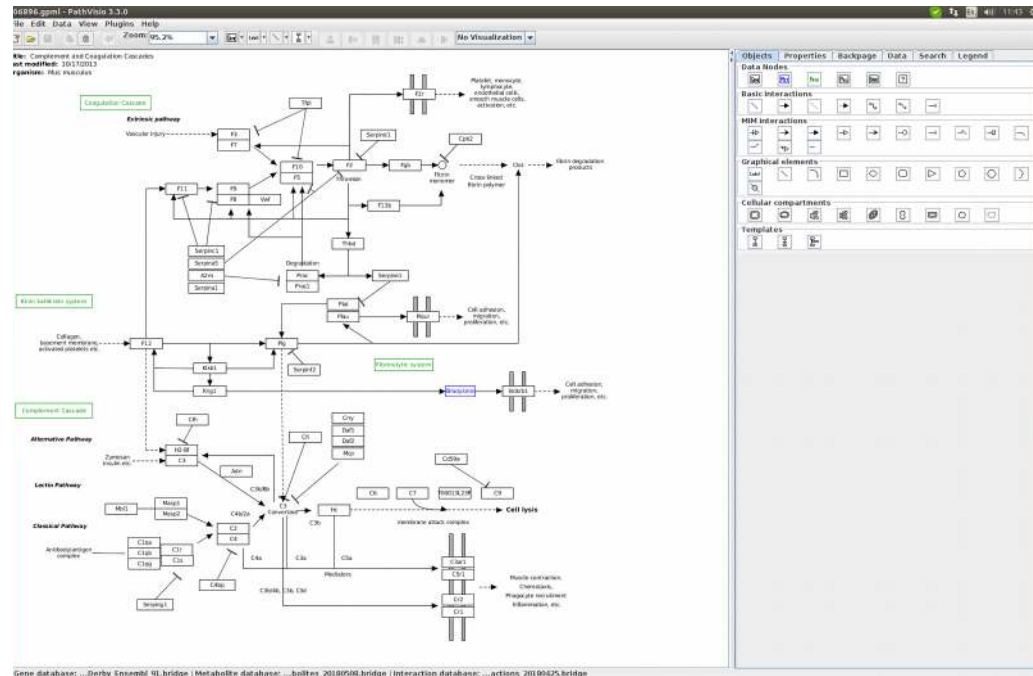


TimiRGeN - Pathvisio GRN creation guide:

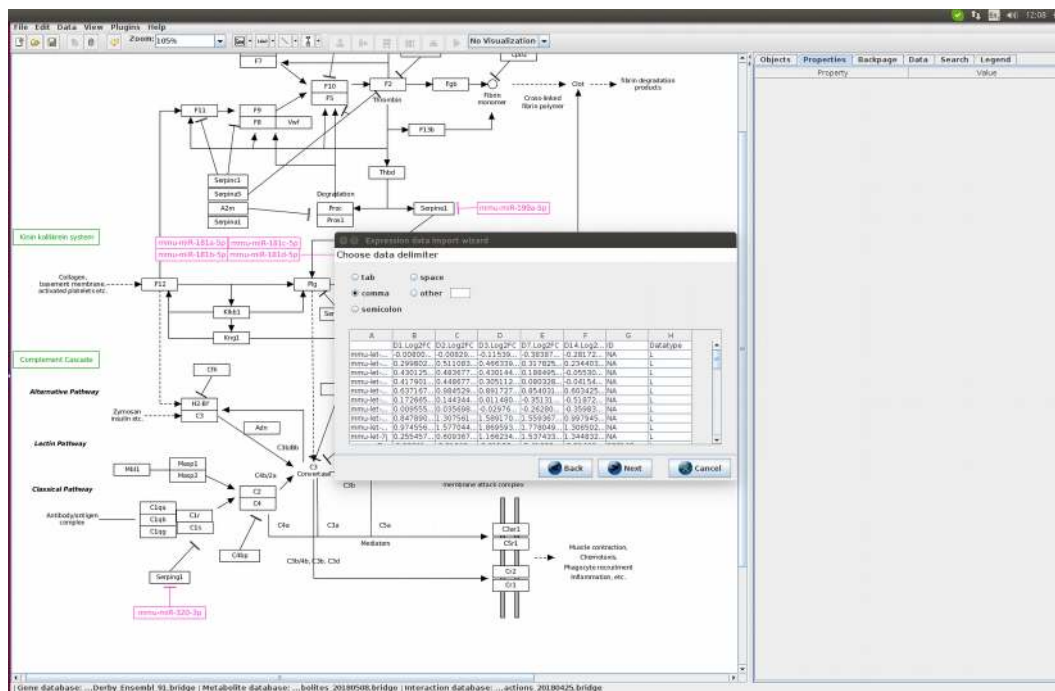
- 1) Open selected pathway in Pathvisio. Use the set up instructions found on the pathvisio website. You can download your pathway as a gpml format from wikipathways or use the wikipathways app in pathvisio to import the pathway (1, 2).



