-extracted from original clinical sample. RVA VP7 genotyping using the semi-nested multiplex PCR<sup>23</sup> were performed for both 1st and 2nd extracted RNA of STM430 together with other G1 (STM387) and G12 (STM413) samples. The size of PCR products was determined by D1000 ScreenTape assay on 4150 TapeStation (Agilent Technologies). The result revealed that all G12 samples contain 264 bp-band of G12 RVA. However, both 1st and 2nd STM430 samples contain two bands, 264 bp-band of G12 RVA and 636 bp-band of G1 RVA, indicating mixed infection of G12 RVA and G1 RVA (Figure 3).

## 4 | DISCUSSION

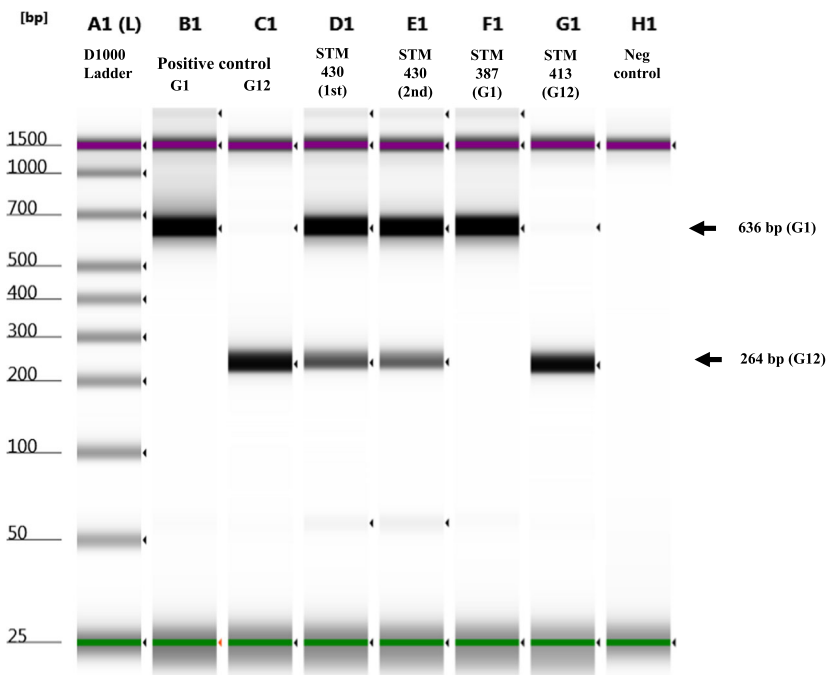
By using RT-PCR Genotyping and NGS analysis, we identified G12 RVAs as mono-infection in four samples (STM371, STM431, STM433, and SOEP379) and a co-infection of G12/G1 mixed-genotype in one sample (STM430). All strains were P[8] and showed a Wa-like genotype constellation, G12-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1. The single sample with the G12/G1 mixed-infection, exhibited two genotype constellations: G12-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1 and G1-P[8]-I1-R1-C1-M1-A1-N1-T1-E1-H1.

In Indonesia, the RVA genotypes G1P[8] and G3P[8] human strains are prevalent.<sup>22,29,30</sup> This may suggest co-infection between G1P[8]/G3P[8] and other G-types, such as the G12 isolated in this study. The finding of mixed-genotypes in this study showed that the NGS method is not only useful for whole genome-based analyses, but can also reveal the possibility of the occurrence of multiple isolates/strains/species. Other than, NGS analysis can also prove that there is

VP4



**FIGURE 2** Phylogenetic tree analysis of VP4 genes detected in five samples collected in Surabaya, Indonesia. *Black inverted triangles and Bullets*: The G12 and G1 RVA strains sequenced in this study, respectively. The reference strains obtained from the GenBank database are represented by the accession number, strain name, country, and year of isolation. Scale bar: 0.020 substitutions per nucleotide. RVA, Rotavirus A.



**FIGURE 3** The VP7 genotyping of STM430. To confirm the mixed infection for STM430 sample, the RNA was re-extracted from original clinical sample. RVA genotyping using the semi-nested multiplex PCR were performed for both 1st and 2nd extracted RNA of STM430 together with other G1 (STM387) and G12 (STM413) samples. The size of PCR products was determined by D1000 ScreenTape assay on 4150 TapeStation (Agilent Technologies). RVA, Rotavirus A.

no contamination on RT-PCR Genotyping results with more than one band in the gel image of electrophoresis.

