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BIOGRAPHY:

- **Postdoctoral Research Fellow in Singapore Centre for Environmental Life Sciences Engineering, NTU.**
- **Excellent team player with experience in project management and strong builder of collaborations in different aspects of basic and applied research leading to long-lasting research projects and peer reviewed scientific publications.**
- **Creative and self-motivated individual with easy-integration in a multicultural environment with unique combination of detail-oriented mindset, driven personality, analytical skills and proven ability to beat tight deadlines by working in a fast-paced work environment**

SKILL HIGHLIGHT: Project Management| Research Industry Experienced| BSL3+ certified| Infectious Virus generation via reverese genetics| Lentiviral expression system| Site Directed and random mutagenesis| Bacterial protein expression and purification| Affinity and ion exchange chromatography| Monoclonal antibody generation, expression and purification| Affinity maturation of monoclonal antibody by phage display| Western blot, ELISA, Co-immunoprecipitation, Immunofluorescence| Fluorescence microscopy| Mass spectrometry sample preparation and data analysis| RNA Sequencing sample preparation and data analysis| *In vivo* mouse infection model

EDUCATION:

National University of Singapore, Singapore Ph.D **Major** in **Microbiology and Immunology**	Aug 2013 – June, 2018	**GP 4.13/5.0**
National Institute of Technology, Durgapur, India Master of Technology in Biotechnology (**86.8%)**	July 2009 – June 2011	**GPA 8.68/10**
West Bengal University of Technology, Kolkata, India Bachelor of Technology in Biotechnology (**83.2%)**	July 2005 – June 2009	**GPA 8.32/10**

GRADUATE PH.D. THESIS: Characterization and optimization of interaction of monoclonal antibodies with Influenza A hemagglutinin.

Department: Yong Lu Lin School of Medicine, Department of Microbiology and Immunology, National University of Singapore
Primary Responsibilities:

- Characterization of binding and neutralizing efficacy of monoclonal antibody against avian influenza virus, H5N1 hemagglutinin protein. Epitope mapping of the antibody and design of immunogens for prospective use as vaccine candidates.
- Characterization of binding and neutralizing efficacy of monoclonal antibody against avian influenza virus, H7N7 and H7N9 haemagglutinin and affinity maturation by phage display panning. Analyzing efficacy of the ScFvs for monoclonal antibody therapy.
- Development of point of care influenza diagnostic kit targeting haemagglutinin.
  Technical expertise: **Wet lab:** Phage display panning protocols for affinity maturation of antibodies; Generation of chimeric virus and *In vitro* microneutralization assay in BSL3; Protein expression and purification through bacterial and mammalian expression system; Ion-exchange and affinity chromatography; Site-directed and random mutagenesis protocols; Antibody engineering, expression and purification techniques; Development of point of care influenza diagnostic kit; Animal cell culture techniques using 293FT, MDCK, HELA, H1299 cells; Western blotting, ELISA and immunofluorescence assay; Fluorescence microscopy; RNA isolation, cDNA synthesis.
  Dry lab: *In-silico* epitope prediction algorithms e.g. BPAP and BEPro, NCBI BLAST, CLUSTAL Omega and EMBOSS, 3D structure generation using Pymol, image analysis using Image J and Adobe Lightroom, statistical analysis using Microsoft excel and Graph Pad Prism, Microsoft office tools for thesis and manuscript preparation.
  Mentor: Assoc. Prof. Tan Yee Joo, Dept. of Microbiology and Immunology, NUS, Singapore.

POST PHD RESEARCH EXPERIENCE: 2.5 years

- **Singapore Centre for Environmental Life Sciences Engineering, Nanyang Technological University**
  Postdoctoral Research Fellow, 1st November, 2019 – Present
  Primary Responsibilities: Understanding the role of serine proteases in virulence of *Enterococcus faecalis* and *Streptococcus pneumonia.* Utlizing proteomics, genomics and molecular biology tools for identifying substrates for serine proteases, *in vitro* and *in vivo*, for development of inhibitors and/or vaccines against *Enterococcus faecalis* and *Streptococcus pneumonia* infections. Responsible for managing the project supervising two research assistants, preparation of grant proposals.
  Technical expertise: **Wet lab:** ***In vitro***: Development of Protein expression and purification through Enterococcus expression system; co-immuno precipitation; bacterial two-hybrid assay; RNA Seq; ChIP Seq; Phos-tag SDS PAGE; Size exclusion, thin-layer and affinity chromatography; Mass spectrometry sample preparation and analysis. ***In vivo***: Generation of wound infection and gut colonization model in Balb/c mice.

