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siRNA based TLR7/8 activation, MHC class I recycling from endosome and cross presentation of HIV-1 antigen for elevated CD8+ response: An approach for intracellular vaccine

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Toll like receptor (TLR7/8) are potential for production of Interferon type I (INF-I) molecules, which are known for their anti-viral activity. Here we report a synthetic siRNA-fusion peptide based complex that enabled the INF-I production via TLR7/8 and also inhibited Nef mediated MHC class I (MHC-I) down regulation in HIV-1 infected cells. We reported recycling of Nef transported MHC-I from late endosome/early lysosome using TBEVsE (*Tick-borne encephalitis virus soluble* Envelope) peptide with conserved His323 residue. TBEVsE fusogenic complex was able to salvage intact heavy chain-β2m heterodimer with HIV-1 antigen bounded confirmation, resembling the cross presentation of MHC-I. Rescued MHC-I was then circulated back to the cell surface and thus up regulated CD8+ CTL activity in HIV-1 infected cells. The synthetic silencing pathway also differentially silenced MYD88 *in vitro* hindering the initiation of INF-I related inflammosomes. This study indicates that there are in fact possibilities for intracellular vaccine mechanism which can harness innate as well humoral immune system against HIV. It shows great potential since transplantation of engineered haematopoetic stem cells expressing the mechanism we reported here can be a potent weapon against chronic viral infection like HIV.

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Tuberculosis (TB) drug resistance is a global treat now a days

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Background: Tuberculosis (TB) drug resistance is a Global treat now a days. The impact of Multi drug resistant tuberculosis (MDR-TB) is dangerous especially in resource limited countries like Ethiopia because of its financial and skilled human power required for diagnosis and management

Objective: The study aim was to determine risk factors for tuberculosis (TB) caused by multi drug resistant *Mycobacterium tuberculosis* (MDR-TB) in Oromia region, Ethiopia.

Methods: In a 6 months case control study in 2013-14, sputum samples and standardized questionnaire data (demographics, treatment, TB contact history, underlying disease, history of imprisonment) were collected from suspected MDR-TB cases>18 years of age. Sputum was processed locally in the Oromia public health laboratory using standard techniques. Data from MDR-TB cases and TB positive controls were compared using logistic regression analysis. For each factors, their association with outcomes variable was estimated by calculating the odd ratio (OR) together with 95% confidence intervals (95% CI).

Results: Of 439 suspected MDR-TB cases, 265 had confirmed *Mycobacterium tuberculosis* infection, of whom 33% (88) had laboratory, confirmed MDR-TB. Over two thirds (65%) were between18 to 39 years of age. On multivariable analysis occupation (farming), known TB contact history, alcohol use, HIV infection, previous known TB history and previous TB treatment outcome were predictors of MDR-TB.

Conclusion: The rate of MDR- TB was high among suspected cases in the Oromia region of Ethiopia. Local MDR-TB detection capacity and local epidemiology studies are key for detection and guiding use of sparse resources to optimize MDR-TB control. If TB is suspected, the presence of any of the above factors should alert Oromia region clinicians and public health to be screen for the MDR-TB.

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