The RVA strains with rare or uncommon G/P types have been detected after the introduction of RVA vaccine and became dominant genotypes. It was reported that the emergence of G12P[8] RVA as a predominant genotype was newly observed in countries using RotaTeq,<sup>31,32</sup> whereas the dominance of G2P[4] and equine-like G3P[8] was found in countries using Rotarix.<sup>33,34</sup> These findings were obtained in countries with high vaccine coverage and effectiveness. However, emerging of previously rare or novel genotypes was observed in the vaccine era, indicating that the widespread vaccine use may accelerate strain diversities.<sup>35</sup> The RVA strains with new genotypes have also been found in countries with low coverage or no vaccination programs.<sup>36,37</sup>

Indonesia has not yet implemented a RVA vaccine national program. The use of Rotarix and RotaTeq in the private market at a relatively high price would have very limited coverage. We reported that uncommon equine-like G3 RVA strains were predominantly spread in Indonesia.<sup>22,24</sup> An isolate of an uncommon G12 RVA strain was firstly identified in Indonesia in December 2007 and was genotyped as G12P[6],<sup>20</sup> but there was no subsequent report about G12 RVA detection in Indonesia until 2016. During the RVA surveillance in 2017–2018, we detected five G12 RVA strains from hospitalized children. In the present study, we conducted a complete molecular characterization of these five G12 RVA Indonesian strains by NGS.

With the present phylogenetic analyses using the full-genome sequence of the 11 gene segments, we obtained direct evidence of the five strains' relatedness to other strains, even within the same genotype. The shifting of RVA genotypes was demonstrated by the difference in VP7 gene of G12 RVA between strain detected in 2007 classified in lineage-II and the present study strains isolated in 2017–2018, classified as lineage-III. The findings suggest an evolution of RVA genes may occur after  $\geq 10$  years, particularly regarding changes in VP4 gene and the lineage of VP7. The majority of RNA viruses have been reported to have an evolutionary rate of between  $1.0 \times 10^{-3}$  to  $1.0 \times 10^{-6}$  substitutions/site/year.<sup>38</sup> The evolutionary rate of the African G12 RVA sequences was  $1.678 \times 10^{-3}$ , (95% highest posterior density,  $1.201 \times 10^{-3}$  to  $2.198 \times 10^{-3}$ ) substitutions/site/year.<sup>39</sup>

The nucleotide sequence divergence between lineage-II and lineage-III ranges from 2.6% to 3.2%.<sup>16</sup> However, lineage-II is a minority cluster when compared with lineage-III. G12 RVA lineage-I includes G12 strains from Japan, Argentina, Thailand, and Paraguay, whereas G12 RVA lineage-II consists of strains from the United States, India, Bangladesh, Germany, Uganda, and South Africa.<sup>16,20</sup> Hence, it was also suggested that the population mobility may contribute to genotype distribution.

The lineage-III G12 RVA strains in VP7 gene isolated in Indonesia were closely related to the United States strains, indicating that they might have originated in the United States. Indeed, each of the 11 genes of RVAs analyzed in this study showed the closest references from United States, Bangladesh, and Hungary (Table 2). This finding

suggests that RVAs have genetically diverse population of segmented double-stranded RNA viruses due to the genomic reassortment ability between human strains or inter-species with animal strains.<sup>40</sup> The RVAs strains might be transported across the globe by the increasing mobility of humans and animals. Examples are seen in the RVA genome in the Belgian strain B4633-03, which was nearly identical to the Dhaka25-02 strain and the United Kingdom strain MV404-02, which was closely related to the Dhaka12-03 strain.<sup>16</sup> We compared our five study strains to other G12 strains that are Wa-, DS-1-, AU-1-, and ST3-like strains observed in Asian countries, such as the Philippines, Thailand, and Bangladesh (Table 1); the results indicate that all five study strains belong to Wa-like genogroups without reassortment with inter-genogroups or inter-species.

