

Multi-omics data visualization & integration on dental pulp regeneration

Produced by

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under the supervision of

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Université Claude Bernard

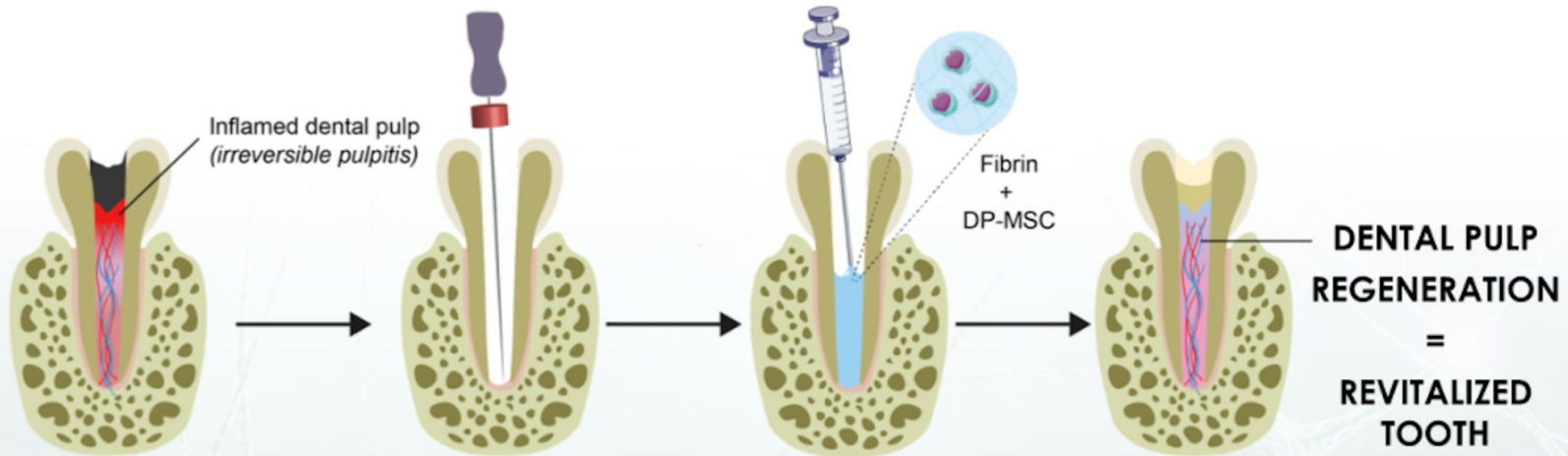


Lyon 1

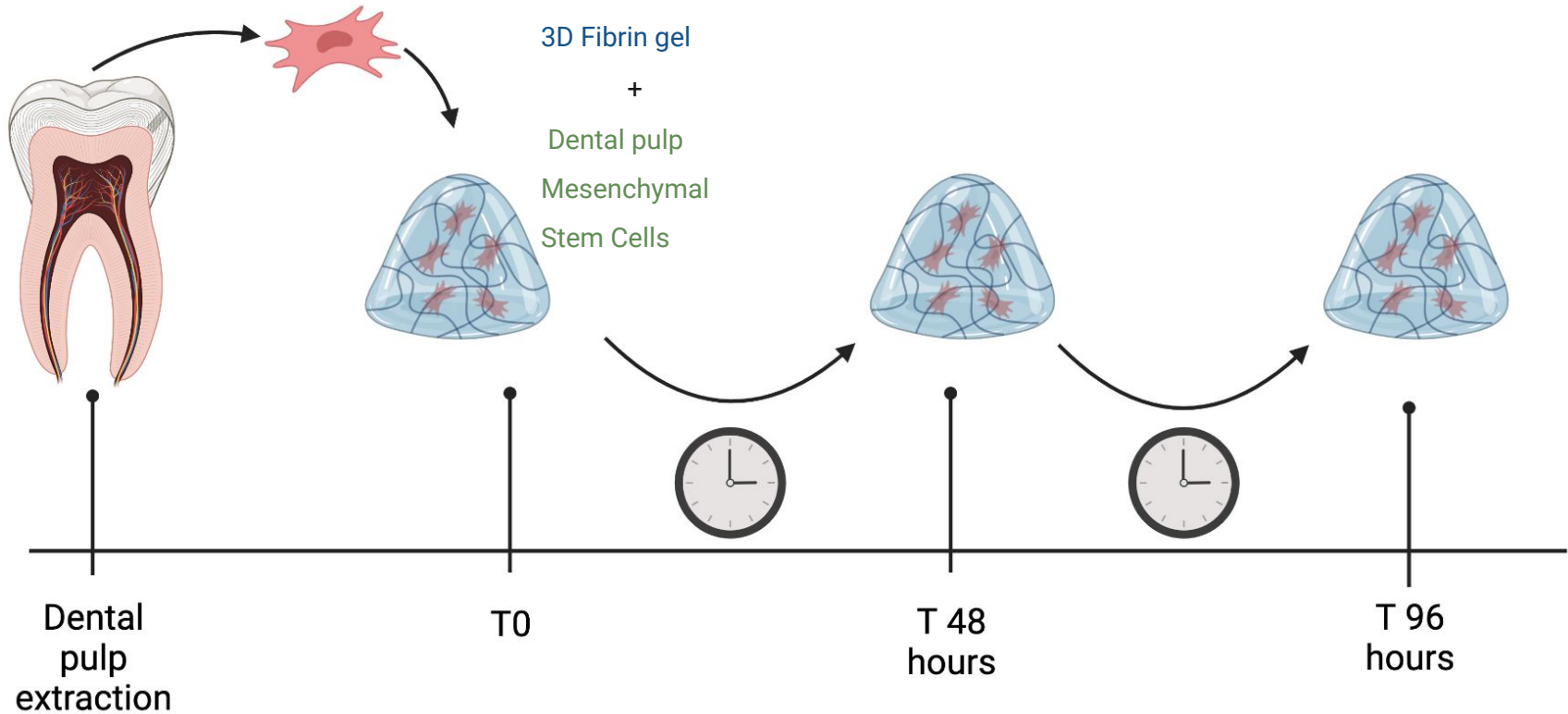


CONTEXT

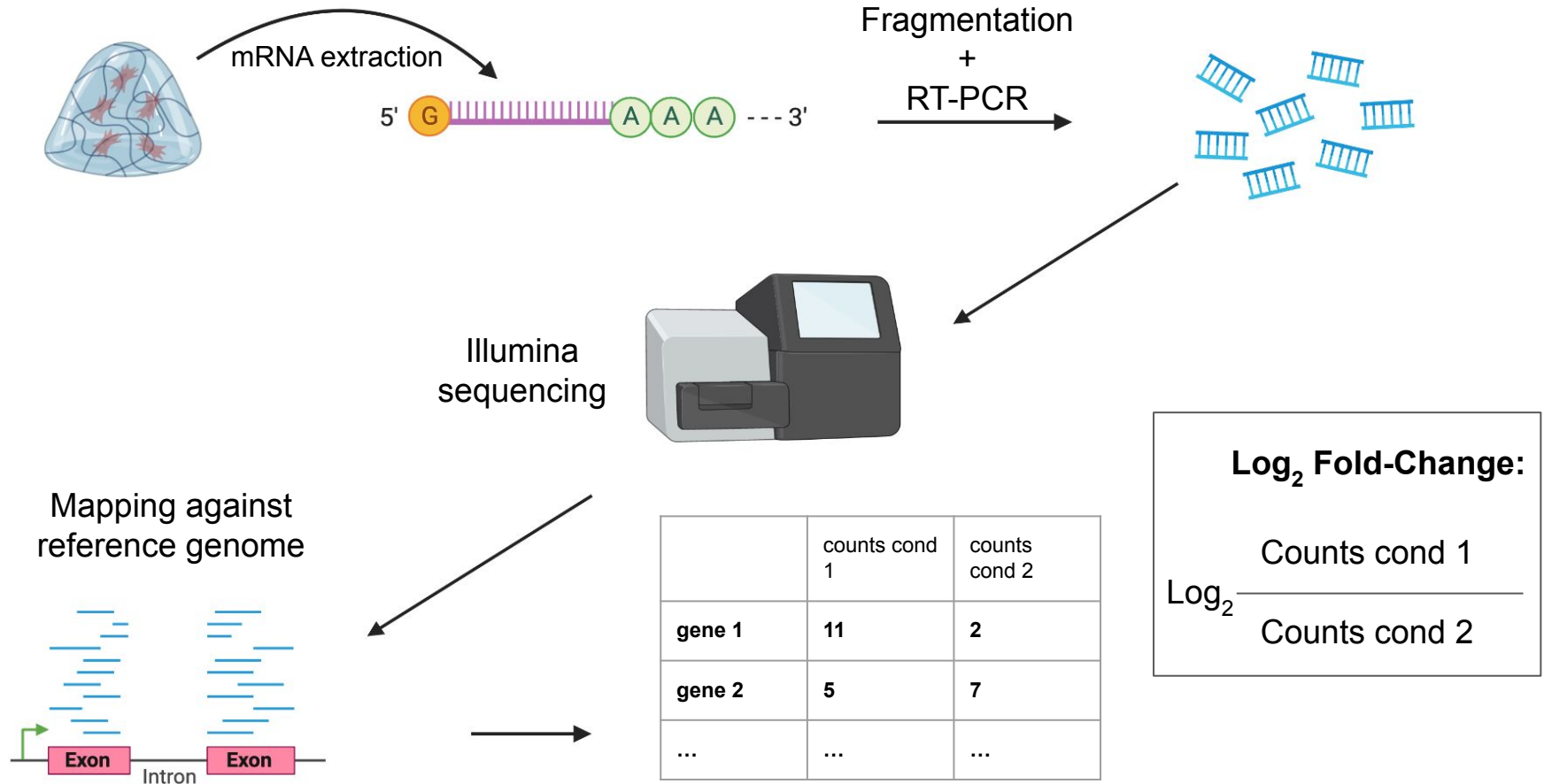
REGENERATIVE ENDODONTIC PROCEDURES (REP)



