HumanIslets Web-Tool



The HumanIslets database can be explored from three complementary views, each accessible from the home page:

- 1. Omics view: compute gene-level and pathway-level associations between an omics dataset and a metadata variable of interest.
- 2. Feature view: query all metadata-omics associations that involve a feature of interest, sorted by statistical significance.
- 3. Donor view: view all metadata and functional outcomes for a specific donor, compared to the distribution of values from other donors.

There is also a data download tool.



The main steps to computing results on this page:

- 1. Select an omics type of interest (ie. proteomics)
- Select a metadata or functional outcome of interest. These are grouped into 9 categories.
 Categorical variables automatically prompt the selection of two specific classes to compare.
- 3. Select any covariates that you would like to adjust for. The tool supports the inclusion of donor metadata (ie. Age, Sex) or technical variables (ie. cold ischemic time, cell culture, etc).
- 4. Optionally choose to do the analysis for a subset of donors.
- 5. Choose a p-value cut-off to determine statistical significance.
- 6. Click 'Submit'!

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۵ ۲		Omics View					Sex 🛞 Cold Is	schemic Time (h) 🧕		
		This tool uses general linear models to covariate variables. Then, results are e	find associations between omics featu tracted from the model for the primary	ures and donor meta / metadata. See the	adata/outcomes using the limma R pack statistical analysis documentation for n	age. A linear model is fit nore details.	ti Organ Characteristic:	s and Processing		
 ب	1	Omics Type:	Bulk protein expression	~			Pancreas weight	(g)		
	2	Primary Metadata:	Donor Characteristics	~	Diabetes diagnosis	~	Fatty infiltration Organ consistence	y		
		Comparison of Interest:	Type 2 V vs. No	Diabetes 🗸 🗸			Interface fo	r selecting ovariates	g multiple	
	3	Control for:	Select covariates		~					
	4	Donors:	● All ○ Subset ◀			Select Donors			×	
ſ	5	P-value cutoff:	0.05	Use adjusted p-v	alues	Apply Filters Upload L	Deta Ausilability			
		1		Г	6 Submit	Note: if enabled, variable filte	ers will exclude donors with missin	g values for that variable	. Show advanced	
						 Sex Diabetes diagnosis 	Male Female No diabetes Type 1	V Type 2		
	Da	ta visualization portal for the HumanIslet	ts project			Age	•	•	lata	Lab
						BMI	•	•		
			Su	pport for e ubset don	extensive filtering to ors included in the analysis	Submit			~ ок	

Controlling for technical covariates can have a big impact on the statistical analysis. We find that culture time and non-endocrine tissue proportion are the most influential variables. Here is an example of controlling for culture time in bulk RNA-seq analysis:

Omics Type:	Bulk gene expression (RNA-seq)	~		1 Select 'Bulk gene expression (RNA-seq)' and
Primary Metadata: Comparison of Interest:	Donor Characteristics Type 2 vs. No Diabete	 ✓ Diabetes diagnosis s ✓ 	~	'Diabetes diagnosis' ('Type 2' vs. 'No Diabetes') for the omics type and metadata of interest.
		Control for:	Culture time (h) ⊗	~
2 Soloct (Cult	urotimo(b)'as	Donors:	cult	Q X
a covariate for:	in the 'Control ' input.	P-value cutoff:	Cell Culture Outcomes	

Click 'Submit'

Control for:	Culture time (h) \otimes		~	
Donors:	cult	Q	×	
P-value cutoff:	Cell Culture Outcomes			
	Culture time (h)			
	Total islet eqivalents after culture (IEQ)			
	Percent IEQ recovery after culture (%)			Submit
	Islet particle index after culture			
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Feature Association Results

3

This statistical analysis resulted in **542** significant features (**282** up and **260** down).

There are 542 mRNAs with significantly different expression values in 'Type 2 versus No Diabetes' in the bulk RNA-seq data, when controlling for culture time.

If we do not control for culture time, we only detect 418 mRNAs as significantly different between Type 2 and No Diabetes.

Feature Association Results

This statistical analysis resulted in 418 significant features (236 up and 182 down).

Download date and time-stamped results tables and copies of the input data and R scripts used for the analysis for locally reproducible results.

Saved_Analysis_2024-06-03T15-54-22

The results can be explored in three different ways. Here is an introduction to the 'Graphical Summary'.



Feature-level plots are interactive. Hovering over a point reveals the donor ID and clicking navigates to the donor-view page for that donor.

The results table is interactive, with many links that generate more detailed plots or navigate to other tool pages/external databases. Click 'SC' to view this feature's gene expression across cell type in our single-cell database comprised of data from 7 publicly available single-cell RNA-seq islet datasets.



ons for HADH

Gene-level associations for HADH

Hover over and click a row to generate an interactive feature-level plot

Type2

SVG PNG PDF 🗸 OK

Non

The pathway analysis tab supports pathway/gene set analysis of the associations results using two different method (ORA and GSEA) for 8 different gene set libraries.



to see the associated statistics, and click to generate a heatmap showing feature-level omics data for that gene set

