

Article

Quantitative Mutation Analysis of Genes and Proteins of Major SARS-CoV-2 Variants of Concern and Interest

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Abstract: Of various SARS-CoV-2 variants, some have drawn special concern or interest because of their heightened disease threat. The mutability of individual SARS-CoV-2 genes/proteins presumably varies. The present study quantified gene/protein mutations in 13 major SARS-CoV-2 variants of concern/interest, and analyzed viral protein antigenicity using bioinformatics. The results from 187 carefully perused genome clones showed significantly higher mean percent mutations in the spike, ORF8, nucleocapsid, and NSP6 than in other viral proteins. The ORF8 and spike proteins also tolerated higher maximal percent mutations. The omicron variant presented more percent mutations in the NSP6 and structural proteins, whereas the delta featured more in the ORF7a. Omicron subvariant BA.2 exhibited more mutations in ORF6, and omicron BA.4 had more in NSP1, ORF6, and ORF7b, relative to omicron BA.1. Delta subvariants AY.4 and AY.5 bore more mutations in ORF7b and ORF8 than delta B.1.617.2. Predicted antigen ratios of SARS-CoV-2 proteins significantly vary (range: 38–88%). To overcome SARS-CoV-2 immune evasion, the relatively conserved, potentially immunogenic NSP4, NSP13, NSP14, membrane, and ORF3a viral proteins may serve as more suitable targets for molecular vaccines or therapeutics than the mutation-prone NSP6, spike, ORF8, or nucleocapsid protein. Further investigation into distinct mutations of the variants/subvariants may help understand SARS-CoV-2 pathogenesis.

Keywords: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); coronavirus disease 2019 (COVID-19); mutations; variant; viral protein; antigenicity



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1. Introduction

As the causative pathogen for coronavirus disease 2019 (COVID-19), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) undergoes constant mutations, resulting in the emergence of various lineages or variants of the virus since the COVID-19 outbreak [1–3]. The rapid evolution of the SARS-CoV-2 virus has caused new problems like repeated infections, evasion of immune protection, and lost or weakened efficacy of vaccines, therapeutics, or diagnostics [4]. The status of SARS-CoV-2 mutations is closely monitored through genomic sequencing of virus samples from infected individuals. Various large-scale analyses of SARS-CoV-2 mutations have been conducted, some focusing on specific genes/proteins of the virus, and others mainly dealing with evolutions, transmissibility, infectivity, or virulence of the variants [5–10].

SARS-CoV-2 accumulates replication errors along the course of its spread, infection, and proliferation. The variants of concern/interest of SARS-CoV-2 refer to the mutants of the virus that harbor specific combinations of viral genome mutations and have the potential of heightened disease threat due to enhanced transmission, infection, virulence, or immune escape [1,11]. Thus, among the numerous hitherto identified SARS-CoV-2 lineages, the variants of concern/interest are more clinically relevant. Epidemiologically, much has also been learned about these SARS-CoV-2 variants [1–3,12].

The SARS-CoV-2 genome comprises approximately 30,000 nucleotides with 12 canonical genes encoding non-structural, structural, or accessory viral proteins of which functions

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The Genetic Basis of Common Diseases Richard A. King,Jerome I. Rotter,Arno G. Motulsky,2002-10-17 Since the first edition of this highly acclaimed text was published in 1992 much new knowledge has been gained about the role of genetic factors in common adult diseases and we now have a better understanding of the molecular processes involved in genetic susceptibility and diseases mechanisms The second edition fully incorporates these advances The entire book has been updated and twelve new chapters have been added Most of these chapters deal with diseases such as gallstones osteoporosis osteoarthritis skin cancer other common skin diseases prostate cancer and migraine headaches that are seen by all physicians Others address the genetic and molecular basis of spondylarthropathies lupus hemochromatosis IgA deficiency mental retardation hearing loss and the role of mitochondrial variation in adult diseases Chapters on the evolution of human genetic disease and on animal models add important background on the omplexities of these diseases Unique clinical applications of genetics to common diseases are covered in the additional new chapters on genetic counseling pharmacogenetics and the genetic consequences of modern therapeutics

