Transcriptomic Signature of Obesity

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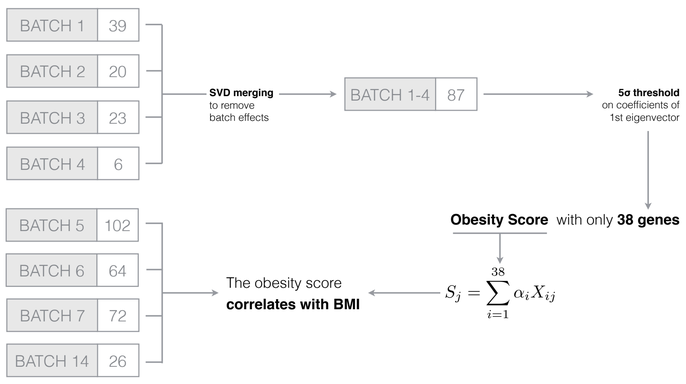
Obesity: Genes or Environment?

Observational studies suggest that obesity might have a Mendelian origin, but it is not clear if gene expression patterns observed in obese subjects are secondary to genetic traits or not.

Well-established cases of Mendelian forms of obesity approximately account for only 5% of the severely obese cases.

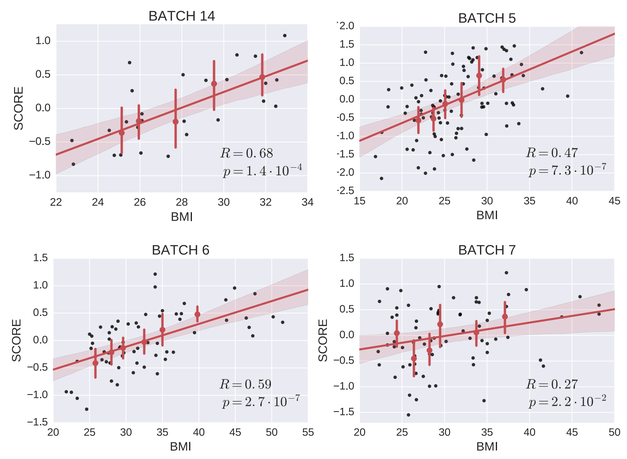
Obesity Score

We merge four datasets (batches 1-4), totalling 87 samples, to construct a robust (5-σ) obesity signature.



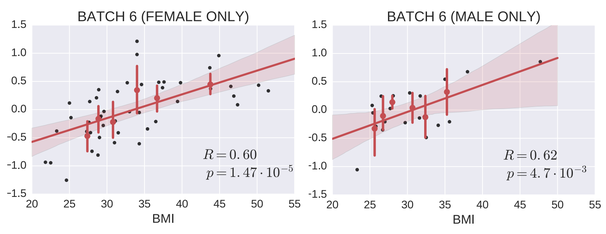
Obesity Score and BMI

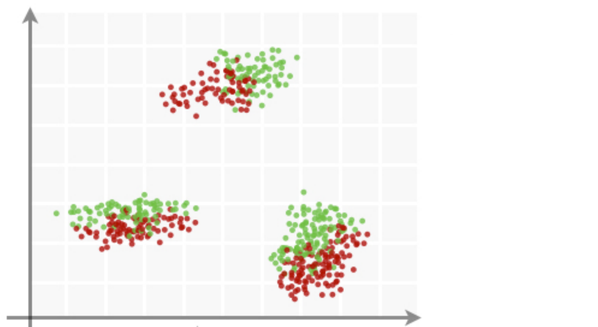
Our score correlates with BMI on four independent datasets (batches 5-7, 14).



Obesity Score and Gender

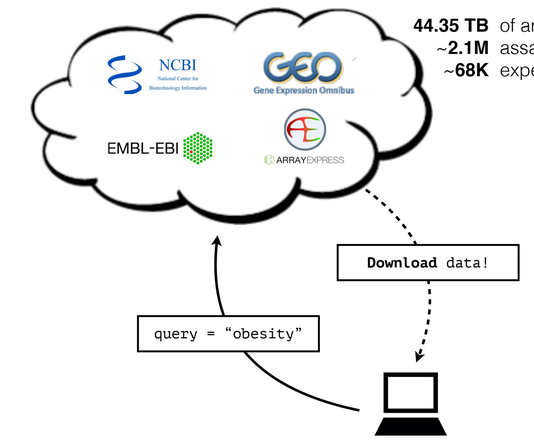
Result do not depend on gender. The obesity score correlates with BMI both for F and M subjects.





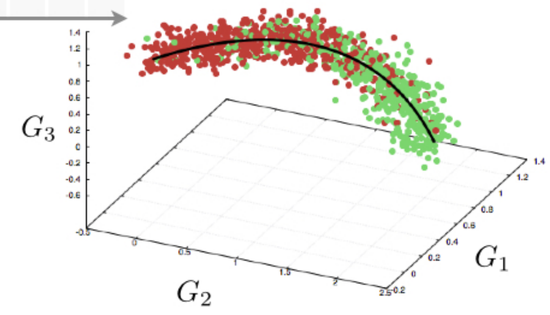
Data Integration

We developed a spectral method to remove **batch-effects** when merging gene expression datasets