Dry lab: EdgeR software package, HTSeq , Samtools and Sorting algorithms for RNA seq analysis; ROTS software package for Mass spectrometry analysis

Supervisor: Kimberly Kline, Associate Professor, Nanyang Technological University & Birgitta Henriques Normark, Professor, Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Sweden.

- **National Institute of Cholera and Enteric Diseases & Okayama University Collaborative Research Center for Infectious Diseases in India**

  Postdoctoral Research Fellow, 1st April, 2019 – 31st October, 2019

  Primary Responsibilities: Studies on emerging and reemerging Infectious diseases, Phase-III. Analysis of the reemergence of infectious Vibrio.cholerae strains in pond water and in the stool samples of patients with chronic Diarrhea in and around Kolkata, India.

  Technical expertise: Isolation of vibrio from environmental water samples, bacterial growth kinetics study, PCR, RNA sequencing for characterization of the vibrios.

  Supervisor: Prof. Keinosuke Okamoto, Director, Okayama Univ. Collaborative Res. Center for Infectious Diseases in India.

- **Department of Chemistry, University of Calcutta, India**

  Postdoctoral Research Associate, 9th July 2018 – 31st March, 2019

  Primary Responsibilities: *In vitro* analysis of effect of prospective siderophore extracted from traditional Indian plants on neuroblastoma and hepatocellular carcinoma cell lines, synthesis and structure determination.

  Technical expertise: Preparation of plant extracts, in-vitro cell culture assays, Flow cytometry analysis.

  Preparation of Grant Proposals. Review manuscripts for submission to Scientific Reports (Nature).

  Supervisor: Prof. Dilip Kumar Maity, Department of Chemistry, University of Calcutta, India

OTHER EXPERIENCE:

- **Cactus Communications Services Pte Ltd, Center of Excellence for Biochemistry, Genetics, and Molecular Biology**

  Freelance Editor, 7th June, 2019 – 31st October, 2019.

  Primary Responsibilities: Review manuscripts and verifying that the standards of the required in the scientific, technical, medical, and academic publishing industry have been met.

PRE PHD RESEARCH EXPERIENCE: 6 Years

- **Plant Tissue Culture and Molecular Biology lab, Biotechnology and Bioresources Division, The Energy and Resources Institute, Delhi, India.**

  Project Associate, October 2012 – July 2013.

  Primary Responsibilities: Estimation of genetic diversity of various plants like Brassica, Sea Buckthorn, chili, jatropha etc.

  Technical expertise: Molecular marker technique, genomic DNA isolation, PCR, AFLP based Bulk Segregant Analysis.

  Supervisor: Shashi Bhusan Tripathi, Fellow, The Energy and Resources Institute, Delhi, India.

- **M.Tech Thesis: Characterization of paper and pulp industry waste water, its toxicity assessment and remediation measures for toxicity reduction.**

  Technical expertise: Wet lab: Isolation of bacterial colonies from effluent samples, biochemical and pathogenic characterization of bacterial isolates, growth kinetics study, assessing bio-remedial efficacy of the bacterial isolate and determination of DNA damage of the treated and untreated effluent on Onion and Chick Pea by COMET assay.

  Dry lab: Optimization of Bioremediation process and analysis using Design expert 7.0, statistical analysis using Microsoft excel and Graph Pad Prism, Microsoft office tools for thesis and manuscript preparation.

  Mentor: Assoc. Prof. Dr. Dalia Dasgupta Mandal, Department of Biotechnology, NIT, Durgapur.

- **B.Tech Thesis: Optimization of kinetics for the enzymatic hydrolysis of starch (rice, corn, potato) into glucose by batch / fed batch process.**

  Technical expertise: Wet lab: Extraction of the enzyme from the stems of *Tinospora cordifolia,* DNSA assay to calculate the activity of the crude enzyme on the particular substrate.

  Dry lab: Microsoft office tools for thesis preparation.

  Mentor: Prof. Subhabrata Sengupta, HOD, Biotechnology Dept., Heritage Institute of Technology, India.