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Neurodegeneration: From Genetics to Molecules Victoria Campos-Peña, Marco Antonio Meraz-Ríos, Rosalinda Guevara-Guzmán, Karla Guadalupe Carvajal, 2016-11-15 Chronic degenerative diseases are one of the major public health problems particularly those affecting the nervous system They are characterized by the degeneration of specific cell populations that include several pathologies which contribute significantly to morbidity and mortality in the elderly population Therefore in recent years the study of neuroscience has gained significant importance Most of these neurodegenerative disorders are the result of a complex interaction between genetic and environmental factors that generate progression and can even determine its severity The presence of mutations in genes as LRRK2 SNCA PARK7 PARK2 or PINK1 is associated with Parkinson s disease Mutations in genes such as APP PS1 and PS2 are associated with familial Alzheimer s disease while HTT gene mutations are the cause of Huntington s disease In most cases this condition is inherited in an autosomal dominant pattern which means one copy of the altered gene in each cell is sufficient to cause the disorder It is known that these mutations can also alter the proteins function however it has not yet been possible to fully understand how some genetic changes cause the disease or influence the risk of developing these disorders Most symptoms seen in these conditions occurs when specific nerve cells are damaged or die generating a loss in brain communication Also many of these mutations generate aggregation of intracellular or extracellular proteins affecting cell function and eventually causing neuronal death It is unclear whether the presence of these aggregates play an important role in nerve cell death during the development of neurodegenerative diseases or if they are simply part of the response of cells to the disease Other mutations affect the mitochondrial function generating alterations in energy production and promoting the formation of unstable molecules such as free radicals Under normal conditions the harmful effects caused by free radicals are offset within the cell However in pathological conditions the presence of mutations can alter this process by allowing the accumulation of radicals and damaging or killing cells On the other hand we also know that these diseases may not have a direct genetic component thus the study of sporadic type neurodegenerative diseases is much more complex Histopathological lesions as well as the cellular and molecular alterations are generally indistinguishable from familial cases For this reason it is important to

understand the genetic and molecular mechanisms associated with this type of pathologies In this sense this issue aims to understand the molecular processes that occur in the brain and how these are influenced by the environment genetics and behavior

Russell & Rubinstein's Pathology of Tumors of the Nervous System 7Ed Roger E. McLendon, Marc K. Rosenblum, Darell D. Bigner, 2006-07-28 This is the leading international professional reference text that also serves as a bench book describing all aspects of the pathology of brain tumours genetics molecular biology epidemiology morphology immunohistochemistry diagnostic criteria and prognosis Beautifully illustrated in colour throughout and comprehensively referenced Russell Rubinstein is regarded as the ultimate source for key information For this seventh edition the book returns to a single clearly organised volume and basic sciences are once again fully integrated within sections devoted to individual tumour entities Entirely revised and updated throughout by a wide range of internationally revered authorities the content reflects the latest tumour classification and grading while neuroradiologic correlation via state of the art neuroimaging techniques continues to be emphasised in all diagnostic entities The offering is completed by a companion CD ROM providing quick and easy access to all the images from the book retrievable by figure number chapter title and keyword searches

Behavioral Neurogenetics John F. Cryan, Andreas Reif, 2012-05-04 This book covers a wide array of topics relevant to behavioral genetics from both a preclinical and clinical standpoint Indeed in juxtaposing both areas of research the reader will appreciate the true translational nature of the field Topics covered range from technical advances in genetic analysis in humans and animals to specific descriptions of advances in schizophrenia attention disorders depression and anxiety disorders autism aggression neurodegeneration and neurodevelopmental disorders The importance of gene environment interactions is emphasised and the role of neuroimaging in unravelling the functional consequences of genetic variability described This volume will be valued by both the basic scientist and clinician alike who may use it as a detailed reference book It will also be of use to the novice to the field to whom it will serve as an in depth introduction to this exciting area of research

Neonatal Neurology , 2019-07-17 Neonatal Neurology Volume 162 in the Handbook of Clinical Neurology series updates the reader on the latest advances in the study of neurological diseases diagnosed in the fetal and neonatal periods With recent advances in magnetic resonance imaging digital electroencephalography recording and genetic testing and diagnosis there is expanding awareness relating to early onset neurological conditions and how their early diagnosis can improve prediction of outcome and subsequent neurodevelopmental outcome This new volume covers diagnosis and management of congenital conditions including brain malformations neuromuscular conditions and genetic epilepsies as well as acquired injury related to peri partum events prematurity critical illness and systemic diseases Provides an in depth understanding of the basic scientific research translational research and clinical consensus across neonatal and fetal medicine Explores how early neurological diagnosis can improve prediction of outcome and how management can improve subsequent neurodevelopmental outcome Features chapters co authored by two experts combining expertise in both