Experimental design

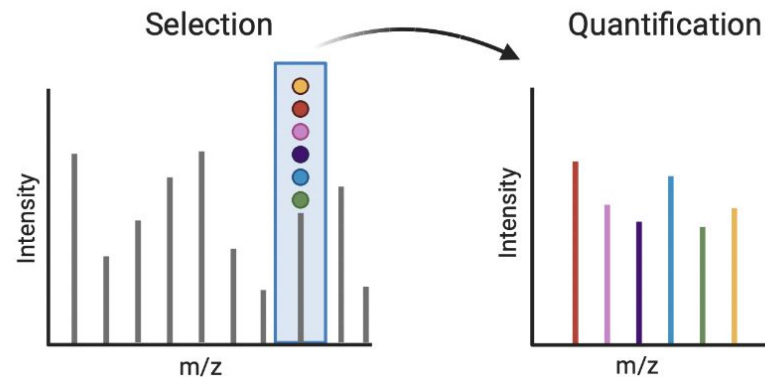
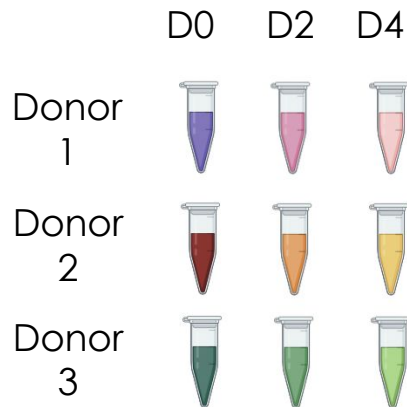


Transcriptomic data



Proteomic data

TMT 9-Plex



LC-MS/MS analysis



Experiment_1.xlsx

Experiment_2.xlsx

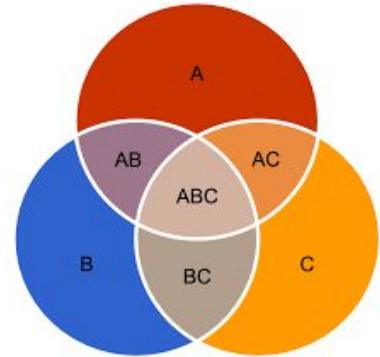
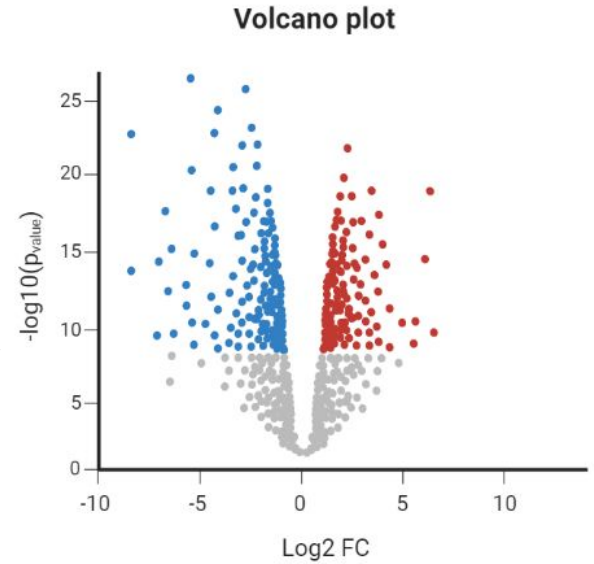
Two replicates with 3 timestamps each time