TEACHING EXPERIENCE: 7 Years

- **Department of Microbiology and Immunology, National University of Singapore**

  Teaching Assistant, September 2013 – May 2017

  Courses involved: Molecular Microbiology of Human Diseases (Spring, 2013, 2014, 2016), Laboratory Techniques in Life Sciences (Spring, 2015), Microbiology (Fall, 2014), Immunology (Fall, 2015).

  Primary Responsibilities: Co-ordinating practical experiments, grading assignments.

- **Department of Molecular and Cell Biology, University of Texas at Dallas, Richardson, Texas, USA**
  Teaching Assistant, September 2011 – May 2012
  Courses involved: Biochemistry I (Fall, 2011), Introduction to Modern Biology (Spring, 2012)
  Primary Responsibilities: Undertaking tutorials for undergraduates, grading assignments.

- **Department of Biotechnology, National Institute of Technology, Durgapur, India**
  Laboratory Assistant, July 2009 – June 2011
  Primary Responsibilities: Designing and coordinating experiments in Immunology Lab as well as Molecular Biology & rDNA Technology Lab.

ACADEMIC HONORS AND AWARDS:

- Awarded **NUS Research scholarship** for the PhD program in Yong Lu Lin School of medicine, NUS.
- **NUS Conference Travel Award**, 2015 and 2017.
- Qualified **GATE** (Graduate Aptitude Test for Engineers) examination of Indian Institute of Technology in 2009 with 92.4 percentile score and availed Ministry of Human Resource and Development (MHRD) scholarship for pursuing M.Tech.
- Received merit award for being declared the **BEST POSTER** in the poster presentation section organized by 16th WEST BENGAL STATE SCIENCE AND TECHNOLOGY CONGRESS, 2009

CERTIFICATIONS:

- Certified for carrying out experiment in BSL3+ level lab by National University of Singapore.
- Certified in Responsible Care and Use of Laboratory Animals by SingHealth Experimental Medicine Centre and SingHealth Office of Research.

JOURNAL PUBLICATIONS: (https://orcid.org/0000-0002-4764-6314)

PUBLISHED

- **Paul, S.S.**, Mok, C.-K., Mak, T.-M., Ng, O.-W., Aboagye, J.O., Wohlbold, T.J., Krammer, F., Tan, Y.-J., 2017. A cross-clade H5N1 influenza A virus neutralizing monoclonal antibody binds to a novel epitope within the vestigial esterase domain of hemagglutinin. Antiviral Res. 144, 299–310. https://doi.org/10.1016/j.antiviral.2017.06.012 (IF: 4.1).

- Zheng, Z., **Paul, S.S.**, Mo, X., Yuan, Y.-R.A., Tan, Y.-J., 2018. The Vestigial Esterase Domain of Haemagglutinin of H5N1 Avian Influenza A Virus: Antigenicity and Contribution to Viral Pathogenesis. Vaccines 6. https://doi.org/10.3390/vaccines6030053 (IF:4.086).

- Behera, M., Paul, I., **Paul, S.S.**, Mandal, T., Mandal, D.D., 2019. Simultaneous o-cresol degradation and biosurfactant production by indigenous bacterial monoculture: kinetics and genotoxic risk assessment. DESALINATION WATER Treat. 144, 116–128. https://doi.org/10.5004/dwt.2019.23508 (IF: 1.32).

- **Paul, S S.**, Takahashi, E., Chowdhury, G., Miyoshi, S.-I., Mizuno, T., Mukhopadhyay, A.K., Dutta, S., Okamoto, K., 2020. Low Viability of Cholera Toxin-Producing Vibrio cholerae O1 in the Artificial Low Ionic Strength Aquatic Solution. Biol. Pharm. Bull. 43, 1288–1291. https://doi.org/10.1248/bpb.b20-00350 (IF:1.863)

- Das, C.; Sen, S.; Singh, T.; Ghosh, T.; **Paul, S S** ; Kim, T.W.; Jeon, S.; Maiti, D.K.; Im, J.; Biswas, G. Green Synthesis, Characterization and Application of Natural Product Coated Magnetite Nanoparticles for Wastewater Treatment. *Nanomaterials* **2020**, *10*, 1615 (IF: 4.358).

