Virome-wide serological profiling reveals association of herpesviruses with obesity

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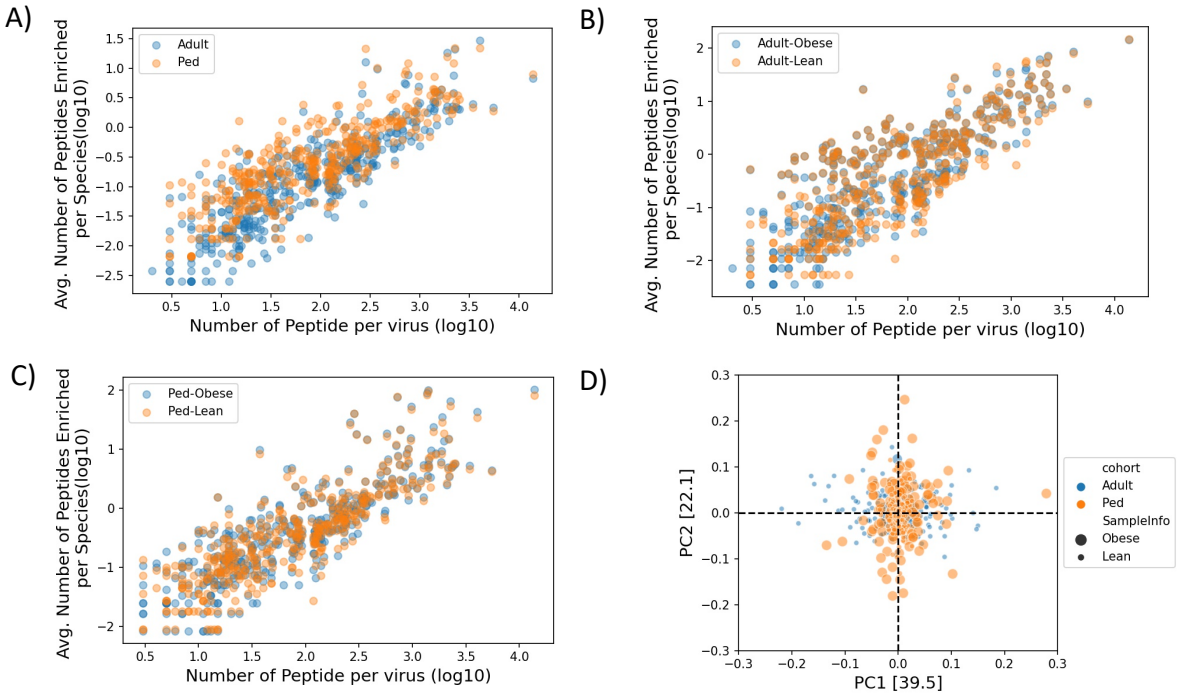
Supplementary Table 1: HSV-1 and -2 peptides significantly associated with obesity in the adult population

