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GPI-anchored CCL28 as a strong mucosal immunostimulator with influenza VLPs

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Background: Influenza presents a major health problem, affecting hundreds of millions of people with high morbidity and mortality. Because of the importance of immunological regulations at mucosa, protection provided at the pathogen's entry site, and promising results with different infectious diseases at mucosa, in both clinical and experimental settings, it would be advantageous to study the mucosal adjuvant with influenza antigens.

Methods & Materials: The M1, HA/M1, HA/M1/GPI-CCL28 VLPs were prepared by co-infecting Sf9 insect cells with rBVs expressing M1, HA and GPI-CCL28. The surface expression and in-vitro chemotactic activity towards CCR3+/CCR10+ cells of GPI-CL28 were checked using flowcytometry. All prepared VLPs were characterized and immunized in mice intranasally. The IgG/IgA responses were investigated in sera, tracheal, lung, and intestinal washes. We analyzed CD4+ IFN-γ− cells for proliferation and CD8+ CD107a+ cells for cytolytic activities using FACS at spleen, lung, mediastinal lymph nodes, and peyer's patches. The Th1/Th2 cytokine and IgG/IgA secreting cells were estimated using ELISPOT while total concentration were checked by sandwich ELISA. Protective studies were evaluated in animals across distantly related subtypes.

Results: The HA/M1/GPI-CCL28 VLPs showed in-vitro chemotactic activity for CD3+/CCR3+/CCR10+ cells and CD19+/CCR3+/CCR10+ cells. The end point titer for IgG in sera and IgA in mucosal washes ranged between 51200-102400 and 6400-12800 respectively, in HA/M1/GPI-CCL28 VLPs, significantly (p<0.0001) higher (4-6 fold) than HA/M1 VLPs alone or HA/M1 VLPs with sCCL28 (soluble) with significantly higher IgG/IgA secreting cells. The IgG2a was observed higher than IgG1, indicating Th1 type of immune response. Half the titer was significantly (p<0.001) higher (3-5 fold) in antibodies with HA/M1/GPI-CCL28 VLPs than other formulations. The HA/M1/GPI-CCL28 VLPs induced cell proliferation but not encouraged cytolytic activities. During cytokine estimations, a high IFN-γ and IL-2 with low IL-4 and TNF-α were observed. Protective efficacy was determined by challenging with A/H1N1/2/1918/H3N2 (homologous) and A/Philippines/2/1982/H3N2 (drifted) viruses and showed 100% and 80% survival in respective viruses, with no significant body weight loss, in the group of HA VLPs containing GPI-CCL28.

Conclusion. The GPI-CCL28 in influenza VLPs act as a strong immunostimulator at both systemic and mucosal sites when compared with influenza VLPs without CCL28, or influenza VLPs mixed with sCCL28, with significant protection in animals across distantly related subtypes.

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Serological and molecular investigation of dengue, chikungunya and rift valley fever in febrile and non-febrile patients from northern Mozambique during Dengue outbreak, 2014


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Background: Arboviruses represent the most rapidly spreading mosquito-borne viruses worldwide. In Mozambique, arboviruses have been heavily neglected and for this reason they are never considered in the differential diagnosis of acute febrile illness. A recent dengue outbreak was reported in Pemba, situated in northern Mozambique in 2014, and during the outbreak more than half of dengue suspected cases had their dengue results negative, suggesting other causes of fever of unknown origin. The aim of the study was to investigate the circulation of dengue (DENV), chikungunya (CHIKV), west nile virus (WNV) and rift valley fever (RVF) in febrile and non febrile patients in Pemba, during the outbreak of dengue in 2014.

Methods & Materials: A total of 398 individuals were identified, of which, 300 were non febrile and 98 were dengue suspected cases (febrile) attending the outpatient appointment visit at Pemba Provincial Hospital, between March and April 2014 were enrolled in this study. Blood samples were collected from each participant and initially tested for dengue using IgM anti-dengue commercial ELISA and by real time PCR. All dengue negative samples were then tested for chikungunya, RVFV, WNV using the PCR and indirect immunofluorescence assay (IFA) for IgG detection.

Results: Of the 398 participants 37.7% (37/98) were DENV positive using PCR and all were negative for CHIKV, RVF and WNV when tested by PCR. Among febrile patients, IgG antibodies against CHIKV were detected in 27.5% (27/98) of febrile participants by IFA, 10.2% (10/98) were dual positive for IgG anti-DENV and IgG anti-CHIKV and 3.06% (3/98) were positive for IgG anti-RVF. The percentage of positive results for IgG antibodies against DENV, CHIKV, RVFV among non febrile participants were 26% (78/300), 45.3% (136/300) and 1% (3/300), respectively. No sample was positive for IgG anti-WNV antibody among non febrile patients.
Leishmania disease gap analysis study - Pakistan

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**Background:** Pakistan is rated among one of the high Leishmania prevalent countries. The rising incidence of Leishmania in Pakistan are marked by poverty, poor healthcare, inadequate vector control, refugees, inadequate healthcare system and drug shortages. Disease is being reported from all over the country specially the remote underserved mountainous areas of Sindh, Khyber and Baluchistan provinces.

To address this Pakistan OneHealth Alliance (POHA) in partnership with Ministry of Health Services (MOHS), and partners undertook, first ever, Gap Analysis Study in during April – October 2015. Plan was not only to identify gaps between diagnosis and management, but also, to help suggest a strategic plan to improve diagnosis, treatment, control and disease prevention.

**Methods & Materials:** A multidimensional approach was adopted to undertake this study. Primarily this was a cross sectional study based on questionnaire survey. Questionnaire were developed for multiple levels of healthcare system including community and patients. Data was captured from all over the country including some of the refugees camps.

**Results:** Cutaneous Leishmania (CL) is reportable under in National Health Information Systems. Clear inter provincial differences exist for disease reporting. 15 districts were found very high disease incidence. Unfortunately, for this disease there is neither an exclusive control program or integrated with some other disease. Only 38% of the facilities surveyed had adequate manpower and diagnostic facilities for the disease. There existed issues with availability of efficient detection and response system, staff training and availability of drugs. In about 50% of facilities there existed severe drug shortage. Despite the high cost antimony injection was the main line of treatment for CL. This was followed by glucantime and cryotherapy. These drugs are neither manufactured.

**Conclusion:** Disease control demand greater political commitment by all stakeholders. Aggressive health education campaigns, inter sectoral collaboration, proper vector control, drug supply and preventive measures are desired to address this menace.

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**Synthetic DNA encoded antibody prophylaxis confers rapid protective immunity in vivo against Chikungunya virus infection**

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**Background:** Chikungunya (CHIKV) disease is a serious emerging mosquito-transmitted viral infection responsible for epidemic outbreaks. Currently, no licensed vaccines or therapies are available against this virus, resulting in significant global spread with concurrent population morbidity.

**Methods & Materials:** This study describes a novel immune-based intervention that utilizes in vivo deliver of synthetic DNA plasmids encoding a monoclonal antibody (mAb) targeting the CHIKV envelope protein.

**Results:** Importantly, a single intramuscular injection with a DNA plasmid expressing an anti-CHIKV mAb produced antibodies in mice more rapidly than vaccination with CHIKV-Env-encoding DNA plasmid. DNA-mediated delivery of anti-CHIKV antibodies in vivo based intervention that utilizes concurrent population morbidity.

**Conclusion:** This study illustrates the ability of antibody-encoding plasmids to induce rapid protection against CHIKV highlighting the potential of this novel immunoprophylaxis and therapeutic applications platform for other emerging infectious pathogens.