Proteomic data

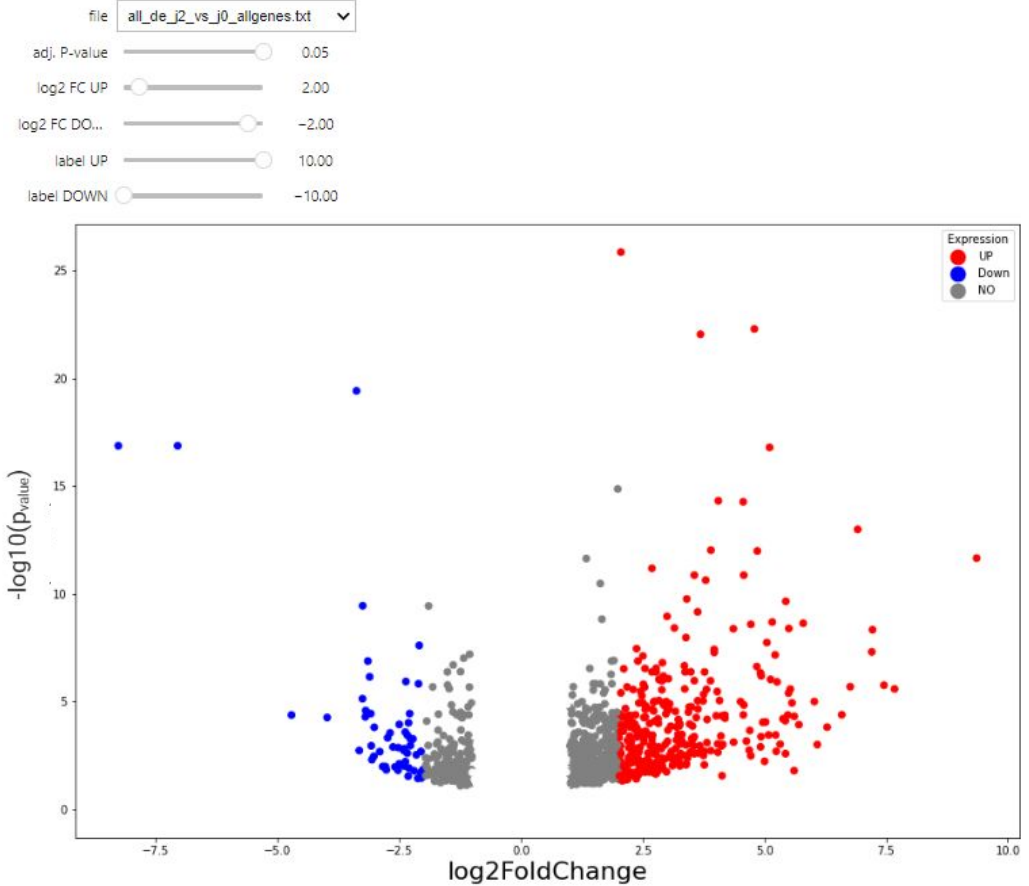
Protein	FDR Confidence	Master	Accession	Description	Contamin	Sum PEP	Coverage	# Peptide	# PSMs	# Unique	# AAs	MW [kDa]	calc. pI	Score	Se	# Peptide
High		Master Protein	P02751	Fibronectin OS=Homo sapiens QX=9606 GN=FN1 PE=1 SV=5		0	1079,65	55	92	607	92	2477	272,2	5,5	2264,21	92
High		Master Protein	sp	ALBU_BOVIN		1	573,971	77	46	652	42	607	69,2	6,18	1876,85	46
High		Master Protein	sp	ALBU_HUMAN		1	516,103	75	42	396	38	609	69,3	6,28	1273	42
High		Master Protein	sp	GELS_HUMAN		1	149,977	39	24	80	24	782	85,6	6,28	236,71	24
High		Master Protein	Q9P2E9	Ribosome-binding protein 1 OS=Homo sapiens QX=9606 GN=RP		0	144,903	41	35	82	35	1410	152,4	8,6	219,94	35
High		Master Protein	sp	PPIA_HUMAN		1	91,763	72	10	75	1	164	17,9	7,81	218,43	10
High		Master Protein	sp	GSTP1_HUMAN		1	91,288	61	10	40	10	209	23,2	5,64	180,46	10
High		Master Protein	sp	K1M1_SHEEP		1	88,686	47	19	63	10	412	46,6	4,81	182,94	19
High		Master Protein	P0DOX6	Immunoglobulin mu heavy chain OS=Homo sapiens QX=9606 PE		0	78,102	34	15	64	1	576	63,4	7,87	173,33	15
High		Master Protein	sp	PRDX1_HUMAN		1	76,513	65	12	58	9	199	22,1	8,13	168,52	12
High		Master Protein	sp	SYH_HUMAN		1	67,007	30	13	34	13	509	57,4	5,88	101,76	13
High		Master Protein	sp	RS27A_HUMAN		1	59,727	51	8	76	1	156	18	9,64	208,18	8
High		Master Protein	P04179	Superoxide dismutase [Mn], mitochondrial OS=Homo sapiens Q		0	58,392	54	11	36	11	222	24,7	8,25	121,19	11
High		Master Protein	sp	TRYP_PIG		1	53,07	25	4	38	4	231	24,4	7,18	136,37	4
High		Master Protein	sp	NQO1_HUMAN		1	52,919	36	10	35	10	274	30,8	8,88	110,05	10
High		Master Protein	sp	K2M2_SHEEP		1	47,472	25	14	50	7	491	53,6	5,57	114,28	14
High		Master Protein	Q99873	Protein arginine N-methyltransferase 1 OS=Homo sapiens QX=9		0	35,395	32	10	28	10	371	42,4	5,35	71,52	10
High		Master Protein	sp	B2MG_HUMAN		1	32,511	55	5	15	5	119	13,7	6,52	54,48	5
High		Master Protein	sp	UBE2I_HUMAN		1	32,062	37	4	14	4	158	18	8,66	38,92	4
High		Master Protein	sp	K1HB_HUMAN		1	31,56	16	7	28	1	404	46,2	4,84	71,92	7
High		Master Protein	sp	K2M1_SHEEP		1	26,617	59	5	13	3	109	12,7	4,59	46,82	5
High		Master Protein	sp	KRHB5_HUMAN		1	25,06	16	9	31	2	507	55,8	6,55	61,25	9
High		Master Protein	sp	CATD_HUMAN		1	20,242	14	6	16	6	412	44,5	6,54	35,42	6
High		Master Protein	sp	ANT3_HUMAN		1	14,791	13	5	11	5	464	52,6	6,71	27,63	5
High		Master Protein	sp	K1H6_HUMAN		1	13,875	10	5	10	1	467	52,2	4,94	24,3	5
High		Master Protein	P02765	Alpha-2-HS-glycoprotein OS=Homo sapiens QX=9606 GN=AHSG		0	13,249	20	5	9	5	367	39,3	5,72	14,91	5
High		Master Protein	Q9H3H3	UPF0696 protein C11orf68 OS=Homo sapiens QX=9606 GN=C11		0	12,236	16	4	7	4	292	31,4	6,32	17,31	4
High		Master Protein	O00468	Agrin OS=Homo sapiens QX=9606 GN=AGRN PE=1 SV=6		0	9,413	2	3	5	3	2068	217,2	6,39	10,48	3
High		Master Protein	sp	IGF2_HUMAN	VRAI		8,892	14	2	5	2	180	20,1	9,32	15,3	2
High		Master Protein	Q43847	Nardilysin OS=Homo sapiens QX=9606 GN=NRDC PE=1 SV=3	FAUX		5,947	1	2	3	2	1151	131,6	4,98	7,08	2
High		Master Protein	sp	BID_HUMAN	VRAI		5,852	8	1	1	1	195	22	5,44	3,32	1
High		Master Protein	Q9NZL4	Hsp70-binding protein 1 OS=Homo sapiens QX=9606 GN=HSPBP	FAUX		5,39	4	1	2	1	359	39,3	5,21	6,1	1
High		Master Protein	sp	RETB_HUMAN	VRAI		5,272	9	1	1	1	201	23	6,07	4,56	1
High		Master Protein	Q52UJ0	Protein FAM98B OS=Homo sapiens QX=9606 GN=FAM98B PE=1	FAUX		5,125	4	2	4	2	433	45,5	8,69	8,37	2

