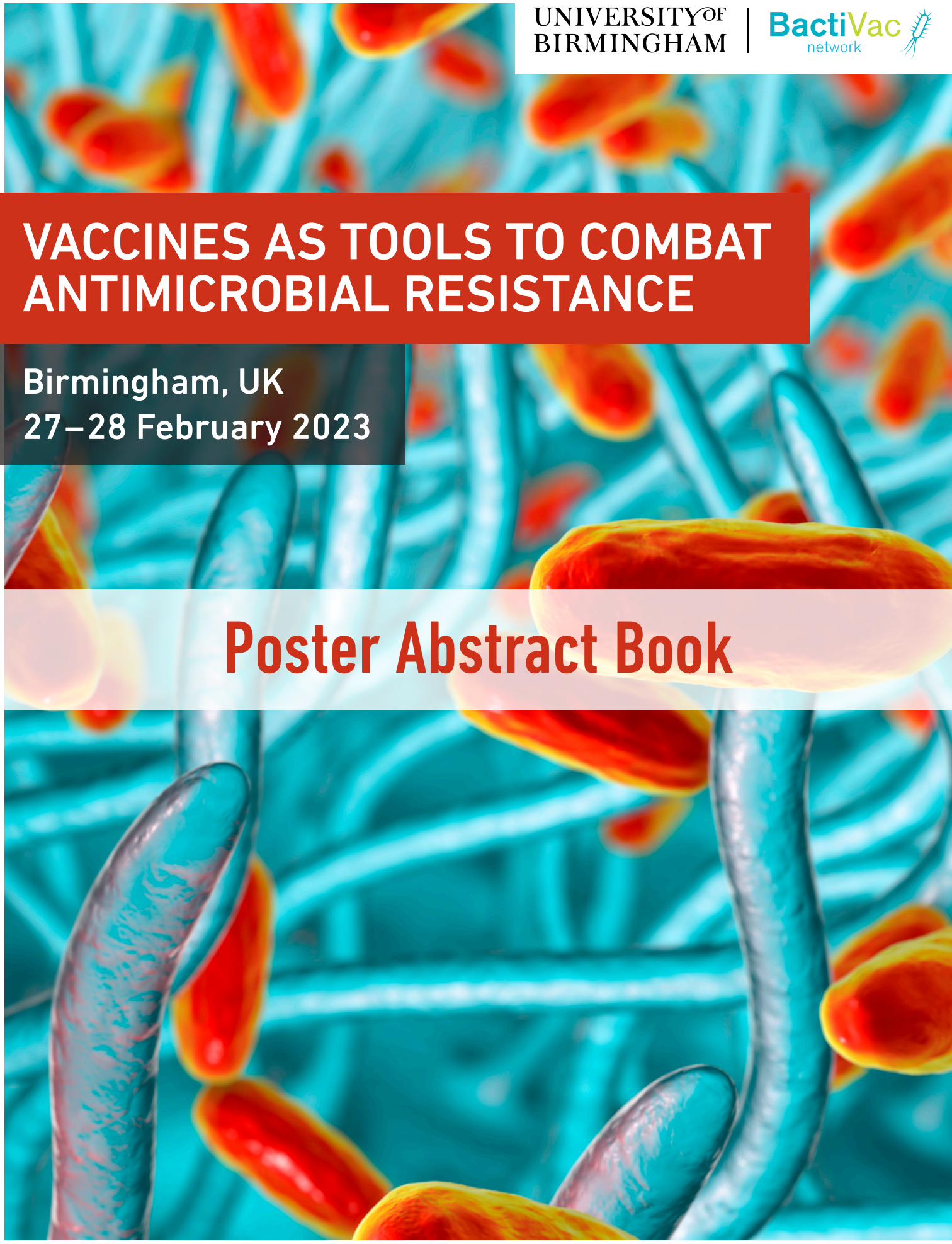

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# VACCINES AS TOOLS TO COMBAT ANTIMICROBIAL RESISTANCE

Birmingham, UK
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## Poster Abstract Book

**FOCUSED MEETING** 2023

Edgbaston Park Hotel and Conference Centre

MICROBIOLOGY SOCIETY

## Poster 01

# Changes in the gut microbiome of Asian seabass (*Lates calcarifer*) following feed-based vaccination against vibriosis

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### Abstract

This study investigates the changes in gut microbiome of Asian seabass following feed-based vaccination against vibriosis. A total of 4,800 fish were equally separated into vaccinated and non-vaccinated groups in duplicate. The vaccinated fish were fed commercial pellets that incorporated with an inactivated *Vibrio harveyi* Vh1 vaccine, while the non-vaccinated fish were fed commercial pellets. The vaccine was administrated at weeks 0 (prime), 2 (booster), and 6 (second booster). Fish of both treatments were challenged on week 10 with $10^8$ CFU/mL of virulent *V. harveyi* Vh1. The gastrointestinal tracts were collected on weeks 0, 2, 6 and 10 (pre- and post-challenge), and were processed for high throughput 16S amplicon sequencing. The alpha diversity of both pre- and post-challenge of both groups showed significant ($p<0.05$) differences, particularly in diversity and richness of microbiota. Phylum Proteobacteria was most dominant among the non-vaccinated fish, both in pre- and post-challenge, while phylum Firmicutes was most dominant among the vaccinated fish. The vaccinated fish was dominated by genus *Cetobacterium* and *Clostridium*, while the non-vaccinated fish by *Vibrio*. LEfSe analysis identified 10 potential taxa markers that differentiated the vaccinated and non-vaccinated fish, where five taxa were associated with each group. Following bacterial challenge, three and seven taxa were associated with vaccinated and non-vaccinated fish, respectively, while the relative percentage survival of the vaccinated fish was 75% compared to 0% for non-vaccinated fish. This study showed that feed-based vaccination contributes to the gut microbiome changes which facilitates the immune response of the fish against bacterial infection.