Set Name	P-value	Adj P-value	Hits	Set Size	Set ID
Ribosome	3.57e-11	8.24e-9	62	117	hsa03010
Carbon metabolism	0.00000195	0.000168	36	71	hsa01200
Vibrio cholerae infection	0.00000246	0.000168	21	33	hsa05110
Biosynthesis of amino acids	0.00000291	0.000168	27	48	hsa01230
Glycolysis / Gluconeogenesis	0.00000535	0.000247	23	39	hsa00010
Pyruvate metabolism	0.0000282	0.00109	17	27	hsa00620
Arginine and proline metabolism	0.0000554	0.00183	17	28	hsa00330
Fatty acid degradation	0.000249	0.00656	16	28	hsa00071
Citrate cycle (TCA cycle)	0.000255	0.00656	11	16	hsa00020
Collecting duct acid secretion	0.000562	0.013	11	17	hsa04966
Epithelial cell signaling in Helicobacter pylori infection	0.00082	0.0166	17	33	hsa05120
Leukocyte transendothelial migration	0.000863	0.0166	24	53	hsa04670
Rap1 signaling pathway	0.00102	0.0181	34	84	hsa04015

Feature View

Statistical associations between each omics type and each metadata/function outcome were computed and stored in a database (>3.8 million relationships). Age, sex, BMI, and culture time were included as covariates in the analysis. The pre-computed results can be queried by either gene symbol or by metadata/functional outcome name.

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û _~	Feature View									
° Q	We computed all omics feature ~ metadate unless one of these variables was the prim	a associations across five diff ary metadata variable. Search	erent omics types and more than 100 met either a gene/protein symbol or metadate	adata variables. Sex, age, BMI, and c variable to retrieve relevant results,	culture tim , sorted by	e were included p-value.	as covariates	in all analyses	s,	
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	.,,		with all matchin	g features						
		Gene/Protein Symbol 🏾 🍸	Metadata Variable 7	Omics type 🛛	Coefficie	nt ↑↓ P-value	rî↓ Adjus	ted p-value ↑↓	Links	
		INSR	Non-endocrine cell proportion (computed)	Bulk protein expression	1.78	4.13e-1	4 2.91e	13	NCBI	T2DKP S
	Data visualization portal for the HumanIslets project	INSR	Purity (%)	Bulk gene expression (Nanostring)	-0.0148	3.61e-9	4.44e	7	NCBI	T2DKP S
		INSR	Culture time (h)	Bulk gene expression (RNA-seq)	-0.0111	2.04e-7	0.000	00159	NCBI	T2DKP S
		INSR	Purity (%)	Bulk protein expression	0.00713	7.15e-7	0.000	00817	NCBI	<u>T2DKP</u>
		INSR	Trapped (%)	Bulk gene expression (Nanostring)	0.01 1	0.0000	0.000	157	NCBI	T2DKP S
["	NSR: insulin receptor ×	INSR	Purity (%)	Bulk gene expression (RNA-seq)	-0.0152	0.0000	0.000	31	<u>NCBI</u>	<u>T2DKP</u> S
	•••]	INSR	Trapped (%)	Bulk gene expression (RNA-seq)	0.0224	0.0000	559 0.002	5	NCBI	T2DKP S
		INSR	Culture time before experiment (days)	Bulk gene expression (RNA-seq)	-0.268	0.0001	3 0.003	51	NCBI	T2DKP S
		INSR	Diabetes diagnosis Type2-None	Bulk gene expression (RNA-seg)	0.652	0.000	0.005	16	NCBI	T2DKP 5
	40 A	INSR	Diabetes diagnosis, Type2-None	Bulk protein expression	0.238	0.0016	3 0.010	5	NCBI	T2DKP §
		INSR	Corrected diabetes status, Type2-None	Bulk gene expression (Nanostring)	0.416	Omics type 🛛)	Coeff	icient	T2DKP §
	Culture time (h)	INCO	Diabatas diagnosis Turo? Nono	Bulk anno overession (Nanostrina)	0.42	Bulk protein	Matab All		-	םשחרד
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Τł	he results table shows all resu	lts for the quer	ied			Bulk gene e:	RNA-sea		11	
fea	ture, sorted by statistical sign	ificance. Intera	ctive			Bulk protein	NNA-Seq		713	
t	able components are the sam	e as on the om	ics			Bulk gene e:	+ Add	Rule	1	
	analysis page					Bulk gene e:	Clear	Apply	52	
						Bulk gene e:	ciear	Apply	.4	
						Bulk gene expres	ssion (RNA-se	q) -0.268	8	



The Donor View page shows a summary of each donor's outcomes, displayed against the distribution of values from different donors across the HumanIslets database. Donors can be searched by either donor ID (ie. R360) or RRID (ie. SAMN14146088).



There are currently nine types of data available to view. More data will be added over time as it is collected.

Each tab shows a summary of a different kind of dataset. For example ...



Data Download

The data download page has two steps: 'Select Donors' and 'Download Data'. In the first step, users can filter donors by metadata, data availability, or a donor list.

Users can filter to include only donors with specific data types available

Clicking the advanced filters link allows users to filter by many more variables

Once the donors have been selected, users can choose the data types that they'd like to download and the format that they want it in.

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∘(Ø →]	Select Dono Click "Submit" with Apply Filters Donor Charact Note: if enabled, v advanced filters Sex Diabetec diag Age BMI HbA1c Submit	Select data types to download Other Outcomes I Electrophysiology Outcomes Ad, y Gene Expression (Nanostring) Proteomics I Onics Data Select data types to download Omics Data Select on the select of the s		Download Data Select datasets: Select data types to download Data format: Comma separated values (.csv) Note: due to its large size, download of single-cell pate differently. Click Download Summary Comma separated values (.csv) Comma separated values (.csv) Text file (.txt) R object (.rds) Excel (.xlsx)					
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