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Concerns in the planning of therapeutic immunizations in HIV infected patients aiming to harness HLA E restricted CD8+T cell HIV suppressive activity

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Recently it has been convincingly shown that Chinese rhesus macaques can be protected from SIV infection by oral SIV/*Lactobacillus* immunization. The protection was due to the induction of HLA E restricted CD8+ T cells, CD8 Treg with anti-SIV specificity. In a subset of monkeys with latent infection, depletion of CD8+ cells allowed viremia to recur which was again controlled as the CD8+ cell count rose. CD8 Treg has been found to target CD4+ T-helper follicular cells, TFH, in germinal centers which normally excluded CD8+ CTL. TFH are the most susceptible cells for SIV/HIV infection and replication, which causes down regulation of HLA A and B but retain HLA C and HLA E expression. A subsequent study of oral SIV/*Lactobacillus* immunization with a very similar protocol performed in Indian rhesus macaques did not show any protection. An explanation may be found in the regulation of CD8 Treg which has a vital role in recognition of 'non-self' and protection from autoimmunity in their 'normal' interaction with TFH. They are thus subject to multiple regulatory mechanisms such as CD94/NKG2A and KIR inhibition. KIR is unique in that gene frequencies vary considerably between populations. Gene frequencies of Mamu-KIR with relevance to SIV infection can vary from 0% to 50% in Chinese and Indian rhesus macaques respectively. In humans certain KIR genes have also been associated with reduced susceptibility and slower HIV disease progression. If KIR genes provide the explanation for the different results of oral immunization in rhesus macaques of Chinese and Indian origin, this must be considered in the planning of human studies, in addition to the uncertainty of induction of CD8 Treg in already infected individuals.

Biography

Eric Sandstrom was graduated from Karolinska Institutet in 1972. He became a Professor at KI with an emphasis on Sexually Transmitted Infections in 1999. His work with HIV began in 1982, in a new STI screening service for gay men in Sweden; this led to an HIV/AIDS clinic with a service ranging from preventive work, outpatient care, inpatient care and hospice service. He has organized a number of clinical trials from phase 1 to multi-centre phase 3 trials with an emphasis on HIV vaccines. He has coordinated a preventive HIV vaccine program with two recently completed trials in Tanzania and Mozambique.

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