## Poster 02

# Immune analysis in juvenile Cyprinus carpio upon experimental infection with heat killed Aeromonas hydrophila through Artemia salina bio-encapsulation

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### Abstract

Commercially important aquatic organisms areaffected by pathogenic microorganisms such as viruses, bacteria, toxic algae, fungi, and protozoan parasites which leads to heavy economic losses to the aqua industry. Infectious bacterial disease in the aqua industry is of major concern next to the viral diseases.In the present study oral vaccination of juvenile Cyprinus carpiowith heat killed Aeromonas hydrophila via live prey Artemia salina were done.Initially A. hydrophila was inactivated using heat at 60ºC for 2hrs and inactivation was confirmed using microbial plating and live and dead assay techniques. Further, the inactivated strains were bio- encapsulated intoA. salina and fed to juvenile C.carpioon the 1st dayof the experimentation and on the 21st day C.carpiowere challenged with A. hydrophila infection and samples were collected. The immune biomarkersincluding lysozyme (LYZ), myeloperoxidase (MPO), respiratory burst activity (RBA), alkaline phosphate activity (AKP), serum antiprotease activity, natural complement haemolytic activity, hematological parameters and histological analysiswere studied. Results showed,increased immune responses with high disease resistance and 100% survival of the animals. Vaccination with bio- encapsulated A. salinasubstantially enhances antibody production and results in significantly enhanced survival compared to control group. Outcome of this study confirmed that, bio-encapsulated vaccine appears to be the most attractive method for releasingvaccines.We conclude thatbio- encapsulated A. salinavaccine more effectively increased the uptake of vaccine and enhanced the efficacy by which the immune system dually enhancesthe immune response of C.carpio.

## Poster 03

# Efficacy of a novel glycovaccine for protection against *Aeromonas hydrophila* infection in Nile tilapia *(Oreochromis niloticus)*

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### Abstract

Vaccination has proved to be effective tools to combat Antimicrobial Resistance (AMR) and in protecting farmed tilapia from disease. Vaccine delivery approaches are much ideal methods to limit AMR in aquaculture. Advanced antigen delivery technologies such as nano vaccines and glycovaccines are exciting alternatives for administering vaccines to tilapia. The present study aimed to assess the effectiveness of a novel lectin-based glycovaccine in protecting Nile tilapia against *Aeromonas hydrophila* by comparing different routes of administration. The glycovaccine was administered to fish by injection, immersion and oral, followed by a booster dose 22 days post-vaccination (dpv). The vaccinated fish were infected with a virulent strain of *A. hydrophila*, and the infection monitored for three weeks. Samples were collected at set time points during the trial to assess specific IgM titres, histopathology, immunohistochemistry, and immune gene expression using RT-qPCR. A significant increase in immune parameters was observed with increased IgM, IgT, IgD, CD4,CD8α, IL1β,and TNFα expression ($p<0.05$) in the head kidney of vaccinated fish. Histopathological examinations showed infiltration of lymphocytes suggestive of gill and gut mucosal immune responses. Relative percentage survival ranged from 70% to 100% in vaccinated fish relative to the unvaccinated control after challenge with *A. hydrophila*. Most protection was observed in fish immunised orally with the *A. Hydrophila* Glyco vaccine. The study's results suggest that this novel glycovaccine can induce a protective immune response against this problematic bacterial disease, offering an easy and safe approach for tilapia farmers to vaccinate their fish against *A. hydrophila*.

## Poster 04

# Safety and immunogenicity of a *Klebsiella pneumoniae* tetravalent bioconjugate vaccine (Kleb4V) administered to healthy adults: A FTIH phase I/II randomized and controlled study

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### Abstract

*Klebsiella pneumoniae* (KP) is the third pathogen, after *E. coli* and *S. aureus* causing hospital acquired infections (Weiner 2020), with the most common being pneumonia and urinary tract infections, followed by blood stream infections, and is also a major cause of antimicrobial resistance. Among the Enterobacteriaceae, KP is the most common producer of carbapenemase (Tzouvelekis 2012) and harbors transmissible carbapenemase genes (Logan 2017) (7.2% of KP isolates from EU resistant to carbapenems and peak of 64.7% in Greece). Preventing KP infections is therefore critical to reduce the spread of AMR. A multivalent bioconjugate vaccine, Kleb4V, has been developed at LimmaTech Biologics, using O antigen-polysaccharides from the 4 most predominant KP serotypes, namely O1v1, O2a, O2afg and O3b, each conjugated to the recombinant *Pseudomonas aeruginosa* Exoprotein A. Kleb4V has been tested for safety and immunogenicity (including antibodies titers and functionality) in a phase I/II trial in Germany (last patient last visit completed in September 2022) and data are expected beginning of 2023. Two vaccine doses have been tested, administered twice with or without adjuvant, in 50-70 years old participants. In parallel, a retrospective study is ongoing to identify the target population at highest risk of KP hospital infections.

## Poster 05

# B-Vac: A robust Software Pipeline for Bacterial Vaccine Candidates Identifications

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### Abstract

To expedite the discovery of bacterial protective antigens (BPA) or bacterial vaccine candidates (PVCs)' identification process, we need to have sophisticated genomics data analysis tools. In this context, we have developed B-Vac: which is a robust and user-friendly vaccine candidate prediction pipeline, that significantly reduced the time and labor associated with the identification of putative bacterial vaccine candidates in bacterial pangenome. B-vac is a python-based pipeline that relied upon modern computational libraries for extensive data analysis and handling. The standalone package is having four essential modules taking input in the form of a proteome/sequences in fasta format. The result outputs include PVCs along with B & T cell epitope sequences that are filter out based on pre-defined and/or customizable criteria.

## Poster 06

# CURRENT STATUS AND CHALLENGES OF FISH VACCINES DEVELOPMENT AGAINST VIBRIOSIS IN MALAYSIA

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### Abstract

Globally, aquaculture currently accounts for 46% of total fish production, with Asia accounting for more than 91% of worldwide aquaculture production. However, intensive farming systems usually increase the stress level in fish due to high stocking density and high feeding levels, resulting in decreased water quality. Disease such as warm-water vibriosis is common and significant in tropical countries as it was commonly found in farmed marine fish and shellfish in the region. Treatment of antibiotic-resistant infections with existing antibiotics has become more challenging with the emergence of multidrug resistance in aquatic microorganisms. In tropical countries such as Indonesia, Thailand, Vietnam and Malaysia, several vaccines against warm water vibriosis have been experimentally tested in marine fish with promising results. However, commercial and licensed fish vaccines against warm-water vibriosis in these regions are still limited. In Malaysian aquaculture, the use of vaccines is still in an early developing phase, with most efforts focused on creating vaccines against bacterial infections, such as vibriosis. The present study gives a brief description of the prevalence of vibriosis in Malaysia and how present vaccines are developed and applied. Limitations and gaps in research and development on fish vaccines are also discussed.

