

RESEARCH ARTICLE

Screening novel antiviral compounds to treat *Clostridioides difficile* infectionsBrice J. Stoltz^{1,2}, Ahmed A. Abouelkhair^{1,2}, Mohamed N. Seleem^{1,2*}

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Data Availability Statement: All relevant data are within the manuscript and its [Supporting Information files](#).

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Abstract

Clostridioides difficile is a major cause of nosocomial infections, often associated with individuals who have gut dysbiosis from previous antibiotic therapies. *C. difficile* infections (CDI) have a high recurrence rate and impose significant financial and mortality burdens on the healthcare system. Therefore, novel anti-*C. difficile* drugs are urgently needed to treat and reduce the severity and recurrence of infection. In this study, we screened a library of 618 antiviral drugs to identify a potential candidate for repurposing as novel anti-*C. difficile* therapeutics. Following our preliminary screening, we identified 9 novel compounds that inhibited *C. difficile* at a concentration of 16 μ M or lower. Among these, 4 antiviral compounds demonstrated the most potent anti-*C. difficile* activity against a panel of 15 *C. difficile* isolates, with minimum inhibitory concentrations (MICs) comparable to the drug of choice, vancomycin. These include rottlerin (MIC₅₀ = 0.25 μ g/mL), α -mangostin (MIC₅₀ = 1 μ g/mL), dryocrassin ABBA (MIC₅₀ = 1 μ g/mL), and obetazimod (MIC₅₀ = 4 μ g/mL). All exhibited minimal to no activity against representative members of the human gut microbiota. Interestingly, α -mangostin, a natural xanthone derived from the mangosteen fruit, exhibited strong bactericidal action, clearing a high inoculum of *C. difficile* in less than an hour. All other drugs exhibited bacteriostatic activity. Given their characteristics, these compounds show great promise as novel treatments for CDI.

Introduction

Healthcare-associated infections are one of the greatest burdens on healthcare systems. Most bacteria responsible for a part of this burden are associated with antimicrobial resistance, with one notable exception: *C. difficile*. Despite lacking a significant antimicrobial resistance profile, *C. difficile* is still considered an urgent threat and one of the deadliest bacterial infections responsible for approximately 30,000 deaths annually, primarily affecting older populations [1–5]. The incidence of *C. difficile* infections (CDI) in the United States has increased over the last two decades and has remained relatively stable from 2021 to 2022, with the COVID-19 pandemic seeing a drop in cases due to improved strategies preventing the spread of

Screening The Novel

Keith Selby, Robert Giddings



Screening The Novel:

Screening the Novel Robert Giddings, Keith Selby, Chris Wensley, 1990 **Screening The Novel** Keith Selby, Robert Giddings, 2016-07-27 The book takes as its theme the relationship between literature and the contemporary means of production and distribution collectively termed the media in particular film and television The intention of the book is to explore and evaluate the mutual opportunities and restrictions in this relationship In the grammar of our culture there seems to be an accepted opinion that print is superior in terms of cultural production to film radio or television that to read a book is somehow a higher cultural activity than seeing a play on television or seeing a film By the same token a novel is a superior work of art to film or television The longer perspective reveals that traditionally there always is a greater respect paid to the previous mode of literary production poetry was superior to drama poetic drama was superior to the novel and film attained cult and classic status initially over television Screening Novel Women Liora Brosh, 2015-12-04 From Hollywood classics like Jane Eyre or Wuthering Heights to the 1990s wave of Jane Austen films adaptations of the British Nineteenth century novel have been sensationally popular This book examines how British and American filmmakers used the domestic novels of the past to construct stable gender ideals for the present **Private Screening** Richard North Patterson, 1985 The nation is stunned silent when presidential hopeful James Kilcannon is shot dead point blank while sharing the stage at a benefit concert with his rock star girlfriend Stacy Tarrant Fiercely independent attorney Tony Lord defends the assassin in a sensational trial that erupts into the media event of the decade But the most shocking gambit ever witnessed in the history of television has yet to unfold As America watches a mysterious and ruthless figure known only as Phoenix takes to the airwaves in the ultimate act of high tech terror Holding the wife of a wealthy newspaper mogul and Stacy s manager hostage Phoenix mounts a televised trial of his own in which Stacy Tarrant and Tony Lord are helpless defendants millions of viewers are jurors and unless his chilling demands are met Phoenix is the unstoppable executioner Copyright Libri GmbH All rights reserved **Photosynthesis Research for Food, Fuel and Future** Tingyun Kuang, Congming Lu, Lixin Zhang, 2013-08-31 Photosynthesis is the process by which plants algae and certain species of bacteria transform solar energy into chemical energy in the form of organic molecules In fact all life on the planet ultimately depends on photosynthetic energy conversion The book provides a compressive and state of the art of very recent progress on photosynthesis research The topics span from atom to intact plants from femtosecond reactions to season long production from physics to agronomy The book is to offer advanced undergraduate students graduate students and research specialists the most recent advances in the all aspects of photosynthesis research The book is intended to offer researchers detailed information on the most recent advances in all aspects of photosynthesis research Tingyun Kuang is a professor at Institute of Botany the Chinese Academy of Sciences CAS and the Academician of CAS Congming Lu is a professor at Institute of Botany CAS Lixin Zhang is a professor at Institute of Botany CAS and the Chief Scientist in the National Basic Research Program of China on

