Innovative HIV-1-specific CD8+ T-cell epitopes revealed in human recipients of conserved-proteome T-cell vaccine

Y. Mohamed [1,2,*], T. Hanke [1]

[1] *The Jenner Institute, University of Oxford*
[2] *Imam Abdulrahman Bin Faisal University*

Background: Optimum characterization of targeted CD8+ T-cell epitopes and their human leucocyte antigen (HLA) class I restriction enlightens iterative improvements of HIV-1 T-cell vaccine designs and may predict early vaccine success or failure. In our study, lymphocytes from volunteers, who had received candidate HIVconsv DNA vectoredvaccines expressing sub-protein conserved regions of HIV-1, were used to define the optimum-length target epitopes and their HLA restriction. In HIV-1-positive patients, CD8+ T-cell responses predominantly recognize immunodominant, but hypervariable and therefore less protective epitopes. The less variable, more protective epitopes in conserved regions are typically subdominant. Therefore, induction of strong responses to conserved regions by vaccination provides an opportunity to discover novel protective epitopes.

Methods: Cryopreserved lymphocytes from vaccine recipients were expanded by stimulation with 15-mer responder peptides for 10 days to establish short term-cell-line STCL) effector cells. These were subjected to intracellular cytokine staining using serially truncated peptides and peptide-pulsed K562 cells, engineered to express individual.

HLA class I alleles, to define minimal epitope sequence and HLA restriction by stimulation of IFN-γ production.

Results: Using lymphocyte samples of 20 vaccine recipients, we defined 8 previously unreported optimal CD8+ T-cell HIV-1 epitopes and their four-digit HLA allele restriction tentatively. Further 13 predicted, but un-reported epitopes with incomplete information were revealed.

Conclusions: The high rate of discovery of novel CD8+ T-cell effector epitopes warrants further epitope mapping in recipients of the conserved-region vaccines in other populations and informs development of HIV-1/AIDS vaccines.

https://doi.org/10.1016/j.jiph.2018.10.129

Eosinophilic gastroenteritis: An atypical cause for chronic diarrhea in human immunodeficiency virus-associated immunosuppression

O. Srivastava [1,*], N. Parikh [1], A. Jhaveri [1], R. Ahlawat [2], I. Bagasrawala [3]

[1] *Jaslok Hospital And Research Centre*
[2] *Marshfield Clinic Children's Medical Center*
[3] *Saifee Hospital*

Eosinophilic gastroenteritis is an uncommon disease in both immunocompetent and immunocompromised patients.

We describe a 57-year-old male with human immunodeficiency virus (HIV) who presented with chronic diarrhea. He had no history of allergies, had significant weight loss, normal systemic examination and a complete blood count showing no eosinophilia. On further evaluation, the diagnosis of eosinophilic gastroenteritis was made by histopathological findings.

Primary Eosinophilic Gastroenteritis has not been reported before in HIV associated immunosuppression and should be kept as a differential diagnosis in HIV patients with chronic diarrhea.

https://doi.org/10.1016/j.jiph.2018.10.130

Detection of Metallo β- Lactamase producing Pseudomonas aeruginosa isolated from patients in Saudi Arabia

M. Al Zayer [1,*], M. AlGhoribi [1,2], E. Al Rashidi [1], N. Alhuseinan [1], B. Al Alwan [3], B. Bakhashween [3], M. Kaaki [4], M. Doud [5], H. Al Sadah [6], A. Ahmed [7], S. Al Johani [2,3], H. Balkhy [1,2,8]

[1] *King Abdullah International Medical Research Center, Riyadh, Saudi Arabia*
[2] *King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia*
[3] *Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City Riyadh, Saudi Arabia*
[4] *Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City Jeddah, Saudi Arabia*
[5] *Department of Pathology and Laboratory, Prince Mohammed Bin Abdulaziz Hospital in Al Madinah, Saudi Arabia*
[6] *Department of Pathology and Laboratory, Imam Abdulrahman Al Faisal Hospital, Dammam, Saudi Arabia*
[7] *Department of Pathology and Laboratory, King Abdulaziz Hospital Al Ahsa, Saudi Arabia*
[8] *Infection Prevention and Control Department, King Abdulaziz Medical City, Riyadh, Saudi Arabia*

Background: Pseudomonas aeruginosa is the most common opportunistic pathogen associated with community and hospital-acquired infections worldwide. Treatment of P.aeruginosa infections is becoming more challenging over years due to its ability to rapidly develop resistance against multiple classes of antibiotics including carbapenems. Carbapenems are considered one of the last resort choice of treatment for severe infections caused by P. aeruginosa. The main resistance mechanism is the production of Metallo β-Lactamase (MBLs), through the acquisition of resistance genes encoding carbapenem-hydrolyzing enzymes related to class B β-Lactamase such as IMP, VIM and NDM. These enzymes are encoded by genes located within mobile genetic elements that facilitate their speared among strains and across species. Therefore, detection of MBL is crucial for the optimal treatment and control of drug resistance among patients.

Objective: To detect the presence of MBLs in P.aeruginosa using genotypic method and to assess the efficiency of phenotypic assays for MBL detection.

Materials and Methods: A total of 184 P.aeruginosa isolates were collected from five different hospitals in Saudi Arabia throughout National Guard Health Affairs AMR surveillance program. Susceptibility testing was performed using the Vitek II system with AST-N292 card, Modified Hodge Test (MHT) and manual MICs. Selected isolates were screened using PCR for the presence of MBLs (IMP, VIM and NDM) encoding genes.