## Poster 07

# Development of a nanoparticle vaccine against *Aeromonas hydrophila* infection for tilapia aquaculture in India

Sreeja Lakshmi[1], David Smith[2], Kim Thompson[2], Preetham Elumalai[3]

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### Abstract

Tilapia aquaculture is a major trade commodity for many low to middle-income countries (LMIC), but intensification of tilapia aquaculture triggers extreme challenges with disease outbreaks followed by high mortality. The infections caused by *Aeromonas hydrophila* has emerged as one of most notifiable diseases for farmed tilapia. Vaccination strategies have proved to be effective tools to protect farmed tilapia.

Our study aims to validate the effectiveness of a novel nanovaccine in Nile tilapia against *A. hydrophila* by comparing i.p, immersion and oral vaccine administration routes. The biophysical characteristics of the synthesised formalin-killed *A. hydrophila* vaccine conjugated with Cobalt nanoparticles were examined by transmission electron microscopy. The nanovaccine was administered to the fishes via injection, immersion and oral delivery systems followed by a booster dose on Day 21. A virulent strain of A*. hydrophila* was injected to the vaccinated fish and subsequent mortality was measured for 3 weeks. The fishes were sampled at fixed time intervals to perform ELISA, histopathological examinations, immunohistochemistry analysis and immune gene expression using RT-PCR. A significant ($P < 0.05$) increase in the IgM antibodies were observed in groups after booster vaccination. Head kidney of vaccinated fishes showed promising expression of immune parameters. Histopathological examinations showed infiltrations of lymphocytes suggestive of mucosal immune responses. Relative percentage survival ranged from 70-100% in vaccinated fish compared to the unvaccinated control after challenge with *A. hydrophila*. The study emphasize a safe potential approach for vaccination strategies employing novel nanovaccines providing protection to fishes and inducing protective immunity against infectious bacterial diseases.

## Poster 08

# RELATIONSHIP BETWEEN BIOFILM FORMATION AND ANTIMICROBIAL RESISTANCE BY BACTERIA ISOLATED FROM CUTANEOUS LEISHMANIASIS WOUNDS

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Kwame Nkrumah University of Science and Technology, Ghana

### Abstract

One of the major concerns associated with cutaneous leishmaniasis wounds is the occurrences of secondary bacterial infections. This results in prolonged treatment of the disease and increase the cost of the disease management. One of the mechanisms of virulence used by bacteria in establishing these infections is biofilm formation, which is also a mechanism of resistance. This study aimed at investigating the biofilm forming ability and possible relationship between biofilm formation and antimicrobial resistance of bacteria isolated from cutaneous leishmaniasis wounds. A total of 23 resistance isolates from cutaneous leishmaniasis wounds were obtained from Department of Pharmaceutics, Kwame Nkrumah University of Science and Technology. Isolates were identified by standard microbiological procedures. Biofilm detection was carried out using the Tissue Culture Plate Method. Antibiotic Susceptibility test of biofilm producing bacteria was performed using the Kirby-Bauer disc diffusion technique using Clinical and Laboratory institute CLSI, 2018 guidelines. 60.87% were weak biofilm producers and 39.13% were moderate biofilm producers. Several relationships were observed between biofilm formation and antimicrobial resistance for each specie. Ciprofloxacin, erythromycin and tetracycline resistance was related to biofilm formation in *Staphylococcus aureus* strains, piperacillin/tazobactam and chloramphenicol in the strains of *Klebsiella pneumoniae* and piperacillin/tazobactam in *pantoea spp*. However, no relationship was observed for higher antibiotic resistance in moderate biofilm producers than weak biofilm producers. The findings of this study has revealed the formation of bacterial biofilm in cutaneous leishmaniasis wounds, and has established the need to assess biofilm formation as a mechanism of virulence in cutaneous leishmaniasis wounds.

## Poster 09

# From the Typhoid Conjugate Vaccine approved against Salmonella Typhi toward a bivalent vaccine candidate targeting both Salmonella Typhi and Paratyphi A

Francesca Micoli, Renzo Alfini, Martina Carducci, Luisa Massai, Roberta Di Benedetto, Daniele De Simone, Francesca Necchi, Simona Rondini, Omar Rossi, Carlo Giannelli

GSK Vaccines Institute for Global Health, Italy

### Abstract

The first vaccine developed at GVGH, the Typhoid Conjugate Vaccine (TCV), was registered in India early 2020 by Biological E as commercial partner, and late in the same year obtained the WHO pre-qualification to enter the GAVI Market. Antibiotic resistant Typhoid is widespread in Nepal and much of Asia. Large-scale implementation of TCV in Nepal aims to reach 95% coverage of nearly 7.5 million children between 15 months to 15 years of age and to significantly reduce the high burden of typhoid in children in the country. A first generation of TCV showed inconsistencies in Phase 1/2 clinical trials and was re-designed to improve the response in the pediatric population. We demonstrated that the polysaccharide size constitutes a critical factor to develop a glycoconjugate vaccine with a strong T-cell dependent response. Our findings will support improved design of future glycoconjugate vaccines. The successful partnership between GVGH and Biological E is continuing with the development of a bivalent vaccine, composed of the licensed TCV and a new conjugate against *S*. Paratyphi A. This combination vaccine will enter Phase 1 clinical trial later this year. The Paratyphi A component has been designed by investigating the role that different polysaccharide characteristics and conjugation parameters can have on the immune response in different animal models. With an overall 212,000 deaths caused by both *S.* Typhi and *S.* Paratyphi A and a growing resistance to antibiotics, we believe that this new bivalent vaccine will play an essential role in protecting children from enteric fever.

## Poster 10

# Production and Evaluation of purD Gene Deleted Brucella abortus as Potential Vaccine Candidate for Control of Brucellosis

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### Abstract

Bovine Brucellosis is an important zoonotic and contagious disease resulting in significant losses therefore, disease mitigation and control measures are of pronounced significance. In this study, we have constructed a purD deleted Brucella abortus. For this, the pRB-K-ΔpurD plasmid cassette was initially constructed using pUC19, kanamycin, and purD upstream and downstream fragments. Then the cassette was electroporated into electro competent Brucella abortus RB51. The ΔpurD mutant was confirmed using PCR analysis. Afterward, the growth kinetics of the mutant was compared with parent RB51. The mutant bacterial growth significantly reduces ($P< 0.05$) as compared to the parent non-mutant bacteria. However, after supplementation of purine bases, the ΔpurD mutant bacteria regain growth in enriched media. For virulence attenuation comparison with the parent RB51 strain, the constructed mutant was evaluated for attenuation estimation and clearance in BALB/c mice. The B. abortus ΔpurD mutant exhibited significant attenuation of virulence and cleared from the mice spleen after 20th DPI when inoculated at the dose of 108 CFU per mice. In contrast to this, the parent RB51 strain induces splenomegaly and showed higher persistence with significantly higher splenic CFUs in the mice group at 10th and 20th DPI as compared to B. abortus ΔpurD mutant. The findings of this study revealed that the highly attenuated B. abortus ΔpurD mutant can be used effectively as a potential live attenuated vaccine candidate for the control of bovine brucellosis both in local and international settings.