photosynthesis *G Protein-Coupled Receptors* Xinfeng Zhao,Qian Li,Jing Wang,Qi Liang,Jia Quan,2023-02-20 This book summarizes the progress made to functional immobilize G protein coupled receptors GPCRs through site specific or orientated recognition in both non covalent and covalent manners The last decade is the dawn of the post structural biology era for G protein coupled receptor research As an emerging approach for state of the art immobilization this book discusses efforts to explore the elegance of naturally occurring biochemical reactions by using their high specificity and robust reactivity in the complex system such as site specific conjugation by covalent recognition between enzymes and their substrates With the perspective of protein drug interactions this book also reviews the applications of protein immobilization with an emphasis on G protein coupled receptors in drug discovery and protein ligand interaction analysis In addition the merits opportunities and disadvantages are analyzed for different immobilization methods and a perspective for future directions is presented Given its scope this book appeals to a broad readership particularly researchers engaged in the field of analytical chemistry bioconjugate chemistry and chemical biology and other related field as well as teachers of relevant majors in colleges and universities **Advances in Escherichia Research and Application: 2012 Edition** ,2012-12-26

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Golden Age were based on novels that never received the acclaim they deserved No one who saw Rod Steiger in The Pawnbroker could forget the actor s wrenching performance but does anyone remember the author of the book on which the film was based The same can be said of Jane Fonda in They Shoot Horses Don t They Greta Garbo in Susan Lenox and Humphrey Bogart in The Treasure of the Sierra Madre This book retrieves these novels and re evaluates the careers of the eight neglected novelists whose works inspired eight different directors among them Stanley Kubrick Sidney Lumet John Huston and Sidney Pollack Each chapter offers detailed analysis on both the original text and the resulting movie Taken together the double examination of novel and film raises some important questions about the nature and problems of cinematic adaptation **Metagenomics** Muniyandi Nagarajan,2017-10-29 Metagenomics Perspectives Methods and

Applications provides thorough coverage of the growing field of metagenomics A diverse range of chapters from international

experts offer an introduction to the field and examine methods for metagenomic analysis of microbiota metagenomic computational tools and recent metagenomic studies in various environments The emphasis on application makes this text particularly useful for applied researchers practitioners clinicians and students seeking to employ metagenomic approaches to advance knowledge in the biomedical and life sciences Case study based application chapters examine topics ranging from viral metagenome profiling metagenomics in oral disease and health metagenomic insights into the human gut microbiome and metabolic syndromes and more Additionally perspectives on future potential at the end of each chapter provoke new thought and motivations for continued study in this exciting and fruitful research area Provides thorough coverage of the rapidly growing field of metagenomics with an emphasis on applications of relevance to translational researchers practitioners clinicians and students Features a diverse range of chapters from international experts that offer an introduction to the field and examine methods for metagenomic analysis of microbiota metagenomic computational tools and research pipelines Highlights perspectives on future potential at the end of each chapter to provoke new thought and motivations for continued study in this exciting and fruitful research area

