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Role of IL18 in HIV Associated Lipodystrophy

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Background

Hypothesis

Modulation of IL18 & NFATc4 by ARVs in adipocytes could play a role in HIVLD

Aims and Objectives

- IL18 and NFATc4 expression *in vitro*
- Targeting IL18 and NFATc4
- Genetic variants in IL18
Materials and Methods

- Differentiating 3T3-F442A murine adipocytes
- Lopinavir [LPV], Ritonavir [RTV], Atazanavir [ATV] and Efavirenz [EFV]
- Telmisartan
- ELISA
- Real-Time PCR

Genetic Association study

- DNA samples
- HIVLD+ n=115
- HIVLD- n=51
- Diagnosis of HIVLD was by clinician’s confirmation / patient’s self-report
- SNP selection: Haplotype tag SNP approach; functional SNPs
- Sequenom MALDI-TOF

Statistical Analysis

- Paired t-test
- Haploview software
Results

* = p < 0.05
Mean values were obtained from 4 independent repeats
Table 1. Single marker Associations-haploview analysis

<table>
<thead>
<tr>
<th>Sl. NO.</th>
<th>SNP ID. No.</th>
<th>P - Values</th>
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Haplotype blocks in IL18 gene in our Cohort of study
Conclusion

- ARV-mediated upregulation in IL18 could play a role in the development of HIVLD

- ARV-induced upregulation of NFATc4, a transcription factor through which IL18 causes inhibition of adiponectin (a marker of insulin sensitivity), could be mechanistically important in the development of insulin resistance.

- Telmisartan offers a potential strategy to treat ARV-induced adverse effects

Future work

- Validation in primary human adipocytes
- Blockade of NFATc4 using siRNA
- IL18 genotyping in bigger & well phenotyped cohort of patients
Acknowledgements

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