Retrovirology

Poster presentation

The MHC Class II Transactivator (CIITA): A "Physiologic" Drug Against HIV-1 Replication

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Optimal vaccination strategies against HIV-1 require the fulfilment of two conditions: a)- the choice of an immunogen including pathogen's antigenic epitopes against which an immune response with neutralizing characteristics can be generated; b) the optimisation of triggering and maintenance of the immune response against the vaccine. Our interest is focussed on the second aspect. The expression of the MHC class-II transactivator (CIITA) whose locus *AIR-1* and corresponding function were discovered in our laboratory, is needed for continuous expression of MHC class-II molecules and consequent antigen presenting function by APC. Unexpectedly, and of great relevance for antiviral functions, we found that CIITA potently inhibits HIV-1 viral replication by a competitive action on the viral transactivator Tat for Cyclin T1, the cellular cofactor used by Tat to elongate viral transcripts. This effect is found in APC and, of greater importance, also in HIV-1-infected T cells. Molecular analysis has revealed that the inhibitory activity of CIITA for HIV-1 Tat maps to the N-terminal region, and particularly to the segment 200–285 included within the P/S/T region of the CIITA activation domain which is then the molecularly defined Cyclin-T1-interacting region. Thus CIITA has a dual role on HIV infection: 1)- it increases APC function for HIV-1 viral antigens; 2)- it decreases viral replication and thus viral spreading in infected individuals. Within this frame CIITA represents the necessary and ideal molecule to control both innate and adaptive immunity against the virus.

Considering the functional importance of a sustained and persistent expression of CIITA in APC, the search for potential synthetic and natural mediators, drugs and biomolecules, that can act on CIITA expression at level of transcription as well as biosynthesis, will be of great importance in tailoring better vaccines against HIV-1, and in controlling and combating HIV-1 infection and spreading.