Functional requirements

- 1 : Identify significantly differentially expressed genes and differentially abundant proteins
- 2 : Identify the functions and associated biological processes by querying a database of annotations (GO database) and performing enrichment tests
- 3 : Comparative analysis between transcripts and proteins
- 4 : Deploying interactive notebook online without visible code



Volcano plots









Volcano plot of the transcripts
fold change between D0 and D2

Table to show the results viewed on the volcano plot

file J2/J0 

Show 10  entries

Search:

symbol 	baseMean 	log2FoldChange 	lfcSE 	pvalue 	padj 
5_8S_rRNA	0	NaN	NaN	NaN	NaN
5S_rRNA	0.038653	-0.001017	0.274193	0.9825698	NaN
7SK	0.517037	-0.019322	0.273432	0.6740422	NaN
A1BG	595.000641	-0.027497	0.221786	0.831401	0.9279159
A1BG-AS1	391.792709	-0.199175	0.182067	0.1597196	0.4158482
A1CF	0.084189	0.011649	0.274288	0.8800164	NaN
A2M	281.240669	6.91734	0.919416	6.1939e-17	1.01879e-13
A2M-AS1	7.184134	-0.163297	0.312138	0.1476119	0.3982945
A2ML1	0	NaN	NaN	NaN	NaN
A2ML1-AS1	0	NaN	NaN	NaN	NaN