- Das C, **Paul S.S**, Saha A, Singh T, Saha A, Im J, Biswas G. Silver-Based Nanomaterials as Therapeutic Agents Against Coronaviruses: A Review. *Int J Nanomedicine*. 2020;15:9301-9315, https://doi.org/10.2147/IJN.S280976 (IF: 5.166).

- **Paul S.S**, Biswas G, 'Repurposed Antiviral Drugs for the Treatment of SARS COVID19: Syntheses, Mechanism of Infection and Clinical Trials', Mini-Reviews in Medicinal Chemistry **2020**, *(E-pub Ahead of Print*) doi: 10.2174/1389557521666201222145842 (IF: 2.915).

ACCEPTED/ IN-PRESS

- **Subha Sankar Paul**, Heykel Trabelsi, Yazen Yaseen, Upasana Basu, Hiyam Adil Altaii and Debarun Dhali, 'Advances in long DNA synthesis,' (Singh- Microbial Cell Factories Engineering for Production of Biomolecules, Elsevier(*Accepted: In Press*))

SUBMITTED

- **Subha Sankar Paul**, Goutam Biswas, 'A Mini Review on the Effectiveness of Peptoids as Therapeutic Interventions against Neurodegenerative Diseases' (Submitted in Neuropeptides (Elsevier))

- Dr. Chee-Keng Mok , **Subha Sankar Paul** , Oi-Wing Ng , James Odame Aboagye , Yee Joo Tan, 'Single and Multi targeting Neutralization of H5N1 Avian Influenza A Virus Non-Structural Protein 1 Using Single Chain Variable Fragment Inhibits Viral Growth' (Submitted in mBio)

CONFERENCE PUBLICATIONS:

Oral Presentation	Poster Presentation
Subha Sankar Paul, Chee-Keng Mok, Tze-Minn Mak, Oi-Wing Ng, James Odame Aboagye, Teddy John Wohlbold, Florian Krammer, Yee-Joo Tan "*A cross-clade H5N1 influenza A virus neutralizing monoclonal antibody binds to a novel epitope within the vestigial esterase domain of hemagglutinin*", Proceedings of 17th International Congress of Virology, IUMS,2017(OR173, Section: Influenza virus, Page No. 32)	Subha Sankar Paul, Sandip Kumar Bose, Argha Nandy, Debdutta Bhattacharya, Ranjana Chowdhury "Studies *on removal of cadmium through biochemical route".* Proceedings of 16th West Bengal State Science Congress, 2009, Research abstracts (Abstract Number: BIOT- 09)
Subha Sankar Paul, Tze-Minn Mak, Yee-Joo Tan "Characterization of a Monoclonal Antibody 4F3 Binding to the Haemagglutinin Proteins of Different Avian Influenza Viruses", Online proceedings of 10th Asia-Pacific Congress of Medical Virology, 2015 (url: http://elite.newhopetek.com.tw/APCMV2015CD/PDF/OS%202-2.pdf)	Subha Sankar Paul, Minati Behra, Debarun Dhali , Dalia Dasgupta Mandal "*The Role of the Bacterial Isolates Pure Culture from Paper and Pulp Industrial Effluents in O-Cresol and Waste Degradation*". Proceedings of Indian Chemical Engineering Congress-CHEMCON-2011(Paper-282, PgNo:263)
Subha Sankar Paul, Debarun Dhali, Dalia Dasgupta Mandal "*A Comparative study of the Toxicity of different Industrial Effluents on the Germination of Chick pea (Cicer arietinum)",* Proceedings of National Conference on Biotechnology and the Environment – NCBE 2010, ISBN:978-93-80697-20-8(Section 6, Page No.-175).	Debarun Dhali, Subha Sankar Paul, Dalia Dasgupta Mandal "*Biodegradation Potential of Bacterial isolates from Industrial Effluents with respect to COD and o-Cresol*", 51st Annual Conference of Association of Microbiologists of India (AMI) 2010, International Symposium on Recent Advances in Cross-disciplinary Microbiology: Avenues Challenges. (Section: Environmental Microbiology, Paper No: EM71, Page NO: 167-168)
Subha Sankar Paul, Chee-Keng Mok, Tze-Minn Mak, Oi-Wing Ng, James Odame Aboagye, Teddy John Wohlbold, Florian Krammer, Yee-Joo Tan "*Defining the binding epitope of a cross-clade H5N1 influenza A virus neutralizing monoclonal antibody 9F4 and comparison of other antibodies targeting the vestigial esterase domain of hemagglutinin",* Proceedings of 1st Microbiology and Immunology Graduate Student Symposium, NUS, 2017	Subha Sankar Paul, Chee-Keng Mok, Tze-Minn Mak, Oi-Wing Ng, James Odame Aboagye, Teddy John Wohlbold, Florian Krammer, Yee-Joo Tan "*A cross-clade H5N1 influenza A virus neutralizing monoclonal antibody binds to a novel epitope within the vestigial esterase domain of hemagglutinin*", Proceedings of 7th Annual Graduate Scientific Congress, NUS, 2017
	Subha Sankar Paul, Tze-Minn Mak, Yee-Joo Tan "Characterization of a Monoclonal Antibody 4F3 Binding to the Haemagglutinin Proteins of Different Avian Influenza Viruses", Proceedings of 6th Annual Graduate Scientific Congress, NUS, 2016