neonatal and fetal neurology *Greenfield's Neuropathology - Two Volume Set* Seth Love,Arie Perry,James Ironside,Herbert Budka,2018-10-08 Greenfield's Neuropathology the world's leading neuropathology reference provides a comprehensive account of the pathological findings in neurological disease their biological basis and their clinical manifestations The book's detailed advice on pathological assessment and interpretation is based on clear descriptions of molecular and cellular processes and reactions that are relevant to the development of the nervous system as well as its normal and abnormal functioning The information is presented in an accessible way to readers working within a range of disciplines in the clinical neurosciences and neuropathological findings are placed within the context of a broader diagnostic process New for the Ninth Edition Features online and downloadable digital formats with rapid search functions annotation and bookmarking facilities image collections and live reference links Contains many color illustrations and high quality clinical photographs to help with interpretation and understanding Includes more than 1000 new photographs and drawings Incorporates new design elements such as alternate colour coding of chapters for easier navigation Known for its thorough yet practical approach Greenfield's continues to provide trusted information to all neuropathologists and those in related specialties including neurologists neurosurgeons general pathologists neuroradiologists and clinical neuroscientists

Atherothrombosis and Coronary Artery Disease Valentin Fuster,Eric J. Topol,Elizabeth G. Nabel,2005 Written by the world's foremost authorities this volume provides comprehensive coverage of current approaches to the prevention diagnosis and management of atherothrombosis and its coronary and noncoronary complications This edition has been thoroughly updated sharply focused on clinical information and trimmed to one manageable volume Coverage begins with a review of risk factors and prevention emphasizing lipid abnormalities hypertension smoking diabetes and obesity Subsequent sections examine the pathogenesis of atherosclerosis markers and imaging acute coronary syndromes chronic stable angina and noncoronary atherothrombosis Clinical presentations medical management and the latest interventional strategies are included

Clinical Image-Based Procedures. Translational Research in Medical Imaging Marius Erdt,Marius George Linguraru,Cristina Oyarzun Laura,Raj Shekhar,Stefan Wesarg,Miguel Angel González Ballester,Klaus Drechsler,2014-03-28 This book constitutes revised selected papers from the International Workshop on Clinical Image Based Procedures CLIP 2013 held in conjunction with MICCAI 2012 in Nagoya Japan in September 2013 The 19 papers presented in this volume were carefully reviewed and selected from 26 submissions The workshop was a productive and exciting forum for the discussion and dissemination of clinically tested state of the art methods for image based planning monitoring and evaluation of medical procedures

Diabetes Mellitus Derek LeRoith,Simeon I. Taylor,Jerrold M. Olefsky,2004 Thoroughly revised and updated this Third Edition encompasses the most recent advances in molecular and cellular research and describes the newest therapeutic modalities for type 1 and type 2 diabetes mellitus Chapters by leading experts integrate the latest basic science and clinical research on diabetes mellitus and its complications The text is divided

into ten major sections including extensive sections on therapeutics diabetes during pregnancy and complications New chapters cover stem cell therapy for type 1 diabetes genetics and treatment of obesity new therapies to promote insulin action vasculopathy islet cell protocols triglycerides in muscle hypoglycemia in the adult and the Diabetes Prevention Program

Pediatric Critical Care Medicine Derek S. Wheeler, Hector R. Wong, Thomas P. Shanley, 2014-04-26 The second edition of *Pediatric Critical Care Medicine* spans three volumes with major sections dedicated to specific organ systems Each major section consists of separate chapters dedicated to reviewing the specific disease processes affecting each organ system Each chapter concludes with a comprehensive list of references with brief concise remarks denoting references of special interest and of interest Consequently the books are unique in their comprehensive coverage of pediatric critical care and their ease of use and will be of value to those studying towards pediatric critical care examinations and those who are already qualified

Molecular Medical Microbiology Yi-Wei Tang, Dongyou Liu, Max Sussman, Ian Poxton, Joseph Schwartzman, 2014-09-14 The molecular age has brought about dramatic changes in medical microbiology and great leaps in our understanding of the mechanisms of infectious disease *Molecular Medical Microbiology* is the first book to synthesise the many new developments in both molecular and clinical research in a single comprehensive resource This timely and authoritative three volume work is an invaluable reference source of medical bacteriology Comprising more than 100 chapters organized into 17 major sections the scope of this impressive work is wide ranging Written by experts in the field chapters include cutting edge information and clinical overviews for each major bacterial group in addition to the latest updates on vaccine development molecular technology and diagnostic technology Topics covered include bacterial structure cell function and genetics mechanisms of pathogenesis and prevention antibacterial agents and infections ranging from gastrointestinal to urinary tract central nervous system respiratory tract and more The first comprehensive and accessible reference on molecular medical microbiology Full color presentation throughout In depth discussion of individual pathogenic bacteria in a system oriented approach Includes a clinical overview for each major bacterial group Presents the latest information on vaccine development molecular technology and diagnostic technology More than 100 chapters covering all major groups of bacteria Written by an international panel of authors who are experts in their respective disciplines