Previous **1** 2 3 4 5 ... 137 Next

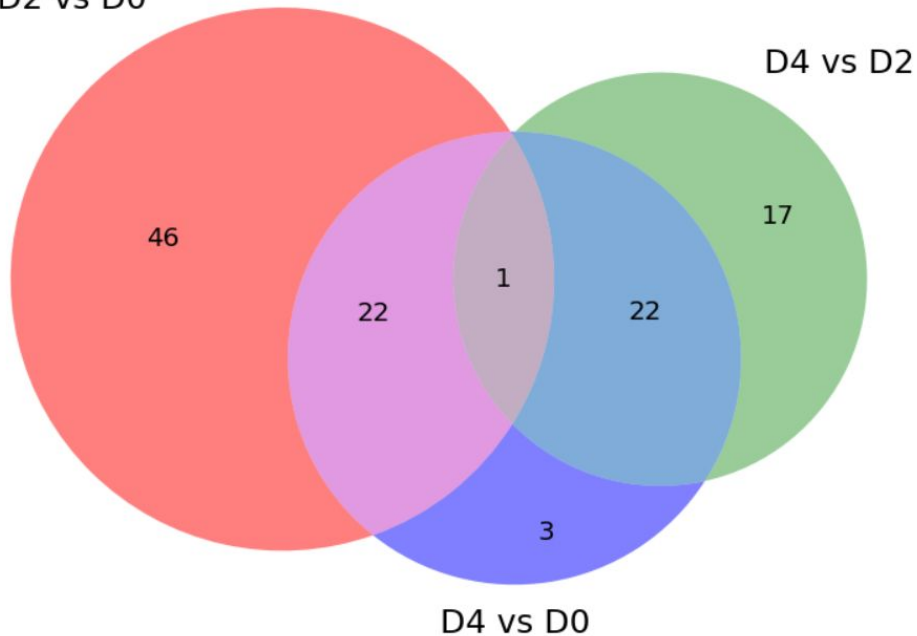
Venn diagrams

file

DE

Venn Diagram

D2 vs D0



file_proteo

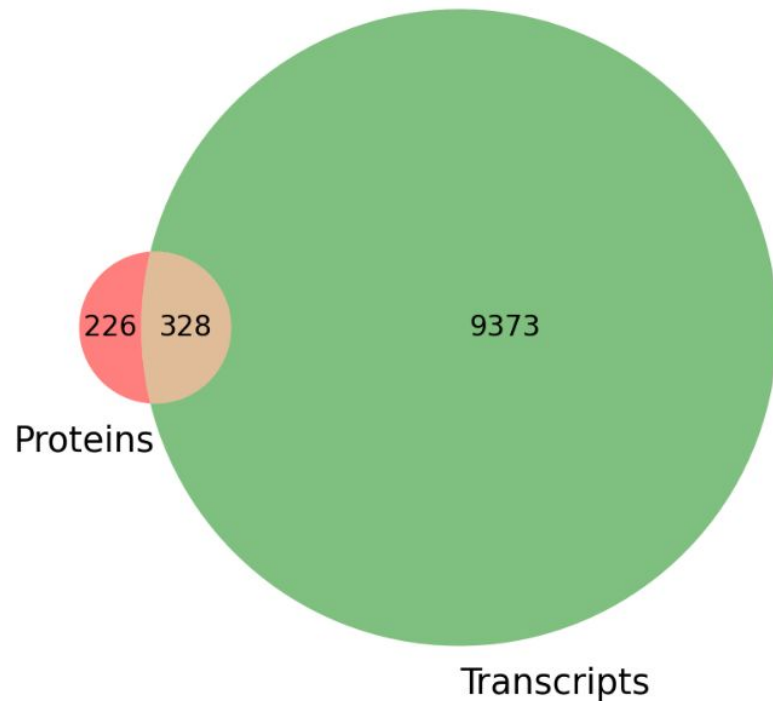
file_transcri...

DE

adj. P-valu...

adj.P-value...

Venn Diagram of the gene symbol sets in transcriptomic vs. proteomic data



Gene Set Enrichment Analysis

- Competitive null hypothesis against Gene Ontology terms
- J2/J0 differentially abundant transcripts enrichment
 - **Glycolysis, signal transduction, perception of EC environment**

	Gene_set	Term	Overlap	Adjusted P-value	Genes
0	GO_Biological_Process_2021	glycolytic process (GO:0006096)	10/29	0.001133	LDHA;TPI1;PKLR;HKDC1;PGK1;ALDOC;ENO2;ALDOA;GAP...
1	GO_Biological_Process_2021	canonical glycolysis (GO:0061621)	9/24	0.001133	TPI1;PKLR;PGK1;ALDOC;ENO2;ALDOA;GAPDH;HK2;PFKP
2	GO_Biological_Process_2021	glucose catabolic process to pyruvate (GO:0061...	9/24	0.001133	TPI1;PKLR;PGK1;ALDOC;ENO2;ALDOA;GAPDH;HK2;PFKP
3	GO_Biological_Process_2021	glycolytic process through glucose-6-phosphate...	9/25	0.001270	TPI1;PKLR;PGK1;ALDOC;ENO2;ALDOA;GAPDH;HK2;PFKP
4	GO_Biological_Process_2021	cellular response to cytokine stimulus (GO:007...	47/482	0.003846	RIPOR2;IL1RN;CCL11;SELPLG;IL24;RORA;AKAP6;CXCL...

	Gene_set	Term	Overlap	Adjusted P-value	Genes
0	GO_Molecular_Function_2021	receptor ligand activity (GO:0048018)	32/307	0.028938	SEMA7A;COLEC10;CCL11;TNFRSF11B;FGF1;AREG;PTHLH...

	Gene_set	Term	Overlap	Adjusted P-value	Genes
0	GO_Cellular_Component_2021	ionotropic glutamate receptor complex (GO:0008...	8/32	0.016052	GRIA1;OLFM2;DLG4;GRIK4;GRIK2;GRIN2C;CNIH3;GRIN1
1	GO_Cellular_Component_2021	collagen-containing extracellular matrix (GO:0...	36/380	0.016052	COL17A1;LRRC15;SEMA7A;SERPINA1;COL13A1;LAMC3;L...
2	GO_Cellular_Component_2021	integral component of plasma membrane (GO:0005...	101/1454	0.018797	ICAM5;ICAM1;SLC8A2;AQP1;MILR1;EDNRA;HTR7;SLC16...
3	GO_Cellular_Component_2021	potassium channel complex (GO:0034705)	12/80	0.031223	KCNF1;KCNJ8;KCNIP2;KCNC3;KCNIP3;GRIK4;ABCC9;GR...

Gene Set Enrichment Analysis

- Competitive null hypothesis against Gene Ontology terms
- J2/J0 differentially abundant proteins enrichment
→ **ECM organization, exocytosis, regulation of fibrinolysis**