- 2) Make sure all NAs are filled. MicroRNAs are poorly annotated in contrast with mRNAs. Use MGI or NCBI databases to fill in missing entrez geneIDs/ ensemble IDs. In case of multiple miRs having the same IDs, use the adjusted IDs created by TimiRGeN when creating the MAPP and Dynamics files. In the case of poorly annotated miRs still persisting perform some sort of manual alteration in the IDs of the miR in the Dynamics and MAPP file. The IDs must match in these files.

miRNA	Gene ID
miR-181a-3p	735252
miR-181b-3p	735253
miR-181c-3p	735254
miR-181d-3p	735255
miR-181e-3p	735256
miR-181f-3p	735257
miR-181g-3p	735258
miR-181h-3p	735259
miR-181i-3p	735260
miR-181j-3p	735261
miR-181k-3p	735262
miR-181l-3p	735263
miR-181m-3p	735264
miR-181n-3p	735265
miR-181o-3p	735266
miR-181p-3p	735267
miR-181q-3p	735268
miR-181r-3p	735269
miR-181s-3p	735270
miR-181t-3p	735271
miR-181u-3p	735272
miR-181v-3p	735273
miR-181w-3p	735274
miR-181x-3p	735275
miR-181y-3p	735276
miR-181z-3p	735277
miR-181aa-3p	735278
miR-181ab-3p	735279
miR-181ac-3p	735280
miR-181ad-3p	735281
miR-181ae-3p	735282
miR-181af-3p	735283
miR-181ag-3p	735284
miR-181ah-3p	735285
miR-181ai-3p	735286
miR-181aj-3p	735287
miR-181ak-3p	735288
miR-181al-3p	735289
miR-181am-3p	735290
miR-181an-3p	735291
miR-181ao-3p	735292
miR-181ap-3p	735293
miR-181aq-3p	735294
miR-181ar-3p	735295
miR-181as-3p	735296
miR-181at-3p	735297
miR-181au-3p	735298
miR-181av-3p	735299
miR-181aw-3p	735300
miR-181ax-3p	735301
miR-181ay-3p	735302
miR-181az-3p	735303
miR-181ba-3p	735304
miR-181bb-3p	735305
miR-181bc-3p	735306
miR-181bd-3p	735307
miR-181be-3p	735308
miR-181bf-3p	735309
miR-181bg-3p	735310
miR-181bh-3p	735311
miR-181bi-3p	735312
miR-181bj-3p	735313
miR-181bk-3p	735314
miR-181bl-3p	735315
miR-181bm-3p	735316
miR-181bn-3p	735317
miR-181bo-3p	735318
miR-181bp-3p	735319
miR-181bq-3p	735320
miR-181br-3p	735321
miR-181bs-3p	735322
miR-181bt-3p	735323
miR-181bu-3p	735324
miR-181bv-3p	735325
miR-181bw-3p	735326
miR-181bx-3p	735327
miR-181by-3p	735328
miR-181bz-3p	735329
miR-181ca-3p	735330
miR-181cb-3p	735331
miR-181cc-3p	735332
miR-181cd-3p	735333
miR-181ce-3p	735334
miR-181cf-3p	735335
miR-181cg-3p	735336
miR-181ch-3p	735337
miR-181ci-3p	735338
miR-181cj-3p	735339
miR-181ck-3p	735340
miR-181cl-3p	735341
miR-181cm-3p	735342
miR-181cn-3p	735343
miR-181co-3p	735344
miR-181cp-3p	735345
miR-181cq-3p	735346
miR-181cr-3p	735347
miR-181cs-3p	735348
miR-181ct-3p	735349
miR-181cu-3p	735350
miR-181cv-3p	735351
miR-181cw-3p	735352
miR-181cx-3p	735353
miR-181cy-3p	735354
miR-181cz-3p	735355
miR-181da-3p	735356
miR-181db-3p	735357
miR-181dc-3p	735358
miR-181dd-3p	735359
miR-181de-3p	735360
miR-181df-3p	735361
miR-181dg-3p	735362
miR-181dh-3p	735363
miR-181di-3p	735364
miR-181dj-3p	735365
miR-181dk-3p	735366
miR-181dl-3p	735367
miR-181dm-3p	735368
miR-181dn-3p	735369
miR-181do-3p	735370
miR-181dp-3p	735371
miR-181dq-3p	735372
miR-181dr-3p	735373
miR-181ds-3p	735374
miR-181dt-3p	735375
miR-181du-3p	735376
miR-181dv-3p	735377
miR-181dw-3p	735378
miR-181dx-3p	735379
miR-181dy-3p	735380
miR-181dz-3p	735381
miR-181ea-3p	735382
miR-181eb-3p	735383
miR-181ec-3p	735384
miR-181ed-3p	735385
miR-181ee-3p	735386
miR-181ef-3p	735387
miR-181eg-3p	735388
miR-181eh-3p	735389
miR-181ei-3p	735390
miR-181ej-3p	735391
miR-181ek-3p	735392
miR-181el-3p	735393
miR-181em-3p	735394
miR-181en-3p	735395
miR-181eo-3p	735396
miR-181ep-3p	735397
miR-181eq-3p	735398
miR-181er-3p	735399