RESEARCH INTERESTS: Infectious disease biology, proteomics, virology, antibody and protein engineering, expression and purification, antibody based therapeutics studies, antibody affinity maturation by phage display, vaccine design, molecular biology, immunology and reverse genetics technology.

TEACHING INTERESTS: Virology, Bacteriology, Applied microbiology, Molecular Biology, Medical Microbiology, Recombinant DNA Technology, Immunology,Molecular Mechanisms of Gene Expression, General Biology, Molecular Parasitology and Vector Biology, Protein and Enzyme Bioengineering , Genetic Engineering Techniques, Cell and Tissue Culture Technology , Molecular Immunology, Immunotechnology, Proteomics and transcriptomics.

EXTRACURRICULAR ACTIVITIES:

- Actively participated in organization of National conference on Biotechnology and Environment, 2010 by Dept. of Biotechnology, NIT, Durgapur with primary responsibility being co-ordination of the technical paper presentation sessions (Oral).
- Presently member of NTU School of Biological Sciences Postdoc Club.

Note

Low Viability of Cholera Toxin-Producing *Vibrio cholerae* O1 in the Artificial Low Ionic Strength Aquatic Solution

Subha Sankar Paul,[a,#] Eizo Takahashi,[b,#] Goutam Chowdhury,[c] Shin-ichi Miyoshi,[d] Tamaki Mizuno,[d] Asish K. Mukhopadhyay,[c] Shanta Dutta,[c] and Keinosuke Okamoto*[,a]

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It has been well known that *Vibrio cholerae* inhabit in environmental water. As many patients infected with cholera toxin-producing *V. cholerae* O1 (toxigenic *V. cholerae* O1) emerge in Kolkata, India, it has been thought that toxigenic *V. cholerae* O1 is easily detected in environmental water in Kolkata. However, we could not isolate toxigenic *V. cholerae* O1 from environmental water in Kolkata, though NAG Vibrio (generic name of *V. cholerae* non-O1/non-O139) is constantly detected. To clear the reason for the non-isolation of toxigenic *V. cholerae* O1, we examined the viability of *V. cholera* O1 and NAG Vibrios in the artificial low ionic strength aquatic solution. We found that the viability of toxigenic *V. cholerae* O1 in the solution is low, but that of NAG Vibrios is high. Subsequently, we examined the viability of NAG Vibrios possessing cholera toxin gene (*ctx*) in the same condition and found that the viability of these NAG Vibrios is low. These results indicate that the existence of *ctx* in *V. cholerae* affects the viability of *V. cholerae* in the aquatic solution used in this experiment. We thought that there was closely relation between the low viability of toxigenic *V. cholerae* O1 in the artificial low ionic strength aquatic solution and the low frequency of isolation of the strain from environmental water.

Key words *Vibrio cholerae*; cholera toxin; aquatic solution; viability

INTRODUCTION

Cholera disease is a life-threatening acute diarrheal disease caused by *Vibrio cholerae*.[1)] In *V. cholerae*, there are 206 serogroups based on the polysaccharide O-antigen.[2)] Of these 206 serotypes of *V. cholerae*, the serotype of strains causing cholera disease with severe diarrhea is limited to 2 serotypes, O1 and O139. *V. cholerae* O139 induced endemic of cholera diseases in West Bengal region in 1990's. *V. cholerae* O139 has been recognized as pathogenic strain of *V. cholerae* since then.[1)] However, the number of patients infected with *V. cholerae* O139 has been low in recent years in the world (WHO Cholera, http://www.who.int/mediacentre/factsheets/fs107/en/index.html). In contrast, many patients infected with *V. cholerae* O1 has emerged in the world. Especially, the patients have constantly emerged in Kolkata, India in all ages.[3,4)]