	Gene_set	Term	Overlap	Adjusted P-value	Genes
0	GO_Biological_Process_2021	extracellular matrix organization (GO:0030198)	16/300	7.015200e-20	APP;VWF;MMP2;SERPINF2;MMP3;SERPINE1;PLG;THBS1;...
1	GO_Biological_Process_2021	extracellular structure organization (GO:0043062)	13/216	1.340338e-16	APP;VWF;MMP2;MMP3;SERPINE1;THBS1;DCN;COL3A1;CO...
2	GO_Biological_Process_2021	external encapsulating structure organization ...	13/217	1.340338e-16	APP;VWF;MMP2;MMP3;SERPINE1;THBS1;DCN;COL3A1;CO...
3	GO_Biological_Process_2021	platelet degranulation (GO:0002576)	9/125	1.046657e-11	APP;VWF;SERPINF2;SERPINE1;APOA1;PLG;TIMP1;THBS...
4	GO_Biological_Process_2021	regulated exocytosis (GO:0045055)	9/180	2.330239e-10	APP;VWF;SERPINF2;SERPINE1;APOA1;PLG;TIMP1;THBS...
5	GO_Biological_Process_2021	collagen fibril organization (GO:0030199)	7/89	3.065533e-09	COL3A1;COL1A2;COL5A1;COL4A2;SERPINF2;COL6A1;CO...
6	GO_Biological_Process_2021	regulation of complement activation (GO:0030449)	6/50	5.697646e-09	C1QB;C3;C5;C1S;CFP;C1QC
7	GO_Biological_Process_2021	regulation of immune effector process (GO:0002...	6/53	7.175437e-09	C1QB;C3;C5;C1S;CFP;C1QC
8	GO_Biological_Process_2021	regulation of humoral immune response (GO:0002...	6/54	7.175437e-09	C1QB;C3;C5;C1S;CFP;C1QC
9	GO_Biological_Process_2021	negative regulation of fibrinolysis (GO:0051918)	4/9	2.376390e-08	SERPINE1;SERPINF2;PLG;THBS1
10	GO_Biological_Process_2021	supramolecular fiber organization (GO:0097435)	9/351	4.116684e-08	APP;COL3A1;COL1A2;COL5A1;COL4A2;SERPINF2;COL6A...
11	GO_Biological_Process_2021	regulation of fibrinolysis (GO:0051917)	4/13	1.119484e-07	SERPINE1;SERPINF2;PLG;THBS1
12	GO_Biological_Process_2021	positive regulation of blood coagulation (GO:0...	4/17	3.426633e-07	SERPINE1;SERPINF2;PLG;THBS1

Gene Set Enrichment Analysis

- Competitive null hypothesis against Gene Ontology terms
- J4/J2 differentially abundant transcripts enrichment → **mitotic processes**



	Gene_set	Term	Overlap	Adjusted P-value	Genes
0	GO_Biological_Process_2021	microtubule cytoskeleton organization involved...	40/128	4.757960e-16	ERCC6L;BUB1B;CDCA8;TTK;KIF11;CENPA;SKA1;AURKB;...
1	GO_Biological_Process_2021	mitotic spindle organization (GO:0007052)	43/157	2.806952e-15	ERCC6L;BUB1B;CDCA8;TTK;KIF11;CENPA;SKA1;AURKB;...
2	GO_Biological_Process_2021	mitotic sister chromatid segregation (GO:0000070)	27/102	1.061352e-08	CDCA5;NCAPG2;KIF14;NCAPG;CDCA8;NCAPH;CCNB1;NUS...
3	GO_Biological_Process_2021	kinetochore organization (GO:0051383)	9/13	2.860446e-06	CDT1;CENPE;CENPF;CENPW;CENPH;NUF2;CENPA;NDC80;...
4	GO_Biological_Process_2021	centromere complex assembly (GO:0034508)	14/37	3.911693e-06	CENPU;CENPV;CENPW;HJURP;KNL1;CENPA;CENPE;CENPF...
5	GO_Biological_Process_2021	sister chromatid segregation (GO:0000819)	13/34	9.888964e-06	TOP2A;SPAG5;NCAPG2;PLK1;CDCA8;KNSTRN;ZWINT;NDC...
6	GO_Biological_Process_2021	mitotic nuclear division (GO:0140014)	18/74	4.841909e-05	SPAG5;UBE2C;NDE1;NCAPG2;PLK1;CDCA8;KIF11;KNSTR...
7	GO_Biological_Process_2021	regulation of cyclin-dependent protein serine/...	19/82	4.841909e-05	BLM;CDKN2B;CCNF;PLK1;PROX1;PKD2;CDC25C;PKMYT1;...
8	GO_Biological_Process_2021	glycolytic process (GO:0006096)	11/29	9.267617e-05	PFKFB2;GPI;LDHA;TPI1;PGAM1;PGK1;ALDOC;ENO1;ENO...
9	GO_Biological_Process_2021	canonical glycolysis (GO:0061621)	10/24	9.497093e-05	GPI;TPI1;PGAM1;PGK1;ALDOC;ENO1;ENO2;ALDOA;HK2;...

Gene Set Enrichment Analysis

- Competitive null hypothesis against Gene Ontology terms
- J4/J2 overabundant proteins enrichment → **Metabolism, cell morphogenesis**