miR-181es-3p	735400
miR-181et-3p	735401
miR-181eu-3p	735402
miR-181ev-3p	735403
miR-181ew-3p	735404
miR-181ex-3p	735405
miR-181ey-3p	735406
miR-181ez-3p	735407
miR-181fa-3p	735408
miR-181fb-3p	735409
miR-181fc-3p	735410
miR-181fd-3p	735411
miR-181fe-3p	735412
miR-181ff-3p	735413
miR-181fg-3p	735414
miR-181fh-3p	735415
miR-181fi-3p	735416
miR-181fj-3p	735417
miR-181fk-3p	735418
miR-181fl-3p	735419
miR-181fm-3p	735420
miR-181fn-3p	735421
miR-181fo-3p	735422
miR-181fp-3p	735423
miR-181fq-3p	735424
miR-181fr-3p	735425
miR-181fs-3p	735426
miR-181ft-3p	735427
miR-181fu-3p	735428
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miR-181gp-3p	735449
miR-181gq-3p	735450
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miR-181gs-3p	735452
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miR-181gv-3p	735455
miR-181gw-3p	735456
miR-181gx-3p	735457
miR-181gy-3p	735458
miR-181gz-3p	735459
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miR-181hc-3p	735462
miR-181hd-3p	735463
miR-181he-3p	735464
miR-181hf-3p	735465
miR-181hg-3p	735466
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miR-181hj-3p	735468
miR-181hk-3p	735469
miR-181hl-3p	735470
miR-181hm-3p	735471
miR-181hn-3p	735472
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miR-181hp-3p	735474
miR-181hq-3p	735475
miR-181hr-3p	735476
miR-181hs-3p	735477
miR-181ht-3p	735478
miR-181hu-3p	735479
miR-181hv-3p	735480
miR-181hw-3p	735481
miR-181hx-3p	735482
miR-181hy-3p	735483
miR-181hz-3p	735484
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miR-181ib-3p	735486
miR-181ic-3p	735487
miR-181id-3p	735488
miR-181ie-3p	735489
miR-181if-3p	735490
miR-181ig-3p	735491
miR-181ih-3p	735492
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miR-181ik-3p	735495
miR-181il-3p	735496
miR-181im-3p	735497
miR-181in-3p	735498
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miR-181is-3p	735503
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miR-181jf-3p	735516
miR-181jg-3p	735517
miR-181jh-3p	735518
miR-181ji-3p	735519
miR-181jj-3p	735520
miR-181jk-3p	735521
miR-181jl-3p	735522
miR-181jm-3p	735523
miR-181jn-3p	735524
miR-181jo-3p	735525
miR-181jp-3p	735526
miR-181jq-3p	735527
miR-181jr-3p	735528
miR-181js-3p	735529
miR-181jt-3p	735530
miR-181ju-3p	735531
miR-181jv-3p	735532
miR-181jw-3p	735533
miR-181jx-3p	735534
miR-181jy-3p	735535
miR-181jz-3p	735536
miR-181ka-3p	735537
miR-181kb-3p	735538
miR-181kc-3p	735539
miR-181kd-3p	735540
miR-181ke-3p	735541
miR-181kf-3p	735542
miR-181kg-3p	735543
miR-181kh-3p	735544
miR-181ki-3p	735545
miR-181kj-3p	735546
miR-181kk-3p	735547
miR-181kl-3p	735548
miR-181km-3p	735549
miR-181kn-3p	735550
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miR-181kp-3p	735552
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miR-181kr-3p	735554
miR-181ks-3p	735555
miR-181kt-3p	735556
miR-181ku-3p	735557
miR-181kv-3p	735558
miR-181kw-3p	735559
miR-181kx-3p	735560
miR-181ky-3p	735561
miR-181kz-3p	735562
miR-181la-3p	735563
miR-181lb-3p	735564
miR-181lc-3p	735565
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miR-181le-3p	735567
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miR-181lj-3p	735572
miR-181lk-3p	735573
miR-181ll-3p	735574
miR-181lm-3p	735575
miR-181ln-3p	735576
miR-181lo-3p	735577
miR-181lp-3p	735578
miR-181lq-3p	735579
miR-181lr-3p	735580
miR-181ls-3p	735581
miR-181lt-3p	735582
miR-181lu-3p	735583
miR-181lv-3p	735584
miR-181lw-3p	735585
miR-181lx-3p	7355