## Poster 11

# Evolution of anti-protein antibody response after *Streptococcus pneumoniae* nasopharyngeal colonisation of mice

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## Abstract

Background

Nasopharyngeal colonisation of mice results in antibody to a handful of protein antigens and provides limited cross-protection against infection with heterologous strains, whereas human sera contain antibody to multiple protein antigens and is broadly cross-protective. We hypothesised a more broadly protective antibody response requires repeated colonisation events in mice.

Methods

ELISAs, flow cytometry assays of IgG opsonisation, and a protein array of 254 conserved pneumococcal antigens were used to evaluate serum IgG responses after *S. pneumoniae* colonisation of CD1 or C57B/6 mice. Results were compared between colonisation with different S. pneumoniae strains, and between single or multiple colonisation events.

Results

In CD1 mice single colonisation events with strains TIGR4 (serotype 4), D39 (2), BHN418 (6B), OXC-1417 (23F), or EF3030 (19F) induced IgG to a mean of 15.5 (SD 5.7) protein antigens. Although many of the antigens overlapped between strains, there were also significant differences. When measured by ELISA, repeated colonisation events increased the strength of recognition of S. pneumoniae strains, and increased the number of protein antigens recognised (mean number after 3 colonisation events 38.9 SD 14.6, after 5 events 52.4 SD 11.4). Multiple colonisation events in CD1 or C57B/6 mice resulted in distinctive patterns of anti-protein antigen responses.

Conclusions

In mice, the strength of IgG responses to *S. pneumoniae* colonisation and the range of antigens recognised is increased by repeated colonisation events and is partially dependent on host genetic background. Future work will investigate how this affects immunity to infection with homologous and heterologous strains.

## Poster 12

# Antimicrobial Resistance among foodborne pathogens in some selected health facilities and food vending sites in Ghana

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### Abstract

Background: Antimicrobial resistance (AMR) of foodborne pathogens (FBP) in the food chain have become a major problem leading to difficulty in treatment options.

Methods: This study was conducted from January 2019 to March 2020 at Maamobi General Hospital, Kaneshie Polyclinic and various food vending joints in the community. Samples were transported to the Noguchi Memorial Institute for Medical Research (NMIMR) for culture, confirmation using Matrix-Assisted Laser Desorption/ Ionization-time of Flight (MALDITOF) and AMR testing. Diarrhoeagenic *E. coli* (DEC) was tested using PCR.

Results: Among a total of 122 stool samples, 62.3% of *E. coli* was isolated with Ciprofloxacin and Amoxicillin-clavulanate resistance being 35.40% and 10% respectively. Also, 16.4% *E. cloacae* were isolated from the stool samples with a 10% resistance to Amoxicillin-clavulanate. Out of the sixteen *E. coli* isolates recovered in stool, 10 were ESBLs habouring the CTX-M (9), TEM (7) and SHV (1) ESBL genes respectively. Thirty-four of the *E. coli* stool isolates possessed heat labile gene (Lt) of Enterotoxigenic *E. coli* (ETEC).

A total of 115 food were sampled from food vendors, out of which 7.8% and 16.8% *Enterococcus faecalis* and *Enterobacter cloacae* were isolated respectively. Resistance to Amoxicillin-clavulanate was 37.50% and 91.60% among the *E. faecalis* and *E. cloacae* isolates respectively. The TEM gene was found in two *C. freundii* isolates from RTE food.

Conclusion: There is evidence of emerging AMR FBP and ESBLs in Ghana. AMR profiling based on study outcome will help in updating the national standard treatment guidelines for gastroenteritis.

## Poster 13

# Characterization of Antimicrobial Resistant *Klebsiella pneumoniae* from clinical and environmental sources to facilitate future vaccine development

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### Abstract

*Klebsiella pneumoniae* (Kpn) is one of the emerging AMR pathogens that causes infections and widely distributed in environment, community and hospital settings. Vaccination can be the effective defense against this for specially LICs and LMICs where other strategies are challenging.

We have collected 130 Kpn isolates (30 from waste water in human-proximate settings and 13 from outdoor facility and 60 from indoor facility) from March 2022 and performed antibiotic sensitivity tests against 13 antibiotics (Ampicillin, Ceftriaxone, Cefepime, Levofloxacin, Ciprofloxacin, Piperacillin/Tazobactam, Amikacin, Meropenem, Ertapenem, Gentamicin, Cefazolin) using the disk diffusion method. We also subjected the Kpn isolates to whole genome sequencing using the Illumina platform to analyze genomic diversity, the presence of resistance genes and predominant K- and O- type antigens for potential vaccine candidate.

Kpn isolates from clinical sources showed resistance against most of the tested antibiotics; whereas, the environmental isolates were significantly sensitive (p value <0.05, chi-squared test) except ampicillin, imipenem-relebactam, Ciprofloxacin and Piperacillin/Tazobactam. We have completed pangenome analysis of 20 kpn isolates from indoor facility that depicts diverse ST and O-antigen types. Ongoing analyses include sequencing of more isolates from different sources and characterization of the antigen types and virulent genes. Our findings will increase the understanding of the pathogenic potential of Kpn as well as the potential vaccine candidate for defeating this AMR bacteria.

Our initial findings indicate that this diverse set of ST and O-antigen types of Kpn require more analysis to find out the potential vaccine target to reduce the AMR threat.

## Poster 14

# Pre-clinical evaluation of a novel GBS glycoconjugate vaccine candidate.

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### Abstract

Background:

Biovac and WITS-VIDA are developing a novel glycoconjugate vaccine against Group B Streptococcal (GBS) infection.

The typical glycoconjugate vaccine approach can be costly, requires significant process development, and most importantly remains vulnerable to new invasive strains.