	Gene_set	Term	Overlap	Adjusted P-value	Genes
403	GO_Cellular_Component_2021	intracellular organelle lumen (GO:0070013)	11/848	1.141924e-08	GLUD1;HMGCL;FH;ECHS1;HSPA5;MDH2;C1QBP;FGG;SERP...
404	GO_Cellular_Component_2021	mitochondrial matrix (GO:0005759)	8/348	4.144643e-08	GLUD1;HMGCL;FH;ECHS1;MDH2;C1QBP;DLD;ACAT1
0	GO_Biological_Process_2021	cellular amino acid catabolic process (GO:0009...	5/90	1.084072e-05	GLUD1;HMGCL;ECHS1;DLD;ACAT1
1	GO_Biological_Process_2021	branched-chain amino acid catabolic process (G...	3/20	1.281631e-04	ECHS1;DLD;ACAT1
2	GO_Biological_Process_2021	branched-chain amino acid metabolic process (G...	3/20	1.281631e-04	ECHS1;DLD;ACAT1
3	GO_Biological_Process_2021	positive regulation of substrate adhesion-depe...	3/36	5.479377e-04	FGB;C1QBP;FGG
4	GO_Biological_Process_2021	platelet degranulation (GO:0002576)	4/125	5.479377e-04	FGB;FGG;LAMP2;SERPING1
5	GO_Biological_Process_2021	negative regulation of blood coagulation (GO:0...	3/40	5.479377e-04	FGB;FGG;SERPING1
6	GO_Biological_Process_2021	positive regulation of peptide hormone secreti...	3/43	5.854625e-04	FGB;GLUD1;FGG
7	GO_Biological_Process_2021	positive regulation of cell morphogenesis invo...	3/50	6.833829e-04	FGB;C1QBP;FGG
8	GO_Biological_Process_2021	regulation of substrate adhesion-dependent cel...	3/51	6.833829e-04	FGB;C1QBP;FGG
9	GO_Biological_Process_2021	fatty acid beta-oxidation (GO:0006635)	3/52	6.833829e-04	HADHB;ECHS1;ACAT1
10	GO_Biological_Process_2021	malate metabolic process (GO:0006108)	2/7	6.833829e-04	FH;MDH2

Displaying interactive results online


 README.md 

Multi_omics

Summary :

This GitHub repository aims at producing interactive visualizations, analyses and integration of multi-omics data. This data is the result of transcriptomic and proteomic experiments on dental pulp mesenchymal stem cell growth.

To view the results you can click on the button below or clone the repository and launch `script.ipynb` or `gsea.ipynb` on your computer :

 launch `binder`

https://mybinder.org/v2/gh/victordeguise/Multi_omics/HEAD?urlpath=%2Fvoila%2Frender%2Fscript.ipynb

Notebooks:

- `script.ipynb` : Interactive visualisations, currently accessible under the Binder link above, includes:
 - Volcano plots for proteomic and transcriptomic datasets by experience
 - Sortable tables for each experience with filters
 - Venn diagram comparing gene symbols appearing in the different datasets
- `gsea.ipynb` : Enrichment analysis, includes:
 - dotplots for Gene Ontology pathways
 - Sortable tables for each experience with filters

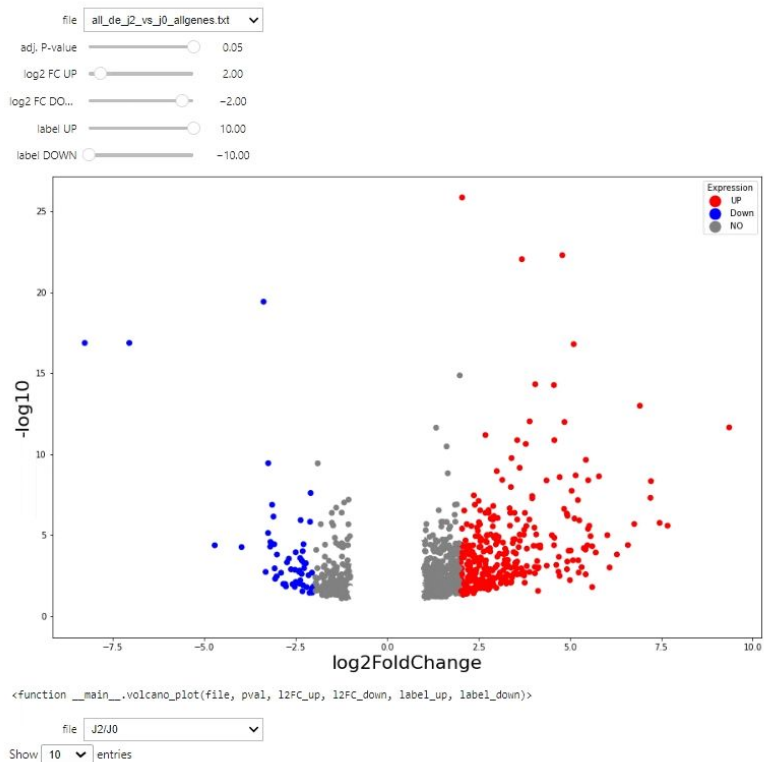
Requirements

voilà



Starting repository: victordeguise/Multi_omics/HEAD
New to Binder? Check out the [Binder Documentation](#) for more information

Transcripto



Search:

Conclusion

To sum up:

- Interactive visualisations accessible for users without programming background
- Functional annotations and geneset comparison between datasets

Limitations:

- Few options for displaying a Jupyter notebook into a webpage
- Data integration is specific to the formats used → limited reusability
- Experimental design was not intended for multi-omic integration → no standard method to combine the two types of data

Further improvements

- Deploying the html page on university's servers with the help of iCap
→ **URL:** <https://momics.univ-lyon1.fr>
- Adding more options for the input format

Thank you for attention !

Any questions ?