

# 19<sup>th</sup> Annual Conference of the British HIV Association (BHIVA)



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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

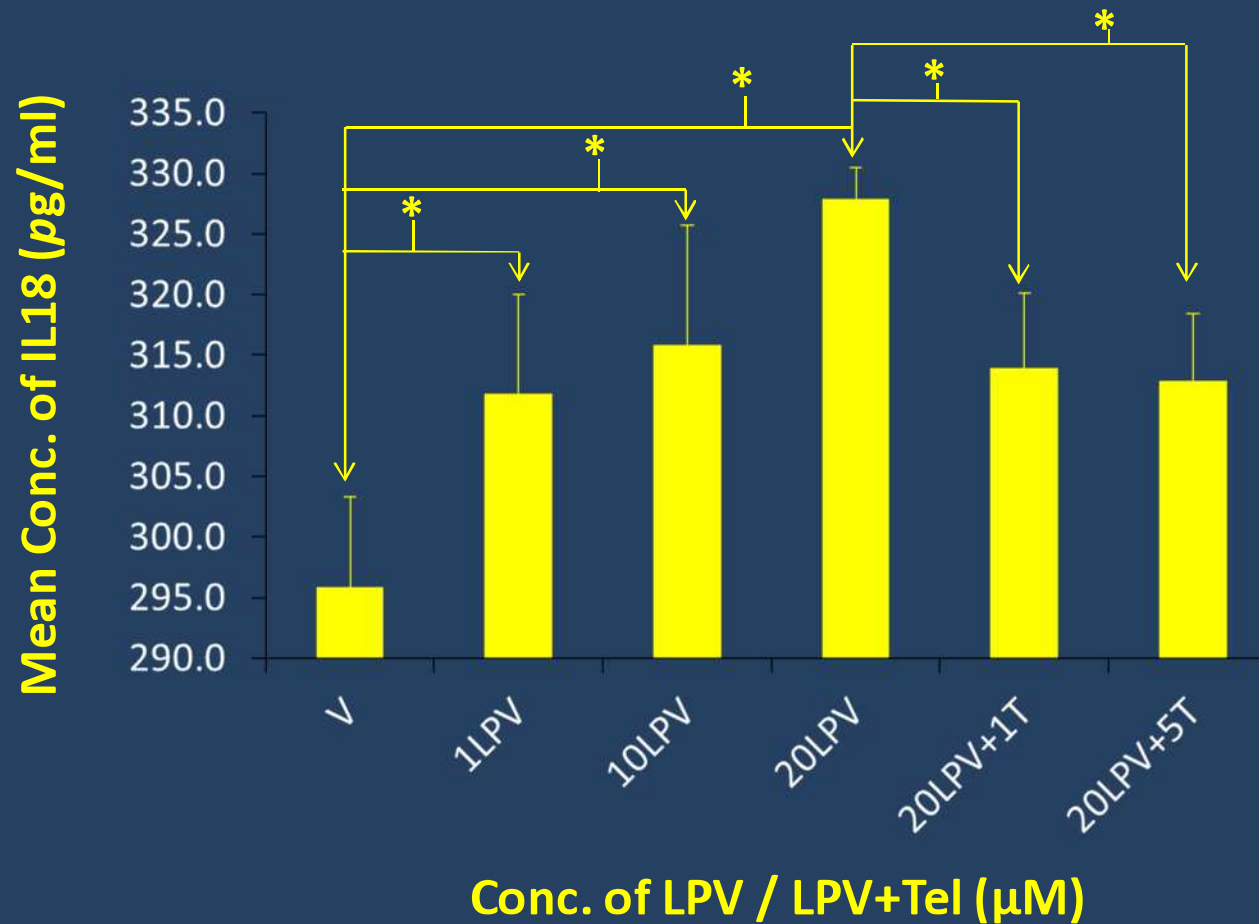
## Genetic Association study

- 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



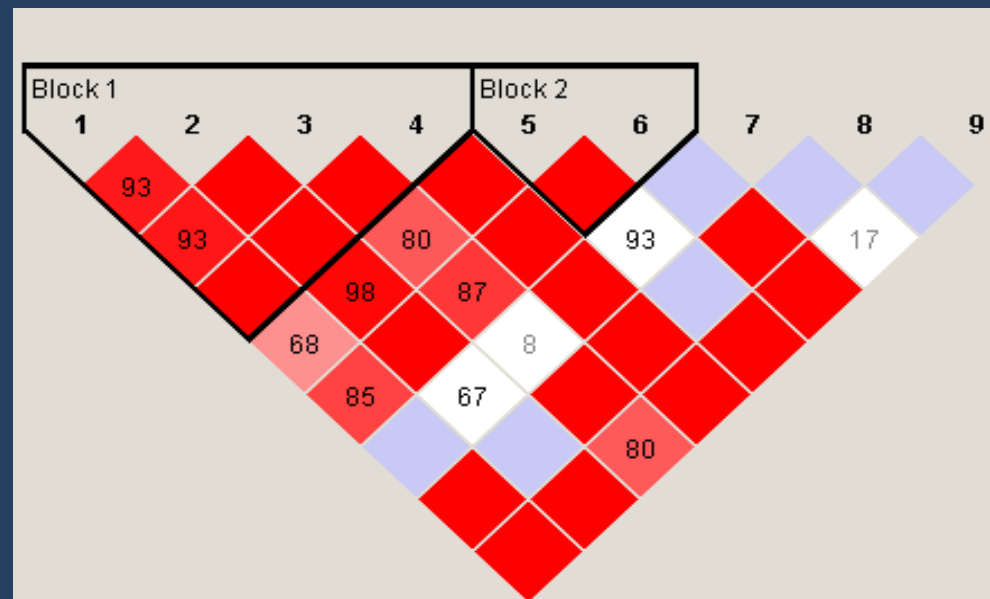
- =  $p < 0.05$
- Mean values were obtained from 4 independent repeats

# Genetic association results

**Table 1. Single marker Associations-haploview analysis**

Sl. NO.	SNP ID. No.	P - Values
1	rs2115763	0.6742
2	rs360719	0.5845
3	rs1946518	0.2353
4	rs1834481	0.5956
5	rs549908	0.4461
6	rs5744280	0.6525
7	rs5744290	0.1828
8	rs5744292	0.2101
9	rs543810	0.4873

**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

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