Biovac has opted to evaluate an alternative approach utilizing a conserved GBS surface protein (gbs2106) as the carrier protein in its glycoconjugate design to:

- Enhance the immune-protection and response generated (in mice) when coupled to GBS capsular polysaccharide (CPS),

- Potentially provide coverage against all ten GBS serotypes,

- Reduce the number of GBS serotypes required for inclusion in a multivalent vaccine formulation.

- Serve as a stand-alone protein subunit vaccine

Method:

Surface protein (gbs2106) and CPS (serotypes Ia, Ib and III) were cultured at a 20 - 30 L scale and purified antigens isolated. The isolated constituents were conjugated, and the drug substance(s) purified, formulated and filled for use in a proof-of-concept, pre-clinical mice study.

Results:

The gbs2106 protein and CPS were isolated in yields of 140 - 170 mg/L and 160 - 180 mg/L, respectively. The target drug substances were generated with a conjugation efficiency of 50 - 60 %. Pre-clinical animal studies are in progress and results to be shared at the meeting.

Conclusion:

A proof-of-concept for producing novel GBS glycoconjugates linked covalently to gbs2106 has been achieved. These conjugates meet the physiochemical characteristics and quality attributes of their TT counterparts.

## Poster 15

# SimCells: Genome-free cells as vaccines against antimicrobial resistance

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### Abstract

Using live bacteria as vaccines or therapeutics has long been seen as an attractive idea, offering a way to target the immune system comprehensively. Unfortunately, the approach is difficult to control, with potentially fatal consequences given the risks associated with replication-capable pathogens. SimCell technology solves this problem by producing bacterial cells that lack genetic material and are therefore unable to divide, but which maintain intact surface features recognised by the immune system. We aim to use SimCells as prophylactic vaccines against one of today's greatest public health threats: antimicrobial resistant (AMR) bacteria.

Here, we described a proof-of-principle study using small-scale manufacturing of Escherichia coli SimCells, which were produced at a purity of less than 1 viable cell per 1 billion SimCells. There was significantly less DNA in E. coli SimCells compared to their wild-type counterparts, as indicated by nucleic acid staining and by qPCR. Using SDS-PAGE and SEM, the SimCell production process was shown to be better at preserving cell protein fingerprints and surface features compared to chemical, thermal, or irradiative bacterial inactivation methods. To assess immunogenicity, E. coli SimCells and UV-irradiated E. coli were administered to immunocompetent mice. Mice administered with E. coli SimCells produced significantly higher E. coli-specific antibodies compared to those administered with UV-irradiated E. coli (two-fold) and the vehicle control (six-fold). This work highlights the potential of utilising SimCells as effective vaccines against AMR pathogens for which antibiotic countermeasures do not exist and lays the foundation for the development of a human E. coli vaccine.

## Poster 16

# Developing a Novel Vaccine Against Multidrug Resistant *Acinetobacter baumannii* Infections

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### Abstract

*Acinetobacter baumannii* is a serious opportunistic pathogen, especially in low- and middle-income countries. Typically causing ventilator-associated pneumonia, *A. baumannii* harbours a myriad of antimicrobial resistance mechanisms causing high rates of morbidity and mortality. Hence, we aim to develop a novel vaccine therapy against *A. baumannii* targeting conserved protein antigens.

We constructed a 900-protein microarray selecting conserved proteins from Thai clinical *A. baumannii* isolates, with a bias to those that are highly expressed during growth in human sera and/or that bioinformatic analyses suggest are likely to be surface expressed. The microarray was probed with sera from mice that had recovered from a non-lethal infection with different *A. baumannii* strains. Probing the array demonstrated specific patterns of antigen recognition for sera from mice infected with different *A. baumannii* strains, although most antigens recognised overlapped between different sera. From these results, ten proteins were identified as potentially good antigens for the development of a vaccine therapy.

Antibodies against the selected protein antigens were raised in rabbits, and initial data show that IgG to four of the selected protein antigens recognise different live *A. baumannii* strains, resulting in significant levels of opsonisation when assessed using flow cytometry. Additionally, preliminary *in vivo* data suggest that antibodies against these antigens are protective in a mouse infection assay.

Overall, our data provide the groundwork for identification and development of a new vaccine therapy targeting the priority antimicrobial resistant pathogen, *A. baumannii*. Future experiments include vaccinating mice with selected protein antigens to determine their protective efficacy.

## Poster 17

# The development of bovine herpesvirus 4 (BoHV-4) vaccine vector platform to control infections in agricultural animals and reduce antimicrobial resistance (AMR)

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### Abstract

Antimicrobial resistance (AMR) is a growing problem worldwide, especially in agricultural settings where pathogens such as *Escherichia coli* (*E. coli*) and *Streptococcus suis* (*S. suis*) are widespread. With no effective vaccines available, antibiotics remain the primary antibacterial intervention. Antibiotic consumption is higher in pigs than in other livestock and over 85% of *S. suis* strains are already resistant to commonly used antibiotics including tetracycline. In clinical mastitis cases in cattle, over 28% of *E. coli* isolates demonstrate antibiotic resistance, with over half resistant to multiple antibiotics. Bacteria are a major cause of disease and productivity loss in animals, but also often represent emerging zoonotic pathogens for humans. In summary, effective vaccines for AMR pathogens are a high priority globally.

Bovine herpesvirus-4 (BoHV-4) vectors are a promising new class of viral vectored vaccines, with a number of positive characteristics. Our recent data has shown the BoHV-4 vector can be modified towards antibody or T cell responses and can be rapidly produced to target a range of pathogens. BoHV-4 vaccines are also suitable for low-cost, simple manufacturing processes that are the ideal solution worldwide, especially in LMICs. Vaccines against these common infections have the potential to reduce farming costs, stabilise food security, and enable farmers to meet likely future legislative demands to reduce antibiotic use.

Our current vaccine platform shows considerable promise towards providing an effective and safe solution with the potential to substantially reduce antibiotic resistance in both animals and in humans.

## Poster 18

# Implementing the monocyte activation test to measure the pyrogen content of vesicle based vaccines

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### Abstract

Background: Ensuring vaccines are safe is of the upmost importance when quality control testing of batches of vaccine for human administration. Traditionally biological medicines were evaluated using the rabbit pyrogen test, but issues with its suitability for vaccines and a move to eliminate animal testing accelerated its replacement with the cell-based Monocyte Activation Test (MAT).