The screenshot displays the KEGG Pathway database interface. The main window shows the 'Complement and Coagulation Cascades' pathway. The diagram is color-coded with green boxes for 'Complement cascade', 'Fibrinolytic system', and 'Hemostatic system'. The right panel shows the 'Objects' and 'Properties' tabs, with the 'Properties' tab selected, displaying the 'Name' and 'Value' columns.



6) Choose Primary identifier column (Green) as ID and column to specify system code as Datatype (red).

Choose column types

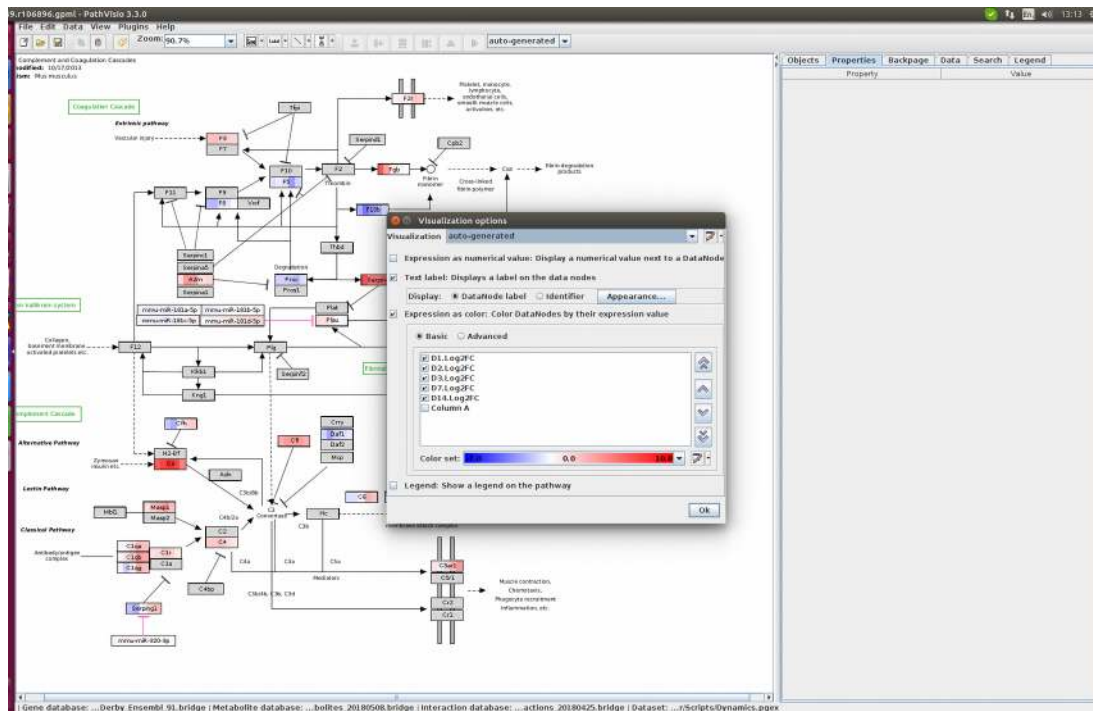
Select primary identifier column: ID

Select a column to specify system code: Datatype

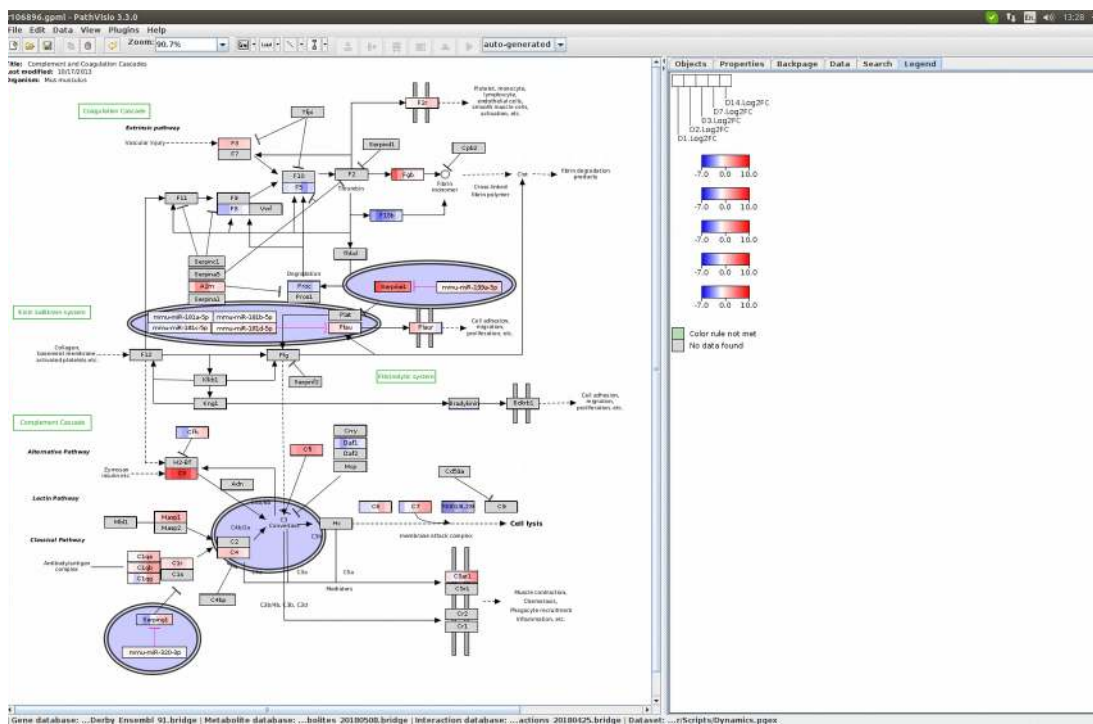
☐ Use the same system code for all rows

	A	B	C	D	E	F	G	H	Datatype
1	mtm-met-1	-0.00050	-0.00025	-0.11539	-0.38187	-0.28172	NA	NA	L
2	mtm-met-2	0.39980	0.31103	0.48533	0.27828	0.23463	NA	NA	L
3	mtm-met-3	0.430125	0.483477	0.420144	0.188495	-0.95530	NA	NA	L
4	mtm-met-4	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
5	mtm-met-5	0.437167	0.484526	0.491727	0.454031	0.403425	NA	NA	L
6	mtm-met-6	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
7	mtm-met-7	0.179655	0.144384	0.011480	-0.35131	-0.51872	NA	NA	L
8	mtm-met-8	0.009555	0.076568	0.02975	-0.29580	-0.75851	NA	NA	L
9	mtm-met-9	0.687895	0.107541	0.585170	0.559267	0.607545	NA	NA	L
10	mtm-met-10	0.474056	0.577044	0.469551	0.738483	0.309502	NA	NA	L
11	mtm-met-11	0.255457	0.409587	0.169234	0.527433	0.344832	NA	NA	L
12	mtm-met-12	0.00050	-0.00025	-0.11539	-0.38187	-0.28172	NA	NA	L
13	mtm-met-13	0.430125	0.483477	0.420144	0.188495	-0.95530	NA	NA	L