The cholera toxin (CT) produced by these virulent strains play an essential role in emergence of symptom by the infection of *V. cholerae* O1 and O139. Therefore, *V. cholerae* causing endemic and pandemic is limited to CT-producing (toxigenic) *V. cholerae* O1 and O139.[1)]

As *V. cholerae* is regarded as a bacteria living in environmental water,[5)] we supposed that possible number of toxigenic *Vibrio cholerae* O1 inhabited in environment water in Kolkata. Then, we examined *V. cholerae* inhabiting in environment water in Kolkata. For these two years, we examined more than 50000 colonies presenting yellow color on thiosulfate-citrate-bile salts-sucrose (TCBS) agar plate from pond water. Many *V. cholerae* non-O1/non-O139 strains, which are commonly designated as NAG Vibrio, have been isolated, but we could not isolate toxigenic *V. cholerae* O1 (data not published). From this result, we inferred that the viability of toxigenic *V. cholerae* O1 in pond water might be inferior to that of NAG Vibrio. Then, we examined the viability of toxigenic *V. cholerae* O1 and NAG Vibrios in the artificial low ionic strength aquatic solution. We used the diluted Page's amoeba saline solution (PAS) as the artificial low ionic strength aquatic solution.

The concentration of Na^+ in almost river water in Japan lies between 3.0 and 7.9 mg/L.[6)] The concentration of Na^+ in PAS (under 100% of ionization degree) is 50.6 mg/L. We used the 11 fold-diluted PAS, in which the concentration of Na^+ is 4.6 mg/L, as the artificial low ionic strength aquatic solution in this experiment.

The result showed that the viability of toxigenic *V. cholerae* O1 is lower than that of NAG Vibrio. Subsequently, to clear the role of cholera toxin gene (*ctx*) in the viability of *V. cholerae*, we examined the viability of NAG Vibrios possessing *ctx* in the same condition. The result indicated that there is relation between the possession of *ctx* of *V. cholerae* and the viability of the bactria in the solution examined.

MATERIALS AND METHODS

Bacterial Strains Twelve strains of *V. cholerae* and one

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A cross-clade H5N1 influenza A virus neutralizing monoclonal antibody binds to a novel epitope within the vestigial esterase domain of hemagglutinin

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[c] Institute of Molecular and Cell Biology, A*STAR (Agency for Science, Technology and Research), Singapore
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ABSTRACT

The sporadic outbreaks of highly pathogenic H5N1 avian influenza virus have raised public health concerns. Monoclonal antibodies (MAbs) against hemagglutinin (HA) have been increasingly used successfully for therapeutic purposes. Previously, MAb 9F4, generated against clade 1 H5N1 HA, was observed to have cross-clade neutralizing efficacy and inhibited viral entry by preventing the pH-mediated conformational change of HA. Furthermore, mouse-human chimeric MAb 9F4 was found to retain high degrees of neutralizing activity. In this study, through escape mutant generation and in-silico prediction, it was revealed that MAb 9F4 binds to a novel epitope in the vestigial esterase sub-domain of HA comprising at least three non-continuous amino acid residues, arginine (R) at position 62, tryptophan (W) at position 69 and phenylalanine (F) at position 79, which interacted with MAb 9F4 in a conformation-dependent manner. Binding and neutralization studies suggested that R62 is the critical residue for MAb 9F4 binding whereas W69 and F79 seem to cooperate with R62 to stabilize the epitope. Mutation of either R62 or W69 did not affect replicative fitness of the virus *in vitro*. Interestingly, MAb 9F4 retained neutralizing efficacy against a clade 2.3.2.1a H5N1 virus consisting of an arginine to lysine substitution at position 62 in HA.