Methods: The MAT uses human monocytic cells, which are exposed to the test substance and release pro-inflammatory cytokines in response to pyrogens. Peripheral blood mononuclear cells (PBMC) are utilised providing an IL-6 readout. When tested over a wide dilution range, the dose-response starts from background levels of IL-6 at through a linearly increasing section, to plateau levels of IL-6 at high concentrations of vaccine. Each batch of vaccine is assigned a relative pyrogen unit (RPU) concentration, which is compared to values of previously tested safe batches.

Results: The first MAT developed at MHRA was implemented for the routine testing of the 4CMenB vaccine in 2015. More recently we developed the method for testing of GMMA based vaccines. Each vaccine behaves differently requiring a bespoke reference, a consequence of the pathogen-specific PAMPs present in the vaccines which stimulate particular target receptors.

Conclusions: The MAT provides essential data on the pyrogenic content of batches of vaccine and provides an indication of the safety profile of each giving a quantitative value based on a human response and negating the need for animal testing.

## Poster 19

# DEVELOPMENT AND ASSESSMENT OF QUANTIFICATION APPROACHES FOR ANTIBIOTIC PRESCRIPTION AND USE IN THE SETTING OF FREQUENT INFORMAL ANTIBIOTIC CONSUMPTION

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## Abstract

Background

Quantifying Antimicrobial Prescription and Use (APU) is often challenging in low-income countries, especially where informal drug consumption (e.g., from market stalls) is commonplace. In the context of evaluating vaccine impact on antimicrobial resistance in Malawi (pneumococcal PCV13 vaccine, and malaria RTS,S/AS01 vaccine), here we have refined a novel multi-component strategy to robustly evaluate APU.

Methods

A cross-sectional, community-based survey in Blantyre district, Malawi, of randomly selected 4-9-month-old healthy children (January-April 2022) implemented three APU quantification approaches: (1) review of patient-retained paper-based health records, (2) direct questioning of parents/caregivers when health records were unavailable, and (3) an antibiotic recognition and use exercise (ARUE) for all participants. Approaches were compared via Cohen's Kappa.

Results

Health records were available for 346/700 children (61.3%, 95% confidence interval, CI, 50.0-72.7) of children. At least one APU occasion was recorded in 46.8% (CI 38.5-55.1) of all children via health records; 22.2% (CI 9.1-35.3) via directly questioned parents/caregivers, and 76.0% (CI 72.8-79.1) via the ARUE. ARUE-health record and ARUE-direct questioning agreement was good (kappa=0.65, P<0.001), and poor (kappa=0.12, P<0.001), respectively. Combining all approaches, APU was reported in 80.8% (CI 78.4-83.3) of total children, with 6.6% (CI 3.6-9.6) of children possessing a health passport having no evidence of a prescription, suggesting informal antibiotic use.

## Conclusion

We have demonstrated the utility of a multi-component APU quantification approach when health record availability is poor. Our findings indicate high antibiotic exposure early in life in this population, with a relatively modest but important contribution from informal sources.

## Poster 20

# EPIDEMIOLOGY OF KLEBSIELLA PNEUMONIAE FROM NEONATAL INFECTIONS, IN KAMPALA UGANDA, TO INFORM VACCINE COVERAGE ESTIMATES

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## Abstract

Background

Globally, *K. pneumoniae* (Kp) causes 17-21% of neonatal sepsis and 23% in Uganda with increasing antimicrobial resistance (AMR). Neonates may acquire *Kp* following exposure to maternal vaginal/gastrointestinal microbiota at delivery. *Kp* is a Gram-negative bacterium, with ≥78 capsular polysaccharides (K antigen) and 12 lipopolysaccharides (O antigen) which are being investigated as vaccine candidates. Our aim was to assess genetic diversity of *Kp* from neonatal infections.

Methods

To examine diversity, virulence, and antimicrobial resistance genes, whole genome sequencing (Illumina) was performed on 28 *Kp* isolates from newborns with invasive disease in Uganda between 2019-2021. 24 draft genomes were assembled (Shovil), and Multilocus sequence typing (MLST), AMR, K-antigen, and O-antigen profiles (Kleborate) were extracted and analyzed, and results were linked to clinical data.

Results.

The case fatality rate among 24 Kp infections was 41% (n=10). Among 16 sequence types (STs), ST2570-1LV and ST39 (n=3), ST14, ST25, and ST1800 (n=2 each) were most frequent. There were 11 K and 4 O type combinations with O2v2: KL149 (n=3), O2v2: KL8, O4:KL131 and O5:KL115 (n=2, each) most frequent. 18 (75%) *Kp* had ESBL genes with blaCTX-M-15 found in 72% (n=13). 10/24 had virulence score of 1 (yersiniabactin only), all ybt16 lineage ICEKp12. ST14, ST39, ST25, ST307, and ST39-1LV (n=2, each) had virulence and AMR genes.

Conclusion.

Our results show diverse K/O types and STs, some of which have not been seen in other regions of LMICs. This highlights the importance of the global neonatal epidemiology of *Kp* to inform potential vaccine coverage.

## Poster 21

# Multispecies Quartet Nanocages Elicit a Broad Antibody Response for Proactive Vaccinology

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## Abstract

A critical issue facing many vaccines is the difficulty of protecting against pathogens with substantial genetic diversity. One solution pioneered to address this problem is an immunization strategy where proteins from several evolutionarily-related pathogens are presented on a single virus-like particle scaffold. Co-display of these antigens elicits a strong antibody response to evolutionarily conserved regions, which are not the major target of conventional vaccines. Here we have generated anemone-like nanoparticles where a quartet of tandemly linked Receptor-Binding Domains from human, bat, and pangolin sarbecoviruses couples on the 60-valent mi3 nanocage through a SpyTag/SpyCatcher spontaneous reaction. These Quartet Nanocages induce a high level of antibodies against antigens from the range of pathogens included on the vaccine, as well as to related pathogens not present in the vaccine. Inducing neutralizing antibodies against pathogens not represented in the vaccine underlines the potential for this strategy to protect against novel variants of the primary pathogen, as well as emergent zoonotic pathogens. Quartet Nanocages also provide improvements in homogeneity in comparison with existing vaccine strategies. In animals primed with a single vaccine antigen, boost immunizations with Quartet Nanocages increased the strength and breadth of an otherwise narrow immune response. The ability to generate a potent antibody response to the primary pathogen, despite using a Quartet immunogen lacking any sequence from the primary pathogen, suggests the potential to generate pre-emptive vaccine libraries, where each member protects against a set of related pathogens. Quartet Nanocages could therefore facilitate proactive protection against an emergent 'Pathogen X'.