Results and Discussion: The results of Vitek II system indicate that 39 isolates were resistant to meropenem and imipenem. PCR analysis showed that 7 out of 39 carry bla VIM resistant gene and none of the isolates found to carry either bla IMP or bla NDM-1

resistant genes. All 7 carried blaVIM resistant P.aeruginosa isolates were found to be MBL producers by MHT and MICs methods. This indicates that the incidence of genes responsible for carbapenemase production in P.aeruginosa is of concern and further molecular investigations are required.

https://doi.org/10.1016/j.jiph.2018.10.110

Bioinformatics Analysis pipeline of Whole-Genome Sequence Data to Investigate Antimicrobial Resistance

A. Alswaji[1,*], M. Alghoribi[1,2], M. Doumith[1], H. Balkhy[1,2,3]

[1] *Infectious Diseases Research Department, King Abdullah International Medical Research Center*
[2] *King Saud bin Abdulaziz University for Health Sciences*
[3] *Infection Prevention and Control Department, King Abdulaziz Medical City*

Background: Next generation sequencing (NGS) is rapidly becoming the technique of choice for the investigation and prediction of antimicrobial resistance (AMR) at an unprecedented scale. Whole-genome sequence data enables the analysis of the genetic information of AMR genes and the assessment of virulence and relatedness among the pathogens carrying these genes. Currently, there is a paucity of microbial genomics and bioinformatics-based research to improve understanding of AMR challenges in the Gulf Health Council (GHC) countries. Here we present the bioinformatics pipeline in development at KAIMRC to identify molecular mechanisms of AMR from genomes sequenced using Illumina platforms.

Methods: The bioinformatics pipeline includes i) read quality assessment and trimming ii) read mapping to reference sequences to detect multi-locus sequence types (MLST), virulence and AMR genes iii) assembly and annotation iv) single-nucleotide polymorphism (SNP) detection and phylogenetic analysis. It was developed using publicly available and open source software and in-house scripts for automation and data management. The pipeline was evaluated on 22 genomes from multidrug-resistant klebsiella pneumoniae isolates recovered from patients at King Abdulaziz Medical city, Riyadh, sequenced locally using Illumina Miseq.

Results: The pipeline showed that the K. pneumoniae isolates comprised of eighteen ST14, two ST147, one ST231 and one ST278. Comparative analysis and phylogenetic tree using SNP identified relatedness among the isolates belonging to ST14. Resistance genes detected including NDM-1, OXA-48, OXA-9, OXA-1, mph(A) and msr(E) using the pipeline correlated with the phenotypic resistance profiles.

Conclusions: The validation of our pipeline showed its potential to accurately detect AMR genes and assess relatedness amongst isolates during outbreaks. It is suitable for the study of any bacterial pathogen although further development is required for the full automation.

https://doi.org/10.1016/j.jiph.2018.10.042

A Snapshot about the Mobile Colistin Resistance (mcr) in The Middle East and North Africa Region

A. Redhwan[1,2,*], M. Choudhury[2], B. Al Harbi[2,3], A. Kutbi[2,4], M. Alfaresi[5], R. AlJindan[6], H. Balkhy[7,8,9], S. Al Johani[10], E. Ibrahim[11], A. Deshmukh[11], M. Ahmed[11,12], A. AlJardani[13], S. Al-Abri[14], J. AlSalman[15], A. Dashti[16], S. Abdelrahman[17], M. Shabban[17], A. Aqel[18], H. AlZoubi[18], H. Sidjabat[2], T. Walsh[19], D. Paterson[2], H. Zowawi[2,7,8]

[1] *College of Health and Rehabilitian Sciences, Princess Nourah University*
[2] *UQ Centre for Clinical Research, The University of Queensland*
[3] *Faculty of Pharmacy, Taibah University*
[4] *Faculty of Medicine, Taif University*
[5] *Pathology and Laboratory Medicine Department, Sheikh Khalifa General Hospital*
[6] *College of Medicine, Imam Abdulrahman Bin Faisal University*
[7] *King Saud bin Abdulaziz University for Health Sciences*
[8] *King Abdullah International Medical Research Centre*
[9] *WHO Collaborating Centre for Infection Prevention and Control, and GCC Center for Infection Control*
[10] *Microbiology, Department of Pathology and Lab Medicine, King Abdulaziz Medical City*
[11] *Department of Neurosurgery, Hamad Medical Corporation, Weill Cornell Medical College*
[12] *The Life Science Centre Biology, School of Science and Technology, Örebro University*
[13] *Public Health Laboratory, Medical Microbiology Department*
[14] *Department of Medicine, The Royal Hospital*
[15] *Samlaniya Medical Complex, Infectious Diseases Unit*
[16] *Medical Laboratory Department, Faculty of Allied Health Sciences, Health Science Center, Kuwait University*
[17] *Faculty of Medicine, Medical Microbiology and Immunology dept. Ain Shams University*
[18] *Faculty of Medicine, Mutah University*
[19] *Department of Medical Microbiology and Infectious Diseases, School of Medicine, Cardiff University, Heath Park*

Background and Purpose: The emergence of colistin resistance among GNB is overwhelming. The recent reporting of the novel plasmid mediated colistin resistance genes (mcr-) is a serious concern and intimidating to accelerate the spread of pandrug resistant bacteria. To date, eight different mcr- genes were described. A number of studies have confirmed the worldwide dissemination of the mcr-1, and other MDR genes in several Enterobacteriaceae, including E.coli, Klebsiella pneumoniae and Salmonella spp. Yet, few data are available on the dissemination of mcr-genes other than mcr-1in human samples, in the MENA Region.

Methods: A multiplex PCR assay was used to screen for the presence of mcr-1 to mcr-5 in large collections of >1,000 GNB of human origin. The isolates were collected from the GCC countries, Egypt and Jordan, for surveillance purposes of MDR GNB. Pooling of the isolates were prepared to expedite the screening process. Positive controls of mcr-2, mcr-4 and mcr-5 genes were synthesized using