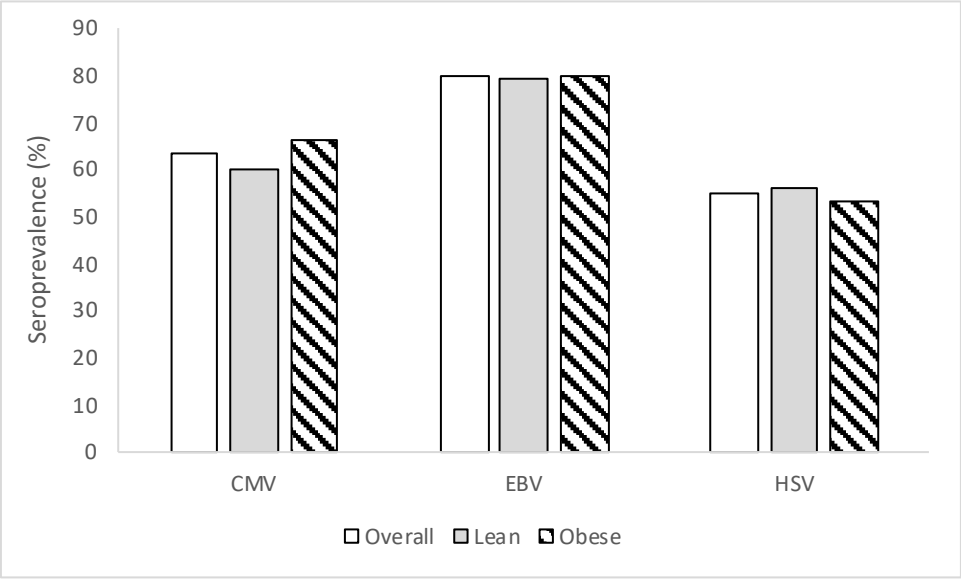
Cohort	Species	UniProt entry	Protein name	Peptide	Prev_Obese	Prev_Lean	log_or	log_pval
Adult	HSV1	P04288	Envelope glycoprotein M (gM)	PIYDEVADDQTDVLYAKIQHPRHLPDDD PIYDTVGGYDPEPAEDPVYSTVRRW	78.0	51.1	1.2	8.6
		P06484	Envelope glycoprotein G (gG) (gG-1)	VSSTTQPQLQTTGRPSHEAPNMTQTGT TDSPTAISLTTPDHTPPMPSIGLEEEEEE	80.2	56.5	1.1	7.1
		P06484	Envelope glycoprotein G (gG) (gG-1)	DSPTAISLTTPDHTPPMPSIGLEEEEEEE GAGDGEHLEGGDGTRDTLPQSPGPAF P	85.0	59.8	1.3	8.7
		Q69091	Envelope glycoprotein D (gD)	RRHTQKAPKRIRLPHIREDDQPSSHQPL FY	86.1	62.0	1.3	8.2
		Q8JQG9	Glycoprotein G (Fragment)	TPPMPSIGLEEEEEEEGAGDGEHLEGG DGTRDTLPQSPGPAFPLAEDVEKDKPN RP	85.7	60.9	1.3	8.7
		Q8JQR0	Glycoprotein G (Fragment)	DGTRDTLPQSPGPAVPLAGDDEKDKPN RPVVPPPGPNNSPARPETSRPKHPPPV SG	79.8	54.3	1.2	8.1
		Q8JQS3	Glycoprotein G (Fragment)	TPPMPSIGLEEEEEEEEEGAGDCEHLK GGDGTRDTLPQSPGPAVPLAGDDEKD KPN	83.9	58.7	1.3	8.5
		Q8JQS3	Glycoprotein G (Fragment)	GDGTRDTLPQSPGPAVPLAGDDEKDKP NRPVVPPPGPNNSPARPETSRPKTPPT SI	72.9	50.0	1.0	6.0
		P06437	Envelope glycoprotein B (gB) (gB-1) (gB1)	PPLGAAPTGDPKPKKNKKPKNPTPPRP AGDNATVAAGHATLREHLRDIKAENTD AN	72.9	47.8	1.1	7.1
		P08665	Envelope glycoprotein B (gB) (gB-1) (gB1)	SAAPSSPGTPGVAAATQAANGGPATPA PPALGAAPTGDPKPKKNKKPKNPTPPR PA	71.1	44.6	1.1	7.7
		P08665	Envelope glycoprotein B (gB) (gB-1) (gB1)	PALGAAPTGDPKPKKNKKPKNPTPPRP AGDNATVAAGHATLREHLRDIKAENTD AN	74.4	49.5	1.1	7.2
		P36318	Envelope glycoprotein D (gD)	RRRTQKGPKRIRLPHIREDDQPSSHQP LFY	82.0	60.9	1.1	6.0
		P06476	Envelope glycoprotein D (gD)	RRTRKAPKRIRLPHIREDDQPSSHQPLF Y	81.3	59.2	1.1	6.4
	HSV2	P89433	Envelope glycoprotein M (gM)	APDHEAELYARVQRPGPVPDAEPIYDT VEGYAPRSAGEPVYSTVRRW	39.2	18.5	1.0	5.7

Supplementary Table 2: HSV-1 and -2 peptides associated with obesity in both adult and pediatric population