## Poster 22

# Using the human immune repertoire Kymouse™ platform for vaccine and monoclonal antibody development for infectious diseases

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### Abstract

The Kymouse™ platform uses highly engineered strains of transgenic mice that contain fully human immunoglobulin loci, providing an experimental model for assessing human antibody responses to different antigens and vaccine candidates. Mice from the Kymouse™ platform can be immunised with defined immunogens, following which secondary lymphoid organs are extracted and undergo single-cell B cell sorting. These B cells are sequenced using NGS and analysed using Kymab's proprietary IntelliSelect® pipeline to identify high quality paired antibody sequences that can be used to express monoclonal antibodies (mAbs) for high-throughput screening. Once lead antibodies have been identified, further deep repertoire mining can be applied to discover related antibodies with unique biological properties.

This platform can be used to test novel antigen configurations and formulations - simultaneously assessing their vaccine potential and mining for potent therapeutic antibodies against infectious diseases. We have active projects in several infectious disease areas, including Coronavirus, malaria, RSV, influenza and *Acinetobacter baumannii*.

Identifying tractable therapeutic antibody or vaccine targets for antimicrobial resistant (AMR) bacteria could provide valuable therapeutic options. Using target agnostic strategies by immunising with bacterial outer membrane vesicles or whole inactivated pathogens, we are able to generate mAbs against relevant surface structures and with therapeutic potential against AMR bacteria.

## Poster 23

# Vaccination and Niche Competition for Targeted Exclusion of Antibiotic Resistant Bacteria from the Gut

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### Abstract

Diarrheal disease is still among the leading causes of morbidity and death worldwide. Moreover, gut pathogens associated with these diseases - such as E. coli and non-Typhoidal Salmonella - can cause invasive infections and are increasingly resistant to antibiotics. Therefore, an alternative strategy for treatment independent of antibiotics is urgently needed.

Live-attenuated vaccines against non-Typhoidal Salmonellosis (NTS) exist for the use in livestock. However, direct translation to humans is challenging as these vaccines pose a major safety concern in immunocompromised individuals. Moreover, these vaccines provide protection from invasive disease but are known to have limited effects on colonization. Instead, we propose a two-pronged strategy that combines a negative selective pressure induced by inactivated oral vaccines, with benign bacterial niche competitors.

We have validated this approach in a murine NTS model and compared it to the classical live-attenuated vaccines. Oral vaccination induces a strong specific IgA response and leads alone to a significant decrease in Salmonella-driven intestinal inflammation. In combination with a niche competitor, we could achieve complete elimination of pathogenic Salmonella from fecal samples and robust protection from intestinal disease. Moreover, a single dose of our Salmonella vaccine could induce robust and long-lasting immunity against Salmonella in domestic pigs. Preliminary data indicates that this technique will be broadly applicable to other Enterobacteriaceae.

Taken together, vaccination/competitive exclusion approaches hold great promise in the prevention, elimination and/or treatment of antimicrobial resistant infections. Moreover, the generation of sterilizing immunity against pathogenic bacteria raises the possibility to drive pathogen extinction.

## Poster 24

# Exopolysaccharides from probiotic strain *Bacillus licheniformis*: insights on antibiofilm efficacy against pathogenic bacteria

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### Abstract

Currently, biofilm formation is a major issue in biomedical and industrial sectors, and it has been attributed to the occurrence of antibiotic resistance development in bacteria. Besides, multidrug-resistant (MDR) bacteria and their related biofilms exemplify a crucial risk to the healthcare system worldwide. So, there is growing attention in research on the discovery of antimicrobial and antibiofilm agents to control the growth of pathogenic bacteria. Though, the utilization of microbial exopolysaccharides has become an alternative of interest as immunostimulatory and antioxidant agents in various industries. Here, we investigated the isolation of exopolysaccharide from *Bacillus licheniformis* Dahb1 and its biomedical applications. Exopolysaccharide from *Bacillus licheniformis* (EPS-*B.lichen*) was extracted using the ethanol precipitation method and structurally characterized. FTIR and $^{1}$H-NMR pointed out the presence of various functional groups and primary aromatic compounds, respectively. EPS-*B.lichen* exhibited strong antioxidant potential confirmed via DPPH radical scavenging assays. Microscopic analysis revealed the antibiofilm activity of EPS-B.lichen (75 µg/ml) was higher against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. These findings pointed out the multipurpose bioactivity of EPS-*B.lichen*, which deserves further consideration for pharmaceutical and biomedical applications.

## Poster 25

# Population-Level Genomic Klebsiella pneumoniae Serotype Surveillance Informs Vaccine Development for neonatal sepsis and Invasive Infections

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### Abstract

Background: K.pneumoniae is an urgent health concern. Vaccines based on surface polysaccharides are highly promising. The study aimed to determine the diversity and distribution of K. pneumoniae O/K antigens in Indian patients to inform vaccine development efforts.

Methods: 195 K.pneumoniae isolates collected from blood of patients in 16 regions of India during 2013-2022 were subjected to genome sequencing. The assembled data was analysed to elucidate O/K-loci types.

Results: 30 different K-loci were identified in the study. KL64(30%), KL51(23%) and K2(8.2%) were predominant while K1 and K2 was 2% and 8% respectively. 46.5%of KL-64 and 89%of KL-51 belong to clonal lineage ST147 and ST231 respectively. Strikingly, virulence and antibiotic resistance genes were present in high proportion(70.3%virulence, 90.8%resistance) among KL51 strains where as their presence was 31.4% and 90.9% in KL64 strains.

Serotypes-O1/O2v1(45%) and-O1/O2v2(30%) were prevalent. 67% of O1/O2v2 strains harboured KL51 loci and were associated with ST231 clonal lineage, which is a predominant lineage in India. The distribution of virulence and resistance genes was 22.7% and 79.8% among O1/O2v1 strains whereas their presence was 58.6% and 69.6% in O1/O2v2 strains.

Conclusion: The study reveals the existence of diverse population pool of K-antigens among the Indian circulating strains of K.pneumoniae which is different from other parts of the world. The study isolates in addition, displayed a high diverse STs, virulome and resistome. On the contrary, O-antigens were less diverse. The diversity of circulating population has to be considered while developing vaccines.