14	mtm-met-14	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
15	mtm-met-15	0.437167	0.484526	0.491727	0.454031	0.403425	NA	NA	L
16	mtm-met-16	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
17	mtm-met-17	0.179655	0.144384	0.011480	-0.35131	-0.51872	NA	NA	L
18	mtm-met-18	0.009555	0.076568	0.02975	-0.29580	-0.75851	NA	NA	L
19	mtm-met-19	0.687895	0.107541	0.585170	0.559267	0.607545	NA	NA	L
20	mtm-met-20	0.474056	0.577044	0.469551	0.738483	0.309502	NA	NA	L
21	mtm-met-21	0.255457	0.409587	0.169234	0.527433	0.344832	NA	NA	L
22	mtm-met-22	0.00050	-0.00025	-0.11539	-0.38187	-0.28172	NA	NA	L
23	mtm-met-23	0.430125	0.483477	0.420144	0.188495	-0.95530	NA	NA	L
24	mtm-met-24	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
25	mtm-met-25	0.437167	0.484526	0.491727	0.454031	0.403425	NA	NA	L
26	mtm-met-26	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
27	mtm-met-27	0.179655	0.144384	0.011480	-0.35131	-0.51872	NA	NA	L
28	mtm-met-28	0.009555	0.076568	0.02975	-0.29580	-0.75851	NA	NA	L
29	mtm-met-29	0.687895	0.107541	0.585170	0.559267	0.607545	NA	NA	L
30	mtm-met-30	0.474056	0.577044	0.469551	0.738483	0.309502	NA	NA	L
31	mtm-met-31	0.255457	0.409587	0.169234	0.527433	0.344832	NA	NA	L
32	mtm-met-32	0.00050	-0.00025	-0.11539	-0.38187	-0.28172	NA	NA	L
33	mtm-met-33	0.430125	0.483477	0.420144	0.188495	-0.95530	NA	NA	L
34	mtm-met-34	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
35	mtm-met-35	0.437167	0.484526	0.491727	0.454031	0.403425	NA	NA	L
36	mtm-met-36	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
37	mtm-met-37	0.179655	0.144384	0.011480	-0.35131	-0.51872	NA	NA	L