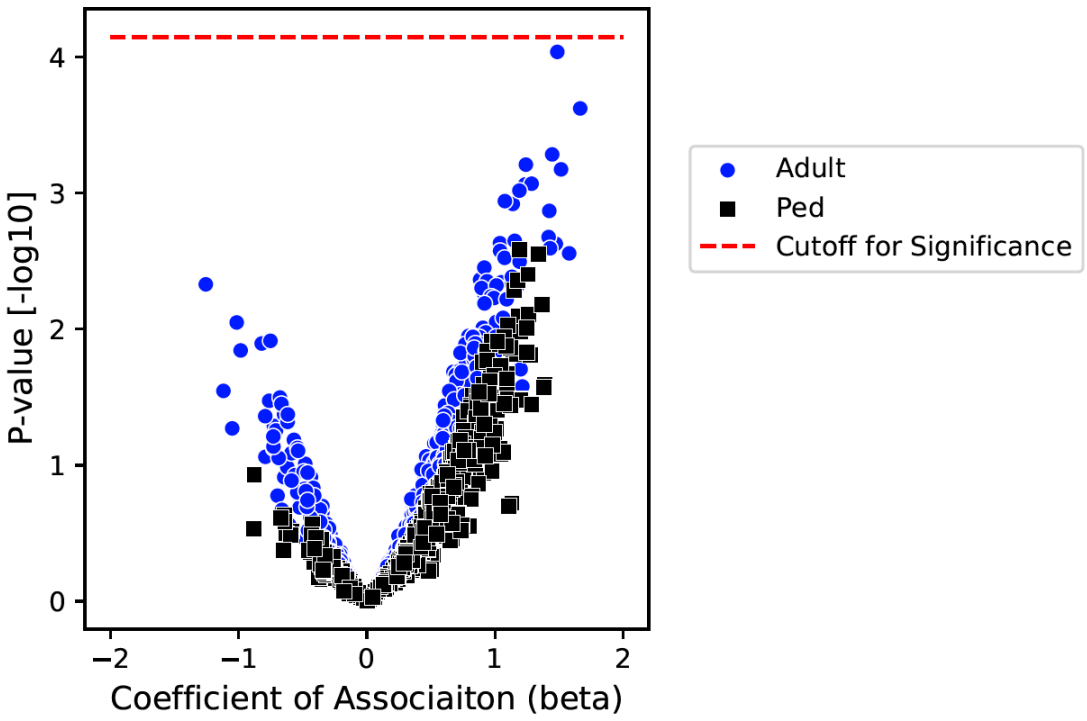
Cohort	Species	UniuProt entry	Protein name	Peptide	Prev_Obese	Prev_Lean	log_or	log_pval
Adult	HSV1	F8RDH2	Tegument protein US11	MSQTQPPAPVGPGDPDVYLKGVPSA GMH**PRGVHAPRGHPRMISGPPQRG** DNDQAAG	45.8	27.7	0.8	3.9
Pediatric	HSV1	F8RDH2	Tegument protein US11	**PRGVHAPRGHPRMISGPPQRGDND QAAGQ**CGDSGLLRVGADTTISKPSE AVRPPTF	23.4	10.8	0.9	1.8
Pediatric	HSV1	P04487	RNA-binding protein (Vmw21)	**PRGVHAPRGHPRMISGPPQRGDND QAAG**QCGDSGLLRVGADTTISKPSE AVRPPTI	20.9	9.9	0.9	1.5
Pediatric	HSV2	P89466	Tegument protein UL46 (Tegument protein VP11/12)	AAWPAESHAPRAPSEDADSIYESVG EDGGRVYEEIPWVRVYENICPRRRLA GGAAL	18.4	7.2	1.1	1.8
Adult	HSV2	P89466	Tegument protein UL46 (Tegument protein VP11/12)	AAWPAESHAPRAPSEDADSIYESVG EDGGRVYEEIPWVRVYENICPRRRLA GGAAL	18.7	7.1	1.1	3.5



Supplementary Figure 1: Enrichmnet profile of peptides with respect to virus library size (Species wise) in adult and pediatric obese and lean groups. Number of peptides in the VirScan library for different viral species (log transformed) in the x-axis plotted against species wise average number of enriched peptides: (A) Adult vs Pediatric cohort (B) Obese versus Lean in adult cohort and (C) Obese versus Lean in the pediatric cohort. (D) Principal component analysis of enriched peptides in obese and lean samples from adult and pediatric cohorts. Here, scatter plot of first two principal components (PC1 and 2) has been shown that describes 57% of variance in peptide enrichment profiles.



Supplementary Figure 2: Seroprevalence of herpes viruses in the pediatric obese and lean population by standard serological methods (N, obese = 120; N, lean = 111)



Supplementary Figure 3: Association of any combination of two viruses with obesity. A total of 43 viral species that are at least 10% prevalent in the overall study population were tested for their association with obesity in the adult and pediatric population by multiple logistic regression analysis, with age and gender as co-variates, and using a two-way interaction model. The co-efficient of association (x-axis) of any combination of two viruses were plotted against respective *p*-values (-log10) (y-axis) after Bonferroni correction for multiple testing. The red dotted line indicates significance threshold after Bonferroni correction. HSV1, herpes simplex virus 1; RVA, rotavirus.