## Poster 26

# NIHR-Global health research unit focusing on antimicrobial resistance bridging the knowledge gap – Experience of GHRU-India unit

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### Abstract

AMR is increasingly predicted to affect health and wellbeing on an international scale. Reducing AMR and preventing the spread of AMR organisms requires understanding the mechanisms of resistance, transmission routes and the epidemiology of AMR organisms. New technologies and greater understanding are required to mitigate against and reduce resistance to effective treatments against infectious diseases. There was lack of India data depicting the circulating high risk clonal lineages of bacterial pathogens.

Since 2017, the centre based in Oxford has coordinated the implementation of an AMR monitoring project at GHRU site in India and has helped improve the detection and tracking of outbreaks and AMR populations. In India, samples have been collected and sequenced through laboratories to create an extensive genome database of more than 5000 samples that helps inform local transmission patterns. Data collected on Streptococcus pneumoniae has provided information on circulating subtypes that are being used to inform vaccine development. GHRU India centre has identified the potential high-risk lineages in India addressing the knowledge gap. Indian Genomic datasets of WHO priority pathogens like K.pneumoniae, E.coli, S.aureus, A.baumannii, P.aeruginosa etc. are now in public domain to inform intervention strategies.

Going forward the need for local data science and engineering and linking of clinical and epidemiological data to genomics is apparent. By linking data and its interpretation we aim to rapidly increase value to public health decision makers at a local level, as well as the routine combination of data aggregated at regional, national, and international levels to inform vaccine design

## Poster 27

# Assessing serological diurnal responses to pneumococcal vaccination in healthy older adults

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### Abstract

Introduction: The aim of this project was to determine whether the diurnal timing of a single dose of Pneumovax® (PPV23) affects the innate and adaptive immune responses in healthy older adults where responses may be impaired due to immunosenesence.

Materials and Methods: 111 adults (> 50) received the PPV23 vaccine (57 AM, 54 PM). Pn-specific IgG, IgA and IgM were measured using an in-house Luminex assay. Pn-specific IgG protection was based on WHO thresholds (≥0.35µg/mL). Cytokine ELISAs (IL-1β, IL-6, IL-8, IL-10 and MCP-1) were performed to determine the innate immune response to vaccination.

Results: Over half of the participants were protected against 8/12 Pn serotypes at baseline (53% AM/PM) and week 1 (72% AM v 74% PM), which was maintained at week 4-52 (84% AM v PM 85%). Pn-specific IgG, IgA and IgM did not vary between AM and PM (ns). IL-6, IL-8 and MCP-1 displayed diurnal variation with significantly higher concentrations demonstrated in the AM (IL-6 baseline: P=0.0155/IL-6 week 1: P=0.0363, IL-8 baseline: P=0.0033/IL-8 Day 1: P<0.0001/IL-8 week 1: P<0.0001 and MCP-1 week 1: P=0.0114). However, higher concentrations of IL-8 (AM) at day 1 (P<0.0004) and week 1 (P<0.008) and lower concentrations of MCP-1 (PM) at week 1 (P<0.0209) were associated with a robust IgG vaccine response.

Conclusion: Timing of PPV23 did not influence Pn-specific antibody concentrations. However, diurnal variation of IL-8 and MCP-1 highlighted associations with robust Pn-specific IgG vaccine responses suggesting that they may prove advantageous when developing future vaccination strategies in healthy older adults.

## Poster 28

# Intradermal Immunization with Heat-Killed Klebsiella pneumoniae Leading to the Production of Protective Immunoglobulin G in BALB/c Mice

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**Abstract**

Introduction: Klebsiella pneumoniae superbug is emerging as a serious health concern as resistance to last-resort antibiotics spreads. To bypass the therapeutic molecules used today, the development of an immunoprophylactic safe approach is of great clinical relevance. This study was conducted to determine the protective efficacy of antibodies elicited by killed vaccine against multidrug-resistant (MDR) K. pneumoniae.

Materials and Methods: In this study, heat-killed MDR K. pneumoniae isolated from different clinical samples were employed for the intradermal immunization of 10 BALB/c mice. Two weeks after the third dose of immunization, the mice were intraperitoneally challenged with live K. pneumoniae and observed for 14 days. Tail blood was collected 7 days after each booster followed by cardiac puncture 14 days post challenge. Bactericidal activity and antigen-binding capacity of the serum antibody produced by the vaccine were evaluated by serum bactericidal antibody (SBA) assay and ELISA, respectively.

Results: In this study, 80% survival rates were observed at 14 days post challenge among the immunized mice. Regarding SBA assay, 100% bactericidal activity of the immunized mouse sera was observed using 50% guinea pig complement at 1:10 serum dilution after 3 hours of incubation, and all the pre- and post challenge immunized serum immunoglobulin G antibody had significantly higher optical density values comparing the control mice in ELISA.

Conclusion: In our study, intradermal immunization with heat-killed MDR K. pneumoniae produced protective antibodies in BALB/c mice. These findings inspire the development of future vaccines against this deadly pathogen in resource limited setting.

## Poster 29

# Colonization and AMR profile of ESKAPE pathogen, Acinetobacter baumannii isolated from healthy veterinary samples

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### Abstract

Introduction

Until 2000's Acinetobacter (A.) baumannii infections were rare and was readily treated. During the COVID-19 pandemic, infections with carbapenem-resistant Acinetobacter species reported to have increased. A. baumannii, one of the six leading nosocomial infections, accounted for 600,000 to 1,400,000 infections globally per year. The clinical samples from animals and humans share identical clones, suggesting that the animals may act as reservoir. however, data from animal origin especially from healthier ones are rarely available to establish A. baumannii interplay between environment, animals and humans. And there is no study reported on these aspects from India.

Methods

This study involves isolation of A. baumannii from five different systems (integumentary, digestive, respiratory, excretory, and urogenital system) of healthier animals (large ruminants, small ruminants, and poultry) in the rural region of Guntur, India. MALDI TOF MS was used for species identification and Kirby Bauer disc diffusion assay was used for AMR profiling for 16 antibiotics, which represented eight different antibiotic classes.

Results

This exploratory research resulted in 51 non-duplicated isolates, which is 49% prevalence. Salivary samples did not yield any isolation. The isolates except those isolated from excretory system (n=10, ~ 20%) possess comparable antimicrobial profiles: resistant to penicillin, aminoglycoside, cephalosporin and lincosamide, intermediate resistance to fluoroquinolone, meropenem (carbapenem) and vancomycin (glycopeptide) and susceptible to tetracycline.

Conclusion

A. baumannii isolated from excretory systems of animals display a unique pattern of antibiotics resistance. Further research is needed to ascertain the clone level colonisation pattern of the strains isolated from various systems of the animals.

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