1. Introduction

Highly pathogenic influenza A viruses (IAVs) of H5 subtypes, most notably H5N1, naturally circulate among migratory aquatic birds and can spread to poultry, leading to massive outbreaks. Ever since the first recorded instance of bird-to-human infection with the H5N1 influenza virus leading to an outbreak in Hong Kong 1997 (Chan, 2002), a total of 856 human H5N1 infections resulting in 452 deaths have been reported to WHO as of 3rd October 2016 (WHO, 2016). The absence of naturally-occurring herd immunity in humans (Peiris et al., 2007) and the thought that the virus needs only acquire a few mutations to achieve transmissibility between mammals (Herfst et al., 2012; Imai et al., 2012; Shelton et al., 2013) have prompted pandemic preparedness against H5N1 viruses.

Traditionally, pandemic preparedness mainly focuses on vaccination measures prior to infection and timely treatment with antiviral drugs (Sambhara and Poland, 2010). The hemagglutinin (HA) surface glycoprotein has been largely utilized as a vaccine antigen (Pica and Palese, 2013). Since the U.S. Food and Drug Administration approved the first H5N1 human vaccine consisting of A/Vietnam/1203/2004 HA in 2007 (FDA, 2013), other egg-dependent or independent vaccines have entered the industrial pipeline and are presently in different stages of development

Abbreviations: IAV, influenza A virus; HA, hemagglutinin; wt, wild-type; MAb, monoclonal antibody; VE, vestigial esterase; VS, vulnerability site; BPAP, bioinformatics predicted antigenic peptides.

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REVIEW

Silver-Based Nanomaterials as Therapeutic Agents Against Coronaviruses: A Review

This article was published in the following Dove Press journal:
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Abstract: Since the identification of the first human coronavirus in the 1960s, a total of six coronaviruses that are known to affect humans have been identified: 229E, OC43, severe acute respiratory syndrome coronavirus (SARS-CoV), NL63, HKU1, and Middle East respiratory syndrome coronavirus (MERS-CoV). Presently, the human world is affected by a novel version of the coronavirus family known as SARS-CoV-2, which has an extremely high contagion rate. Although the infection fatality rate (IFR) of this rapidly spreading virus is not high (ranging from 0.00% to 1.54% across 51 different locations), the increasing number of infections and deaths has created a worldwide pandemic situation. To provide therapy to severely infected patients, instant therapeutic support is urgently needed and the repurposing of already approved drugs is presently in progress. In this regard, the development of nanoparticles as effective transporters for therapeutic drugs or as alternative medicines is highly encouraged and currently needed. The size range of the viruses is within 60–140 nm, which is slightly larger than the diameters of nanoparticles, making nanomaterials efficacious tools with antiviral properties. Silver-based nanomaterials (AgNMs) demonstrate antimicrobial and disinfectant effects mostly by generating reactive oxygen species (ROS) and are presently considered as a versatile tool for the treatment of COVID-19 patients. Other metal-based nanoparticles have been primarily reported as delivery agents or surface modifying agents, vaccine adjuvant against coronavirus. The present review summarizes and discusses the possible effectiveness of various surface-modified AgNMs against animal coronaviruses and presents a concept for AgNM-based therapeutic treatment of SARS-CoV-2 in the near future.

Keywords: silver nanomaterials, coronavirus, silver nanocomposites, antiviral, SARS-CoV

Introduction

Coronaviridae is an emerging family of coronaviruses and comprises two subfamilies, coronavirinae and torovirinae.[1] Coronavirinae is sub-categorized into four genera, namely alpha, beta, gamma, and delta coronaviruses.[2] Until now, humans have been mostly affected by alpha (229E, NL63) and beta genera (OC43, SARS-CoV, HKU1, MERS-CoV and SARS-CoV-2).[3] As a point of fact, the alpha and beta genera infect mammals while the delta and gamma genera mainly infect birds.[4] In 1930, the first bird coronavirus was discovered when domestic chickens were infected by an unknown pathogen named an infectious bronchitis virus (IBV).[5] Later, in 1965, the first human coronavirus was reported[6] with common cold symptoms. In 1968, eight scientists proposed the name "corona" (which means "crown" or "wreath" in Latin) for the newly discovered viruses based on detailed findings of their structures.[7] This structural exploration showed that four types of proteins are present in all coronavirus structures: spike (S), envelope (E), membrane (M), and nucleocapsid (N).[8] A positive sense single-strand ribonucleic acid

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Repurposed Antiviral Drugs for the Treatment of COVID-19: Syntheses, Mechanism of Infection and Clinical Trials

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Abstract: COVID-19 is a public health emergency of international concern. Although, considerable knowledge has been acquired with time about the viral mechanism of infection and mode of replication, yet no specific drugs or vaccines have been discovered against SARS-CoV-2, till date. There are few small molecule antiviral drugs like Remdesivir and Favipiravir which have shown promising results in different advanced stage of clinical trials. Chloroquinine, Hydroxychloroquine, and Lopinavir-Ritonavir combination, although initially was hypothesized to be effective against SARS-CoV-2, are now discontinued from the solidarity clinical trials. This review provides a brief description of their chemical syntheses along with their mode of action and clinical trial results available in Google and different peer reviewed journals till 24th October 2020.