Molecular Diagnostics Wayne W. Grody, Robert M. Nakamura, Frederick L. Kiechle, Charles Strom, 2009-11-06 Advances in genomic and proteomic profiling of disease have transformed the field of molecular diagnostics thus leading the way for a major revolution in clinical practice While the range of tests for disease detection and staging is rapidly expanding many physicians lack the knowledge required to determine which tests to order and how to interpret results *Molecular Diagnostics* provides a complete guide to the use and interpretation of molecular testing in the clinical arena No other available resource offers this emphasis comprehensive scope and practical utility in the clinical setting Serves as the definitive reference for molecular pathologists worldwide Covers a variety of molecular techniques including next generation sequencing tumor

somatic cell genotyping infectious and genetic disease testing and pharmacogenetics Discusses in the detail issues concerning quality assurance regulation ethics and future directions for the science Campbell-Walsh Urology Alan J. Wein, Louis R. Kavoussi, Andrew C. Novick, Alan W. Partin, Craig A. Peters, 2011-09-28 Since 1954 Campbell Walsh Urology has been internationally recognized as the pre eminent text in its field Edited by Alan J Wein MD PhD hon Louis R Kavoussi MD Alan W Partin MD PhD Craig A Peters MD FACS FAAP and the late Andrew C Novick MD it provides you with everything you need to know at every stage of your career covering the entire breadth and depth of urology from anatomy and physiology through the latest diagnostic approaches and medical and surgical treatments Consult this title on your favorite e reader with intuitive search tools and adjustable font sizes Elsevier eBooks provide instant portable access to your entire library no matter what device you re using or where you re located Be certain with expert dependable accurate answers for every stage of your career from the most comprehensive definitive text in the field Required reading for all urology residents Campbell Walsh Urology is the predominant reference used by The American Board of Urology for its board examination questions Visually grasp and better understand critical information with the aid of algorithms photographs radiographs and line drawings to illustrate essential concepts nuances of clinical presentation and technique and decision making Stay on the cutting edge with online updates Get trusted perspectives and insights from hundreds of well respected global contributors all of whom are at the top and the cutting edge of their respective fields Stay current with the latest knowledge and practices Brand new chapters and comprehensive updates throughout include new information on perioperative care in adults and children premature ejaculation retroperitoneal tumors nocturia and more Meticulously revised chapters cover the most recent advancements in robotic and laparoscopic bladder surgery open surgery of the kidney management of metastatic and invasive bladder cancer and many other hot topics Reference information quickly thanks to a new streamlined print format and easily searchable online access to supplemental figures tables additional references and expanded discussions as well as procedural videos and more at www.expertconsult.com Genetic Disorders of the Exocrine Pancreas Peter R.

Durie, Markus M. Lerch, Albert B. Lowenfels, Patrick Maisonneuve, Charles D. Ulrich, 2002-01-01 This publication summarizes important new scientific information and provides guidelines for genetic testing for hereditary pancreatitis as well as guidelines for the prevention screening and treatment of pancreatic cancer in hereditary pancreatitis It also includes chapters on neonatal screening for cystic fibrosis gene mutations in idiopathic pancreatitis and clinical phenotypes of Shwachman Diamond Syndrome This book is required reading for all individuals with an interest in pancreatic disease

Recent Advances in Immunosuppression-Related Swine Diseases Gang Wang, Leyi Wang , Taofeng Du, 2024-07-25 Pigs are important agricultural animals with ancient domestication history and economic value and have become important sources of protein for humans Infectious diseases affect the health of pigs and the stability and productivity of the global swine industry The emergence and reemergence of several contagious swine diseases in recent years have posed a severe

threat to pig production globally Increasing concern has been raised about the immunosuppressive effect caused by immunosuppressive swine pathogens in recent years such as porcine reproductive and respiratory syndrome virus PRRSV porcine circovirus PCV African swine fever virus ASFV classical swine fever virus CSFV pseudorabies virus PRV among others Infection with variant strains of PRRSV PRV and the low virulence strains of ASFV increase the pathogenicity of opportunistic infectious agents causing secondary disease challenges which can result in more complicated clinical symptoms and severe diseases These diseases lead to increased treatment expenses reduced swine herd growth rate and feed conversion rate However with the ongoing viral evolution and the emergence of novel variants current research into the mechanisms underlying immunosuppression remains inadequate highlighting the urgent need for further investigation

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