The branch topology of the equivalent segments from all five Indonesian G12P[8] strains in this study fell within the same monophyletic lineage for all segments, except VP3 and NSP4 of STM430/G12P[8] strain. Clustering within same monophyletic lineage indicate that these G12 strains may have originated from the same ancestor. G12P[8] virus seems to be undergoing further intra-genotype reassortment with G1P[8] virus in a mixed infection STM430 sample. The reassortment events have occurred in its VP3, and NSP4 genes (proved by average coverage in NGS results almost similar to other genes of STM430 G12). However, it is possible that the reassortments also are undergoing in the VP2, NSP2, NSP3, and NSP5 genes (data not shown). In the future, we will conduct other experiments to confirm the undergoing reassortment events in the RVA mixed infection samples. RVA G1P[8] was also found to be predominant in Indonesia.<sup>22</sup> Circulating RVA mixed-genotypes may thus contribute to intra-genogroups events. Our present findings revealed that gene segments of STM430 were closely related to those of RVA G1 strains that we previously isolated in Indonesia.<sup>22</sup> No reassortment for inter-genogroups was observed, even though an equine-like G3P[8]/[6] DS-1-like RVA strain was predominant at a hospital in the suburbs of Surabaya in 2015–2018.<sup>22</sup>

The NSP4 gene of all five G12 strains isolated in this study was closest to RVA/Cow-wt/UGA/BUW-14-A035/2014/G12P which is isolated from domestic animals in Uganda and is human-to-animal RVA transmission.<sup>41</sup> This phenomenon suggests that NSP4 gene reassortment event easily occurs between human and animal strains. Importantly, there is no human possessing an animal strain. Our present findings demonstrate that the genotype constellation of G12 RVA strains are similar. This may be because only a few G12 strains were detected in the study; the further isolation of G12 RVAs throughout Indonesia is necessary.

The detection of G12P[8] RVA has also increased recently in countries with and without high vaccine coverage.<sup>42,43</sup> The G12 genotype was first detected in 1987 in the Philippines,<sup>44</sup> then remained undetected until it re-emerged in Thailand in 1998.<sup>45</sup> Although G12 was considered a rare genotype in the 2000s, G12P[8] is now common genotype in many countries including in Asian countries such as Bangladesh,<sup>46</sup> India,<sup>47</sup> Japan,<sup>48</sup> Korea,<sup>49</sup> Thailand,<sup>45</sup> and Vietnam.<sup>50</sup> The emergence of G12 RVA strains may also have an impact on the efficacy of RVA vaccines. The increasing frequency of

G12 RVAs raises questions about their origin and evolution and how they can spread all over the world. Characterizing the complete genomes may increase our understanding of the relatedness and the evolution of emerging G12 RVA strains, which could be the result of point mutations, genetic rearrangements or reassortment events, and inter-species transmission. Whole genome-based analyses are thus useful to understand the evolutionary dynamics of G12 strains.

## 5 | CONCLUSIONS

To our knowledge, this is the first research article of the complete genome analyses of the G12 strains that have re-emerged in Indonesia. Five G12 RVA strains were obtained in the samples collected in Indonesia in 2017–2018. The results of our analyses demonstrated that G12P[8] is a newly emerging genotype in Indonesia, with genetic backbone of all strains Wa-like; no reassortment event was observed in inter-genogroups or animal strains. Further surveillance studies are necessary to gain more information about the circulating genotypes of human RVA in Indonesia, especially new emerging strains, such as G12 RVA strains.

### AUTHOR CONTRIBUTIONS

**Laura Navika Yamani, Takako Utsumi, Yen Hai Doan, Maria Inge Lusida, and Ikuo Shoji:** designed the study and wrote the manuscript. **Soengeng Soegijanto, Alpha Fardah Athiyyah, Subijanto Marto Sudarmo, Reza Gunadi Ranuh, Soetjipto, Juniastuti:** collected samples. **Zayyin Dinana, Rury Mega Wahyuni, and Emily Gunawan:** carried out RVA detection and genome analysis. **Laura Navika Yamani, Yen Hai Doan, Kazuhiko Katayama, and Chieko Matsui:** performed NGS sequencing. **Laura Navika Yamani, Yen Hai Doan, Chieko Matsui, Rheza Gandhi Bawono:** conducted sequence data analysis. **Lin Deng, Takayuki Abe, Hiroyuki Shimizu, Koji Ishii, Kazuhiko Katayama, Maria Inge Lusida, Ikuo Shoji:** gave critical revision of the article. All the authors contributed to the interpretation of the data, writing of the manuscript, and approved the final manuscript.

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### CONFLICTS OF INTEREST

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study will be available at Kernel-Kobe University Repository (<https://da.lib.kobe-u.ac.jp/da/kernel/>). The sequence results were deposited in the DDBJ/GenBank database with accession numbers LC581220 to LC581275.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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