Keywords: SARS-CoV-2, coronavirus, antiviral drugs, repurposed drugs, Remdesivir, synthesis

1. INTRODUCTION

Towards the end of 2019, a novel coronavirus SARS-CoV-2, the causative virus for COVID-19, with the manifestation of viral pneumonia, caused an epidemic[1], which soon spread worldwide. As of 24th October 2020, 41,570,883 confirmed cases have been reported worldwide[2]. This virus reported an infection fatality rate (ranges from 0.00%- 1.63% depending on place)[3], which is lower compared to Middle East Respiratory Syndrome (MERS-CoV) (10%) and Severe Acute Respiratory Syndrome (SARS-CoV) (37%). This novel coronavirus has been reported to be highly infectious and has already affected majority of the countries in the world, turning itself into a pandemic. Particularly, the sudden spread of the COVID-19 outbreak across Europe and the whole world thereafter from late March, is of great concern.

SARS-CoV-2 consists of a single-strand, positive-sense RNA and belongs to the coronaviridae family[4]. Coronaviruses are reported to infect different host ranging from birds to mammals, which can manifest as common cold to more severe symptoms such as viral pneumonia and severe acute respiratory syndrome caused by MERS-CoV and SARS-CoV[5]. SARS-CoV-2, a new type coronavirus, has higher sequence identity with SARS-CoV (>79%) than that with MERS-CoV (50%)[4]. All coronaviruses including SARS-CoV-2, consists of four common structural proteins: the spike protein (S), the nucleocapsid protein (N) the membrane protein (M) and small envelope protein (E). Apart from these, RNA-dependent RNA-polymerase (RdRp), papain-like protease (PLpro), 3-chymotrypsin-like protease (3CLpro) and helicase are also found in almost all coronaviruses[6]. During the

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vaccines

MDPI

Review

The Vestigial Esterase Domain of Haemagglutinin of H5N1 Avian Influenza A Virus: Antigenicity and Contribution to Viral Pathogenesis

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Abstract: Initial attempts to develop monoclonal antibodies as therapeutics to resolve influenza infections focused mainly on searching for antibodies with the potential to neutralise the virus in vitro with classical haemagglutination inhibition and microneutralisation assays. This led to the identification of many antibodies that bind to the head domain of haemagglutinin (HA), which generally have potent neutralisation capabilities that block viral entry or viral membrane fusion. However, this class of antibodies has a narrow breadth of protection in that they are usually strain-specific. This led to the emphasis on stalk-targeting antibodies, which are able to bind a broad range of viral targets that span across different influenza subtypes. Recently, a third class of antibodies targeting the vestigial esterase (VE) domain have been characterised. In this review, we describe the key features of neutralising VE-targeting antibodies and compare them with head- and stalk-class antibodies.

Keywords: influenza; neutralising antibodies; vestigial esterase; antibody dependent cell-mediated cytotoxicity; pH-induced conformational changes

1. Introduction

Being the major surface glycoprotein present on the envelope of the influenza A virus (IAV), many studies have been devoted to understanding the structure of HA and its antigenicity. HA is a type 1 transmembrane protein that is assembled as a homotrimer in the endoplasmic reticulum and transported to the plasma membrane via the secretory pathway. HA is further cleaved into HA1 and HA2 by a protease provided by the host system. The two subunits remain linked by a disulphide bridge [1]. Structurally, each subunit consists of a membrane-proximal helix-rich stem structure primarily composed of HA2 with some HA1 residues, and a membrane-distal receptor-binding globular domain comprised of HA1 [2].

In terms of antigenicity, antibodies against HA are mainly responsible for protection via vaccination [3,4]. With advances in monoclonal antibody (mAb) technologies, large numbers of