DNA-Encoded Libraries Andreas Brunschweiler, Damian W. Young, 2022-11-25 This book deals with the recent advances in DNA Encoded Library DEL technology that has emerged as an alternative to high throughput screening HTS over the last decade and has been heralded as a disruptive technology for drug discovery The book aims to provide a comprehensive overview of all of the major components of the DEL process from conception to bench execution and clinical investigations The contributions from experts in the field combine different perspectives from academia and industry The book will be of interest to researchers in the drug discovery field as well as to graduate students and scholars who are interested in this rapidly improving technology

Screen Adaptations: Jane Austen's Pride and Prejudice Deborah Cartmell, 2010-08-10 The study of literature on screen is a growing area of study in schools and universities Many students have to produce critical essays comparing the novel and film versions of a particular text The Screen Adaptations series offers a wealth of study material from the literary context of the original work through to thought provoking comparisons of the screen versions critical commentary and the afterlife of the films *Pride and Prejudice* is a classic piece of literature and any new adaptation is a major event With several well known TV and film versions available featuring stars such as Keira Knightley as well as a Bollywood version discussions around how these films interpret the story themes and characters is a popular classroom choice for students and teachers alike This new title in the Screen Adaptations series provides a rich source of material to help students understand and write about the reciprocal relationship between film and literature It offers in depth analysis of the various screen versions and alternative readings as well as critical insight and an interview with writer Andrew Davies best known for his 1995 BBC adaptation Following from Shakespeare Jane Austen on screen is now an established part of literary studies and the volume will conclude with a survey of the growing body of literature in the field

Theoretical and Computational Chemistry Editor's

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chapters of the book are organized according to the following practical and easy to consult format introduction chapter topics and text conclusions take home lessons and references cited for further reading *Alcohol and Alcohol-related Diseases* Sebastian Mueller, Markus Heilig, 2023-10-24 Alcohol is one of the major risk factors for negative health outcomes worldwide It accounts for more than 60 alcohol related diseases ranging from addiction through liver cirrhosis to cancer Collectively these conditions account for mortality and morbidity that make alcohol use one of the leading preventable causes of disability adjusted life years DALYs lost globally In this book an international faculty covers all aspects of alcohol related disorders ranging from addiction alcohol use disorders AUD to alcohol related diseases of other organs such as liver heart or cancer A special focus is to reach out to primary care physicians who are in the front line of this major health problem The book also provides an update for addiction specialists as well as specialists in internal medicine gastroenterology and hepatology The book is divided into sections that include epidemiology alcohol use disorders and addiction alcohol related liver disease alcoholic hepatitis primary care and interdisciplinary approaches and other alcohol related diseases Besides current diagnostic measures and treatment strategies the book deals with the many underlying molecular and genetic mechanisms of alcohol toxicity Novel insights include prospective data on all cause mortality and the emerging major role of alcohol mediated hemolysis and enhanced red blood cell turnover The book also aims at guiding policy makers to handle the topic of alcohol in our society more responsibly Biostimulants in Agriculture Youssef Rouphael, Giuseppe Colla, 2020-03-24

The Twentieth-Century Spanish American Novel Raymond Leslie Williams, 2005-03-01 Spanish American novels of the Boom period 1962 1967 attracted a world readership to Latin American literature but Latin American writers had already been engaging in the modernist experiments of their North American and European counterparts since the turn of the twentieth century Indeed the desire to be modern is a constant preoccupation in twentieth century Spanish American literature and thus a very useful lens through which to view the century s novels In this pathfinding study Raymond L Williams offers the first complete analytical and critical overview of the Spanish American novel throughout the entire twentieth century Using the desire to be modern as his organizing principle he divides the century s novels into five periods and discusses the differing forms that the modern took in each era For each period Williams begins with a broad overview of many novels literary contexts and some cultural debates followed by new readings of both canonical and significant non canonical novels A special feature of this book is its emphasis on women writers and other previously ignored and or marginalized authors including experimental and gay writers Williams also clarifies the legacy of the Boom the Postboom and the Postmodern as he introduces new writers and new novelistic trends of the 1990s

Unveiling the Energy of Verbal Artistry: An Emotional Sojourn through **Screening The Novel**

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