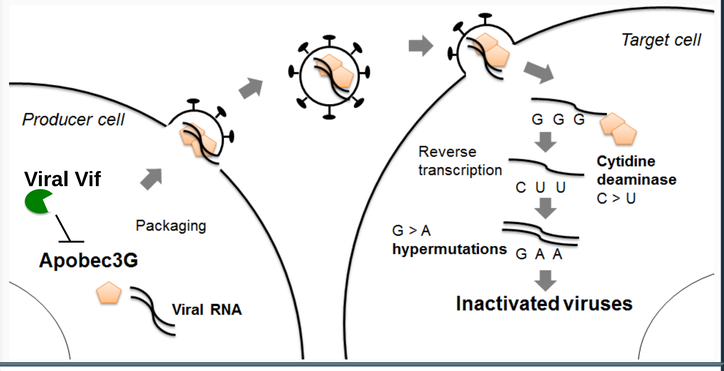
Non-human primate A3Cs potently inhibit lentiviruses

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Background

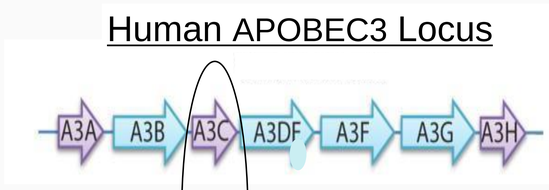
APOBEC3s are cytidine deaminases

- incorporate into virions, mutate viral genomes
- lentivirus Vif protein counteracts this



Function of A3C is unknown

Human APOBEC3 Locus



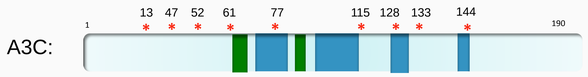
Inhibits:

	A3A	A3B	A3C	A3DF	A3F	A3G	A3H
Lentiviruses	-	-	-	+	+	+	+
Endogenous retroelements	+	+	-	+	+	+	+

A3C is under positive selection in primates



Positive selection across gene (p<0.00001)



= Vif:A3 binding =deaminase domain * = positive selectionPr>0.95

This is consistent with A3C having a role against pathogens

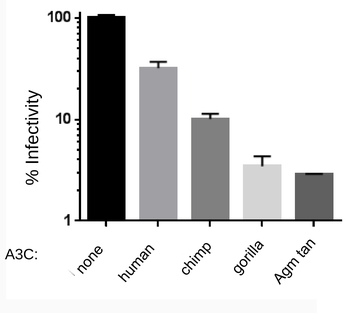
Hypothesis:

A3C is an anti-lentiviral protein in non-human primates

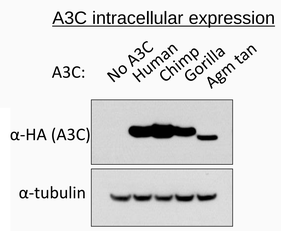
Results

Non-human primate A3Cs restricts HIV-1

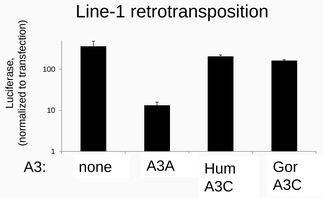
A3C restriction of HIV-1 Δ*vif*



A3C intracellular expression



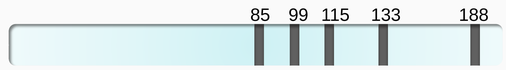
Line-1 retrotransposition



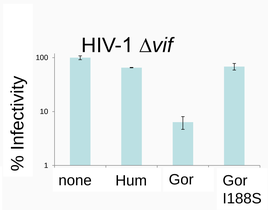
Gorilla A3C does not more potently block an endogeneous retroelement, Line-1

What amino acids confer gorilla A3C antiviral activity?

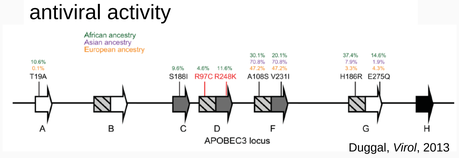
Residue differences between gorilla and human A3C:



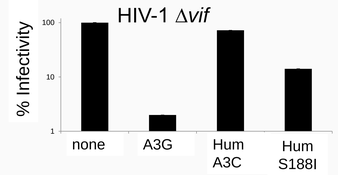
Isoleucine 188 contributes to A3C antiviral activity



A common SNP in human A3C increases antiviral activity



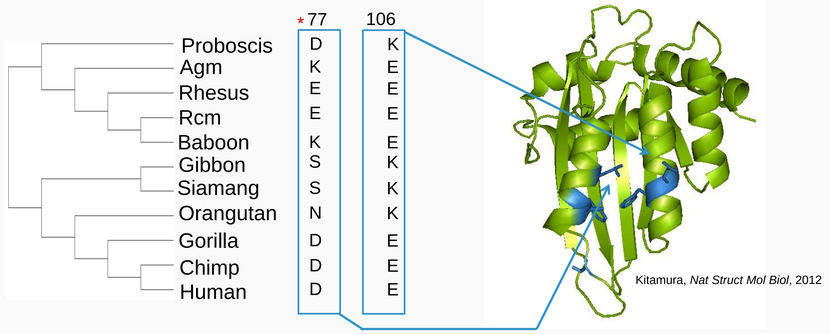
Duggal, *Virol*, 2013



Isoleucine 188 was lost in the human/chimp lineage



A3C may be in genetic conflict with Vif



* = positive selection Blue Residues= Residues required for HIV-1 Vif antagonism of A3C

HIV-1 Vif requires D77 and E106 to antagonize human A3C

Is sequence variation at these sites driven by Vif?

Testing the resistance/susceptibility of primate A3Cs to lentiviral Vif proteins

Conclusions

Functional and evolutionary data indicate that A3C is an anti-lentiviral protein in non-human primates

A3C lost activity in the human/chimp lineage

Acknowledgements

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