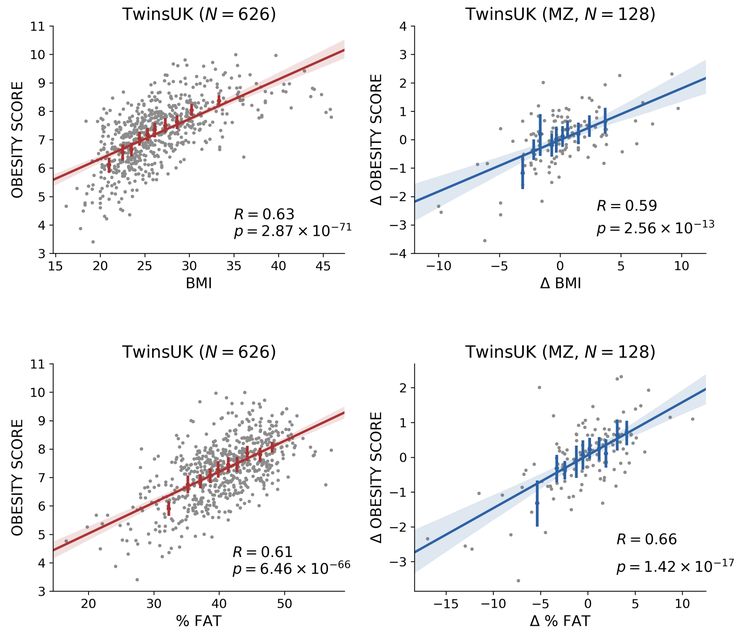
Dimensionality Reduction

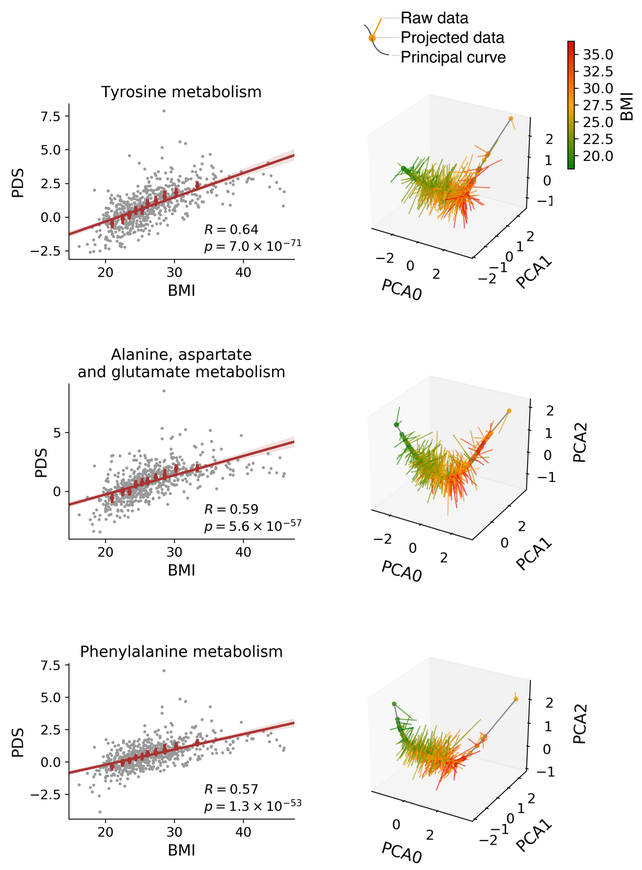
We use Pathway Deregulation Scores (PDS) to reduce the number of dimensions from tens of thousands of genes to just hundreds of pathways.



Obesity Score and Twins

We further validate our results with the TwinsUK dataset (N=626). The obesity score correlates with BMI and %FAT.





Datasets

Batch	Lean	Overweight	Obese	Total	Gender	BMI	Tissue	Accession code	Ref.
Batch 1	20	0	19	39	19 M / 20 F	categorical	Adipose	GSE2508	6
Batch 2	10	0	10	20	All F	categorical	Adipose	GSE26637	7
Batch 3	6	(10)	17	23	Unknown	numerical	Adipose	GSE27949	8
Batch 4	3	0	3	6	Unknown	categorical	Adipose	GSE48964	9
Batch 5	42	39	21	102	49 M / 53 F	numerical	Adipose	GSE62117	10
Batch 6	5	24	35	64	19 M / 45 F	numerical	Adipose	GSE64567	11
Batch 7	14	28	30	72	All F	numerical	Normal breast	GSE33526	12
Batch 8	131	131	142	404	All F	categorical	Breast tumor	GSE78958	13
Batch 9	–	–	–	979	All F	none	Breast tumor	–	?
	–	–	–	114	All F	none	Normal breast	–	?
Batch 10	0	0	18	18	All F	categorical	Adipose	GSE65540	28
	0	0	18	18	All F	categorical	Monocytes	GSE66306	28
Batch 11	–	–	–	275	Unknown	none	Adipose	–	?
	–	–	–	488	Unknown	none	Blood	–	?
Batch 12	12	0	36	48	All F	categorical	Monocytes	GSE32575	14
Batch 13	0	0	12	12	Unkwon	categorical	Monocytes	GSE54350	30
Batch 14	4	14	8	26	16 M / 10 F	numerical	Adipose	E-MEXP-1425	23

References

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2. F. Font-Clos, S. Zapperi and C. A. M. La Porta. 2017. "Integrative Analysis of Pathway Deregulation in Obesity." NPJ Systems Biology and Applications 3 (June): 18.

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4. A. Livshits, A. Git, G .Fuks, C. Caldas, and E. Domany. 2015. "Pathway-Based Personalized Analysis of Breast Cancer Expression Data." Molecular Oncology 9 (7): 1471–83.

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