IFN α tips the balance towards APOBEC3G

The cytidine deaminase **APOBEC3G** is a host protein that becomes packaged into HIV virions, where its enzymatic activity induces degradation of HIV DNA. HIV counters this form of host defence through virion infectivity factor (**Vif**), which targets APOBEC3G for proteasomal degradation. However, in a report published in *The Journal of Experimental Medicine*, it has now been shown that interferon- α (IFN- α) can increase the expression of APOBEC3G by macrophages to such an extent that the effects of Vif are overcome and HIV replication is markedly decreased.

IFN- α can inhibit the infection of macrophages by HIV in many ways. So, because IFN- α has been shown to induce the expression of an RNA-specific adenosine deaminase, Peng *et al.* set out to determine whether IFN- α could limit HIV infection of macrophages by inducing the expression of cytidine deaminases that can target HIV DNA. Indeed, IFN- α was found to increase the amount of APOBEC3G (both mRNA and protein) expressed by human primary monocyte-derived macrophages, and this increase correlated with a decrease in viral replication. IFN- α was also shown to induce the expression of several other members of the APOBEC3 family: APOBEC3A and APOBEC3F. The promoters of the genes encoding these three APOBEC3 proteins were found to contain IFN-stimulated response elements (ISREs), indicating that IFN- α regulates the amount of these

APOBEC3G: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=60489

Vif: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=155459

APOBEC3 proteins expressed by macrophages by inducing transcription. Because APOBEC3F has similar anti-HIV activity to APOBEC3G, the induction of these two APOBEC3 proteins is likely to provide another mechanism by which IFN- α inhibits the infection of macrophages by HIV. Consistent with this notion, knockdown of *ApoBec3G* expression by small interfering RNA markedly reduced the ability of low doses of IFN- α to inhibit the infection of macrophages by HIV, although at high doses of IFN- α , inhibition of infection was still observed, probably because other IFN- α -induced antiviral mechanisms were activated.

These data indicate that IFN- α induction of APOBEC3G expression by macrophages tips the delicate balance between APOBEC3G and Vif in favour of APOBEC3G, and that this is one mechanism by which IFN- α mediates its anti-HIV

effects in macrophages. Because APOBEC3G has also recently been shown to inhibit the replication of hepatitis B virus, the authors suggest that IFN- α -mediated induction of APOBEC3G expression by macrophages might be a widely used antiviral host-defence mechanism.

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