38	mtm-met-38	0.009555	0.076568	0.02975	-0.29580	-0.75851	NA	NA	L
39	mtm-met-39	0.687895	0.107541	0.585170	0.559267	0.607545	NA	NA	L
40	mtm-met-40	0.474056	0.577044	0.469551	0.738483	0.309502	NA	NA	L
41	mtm-met-41	0.255457	0.409587	0.169234	0.527433	0.344832	NA	NA	L
42	mtm-met-42	0.00050	-0.00025	-0.11539	-0.38187	-0.28172	NA	NA	L
43	mtm-met-43	0.430125	0.483477	0.420144	0.188495	-0.95530	NA	NA	L
44	mtm-met-44	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
45	mtm-met-45	0.437167	0.484526	0.491727	0.454031	0.403425	NA	NA	L
46	mtm-met-46	0.417901	0.448677	0.309112	0.080258	-0.44154	NA	NA	L
47	mtm-met-47	0.179655	0.144384	0.011480	-0.35131	-0.51872	NA	NA	L
48	mtm-met-48	0.009555	0.076568	0.02975	-0.29580	-0.75851	NA	NA	L
49	mtm-met-49	0.687895	0.107541	0.585170	0.559267	0.607545	NA	NA	L
50	mtm-met-50	0.474056	0.577044	0.469551	0.738483	0.309502	NA	NA	L

7) Select a suitable colour palate to represent the time series. The segments will be shown in an order which matches the Dynamic file. (Data > Visualization options)



8) Isolate key parts of the pathway for bottom-up GRN construction. In this example, the interactions of the miR-mRNA target's can be seen to effect the biogenesis of C3 convertase.



References

- 1) Slenter DN, Kutmon M, Hanspers K, et al. WikiPathways: a multifaceted pathway database bridging metabolomics to other omics research. *Nucleic Acids Res.* 2018;46(D1):D661D667. doi:10.1093/nar/gkx1064
- 2) van Iersel MP, Kelder T, Pico AR, et al. Presenting and exploring biological pathways with PathVisio. *BMC Bioinformatics.* 2008;9:399. Published 2008 Sep 25. doi:10.1186/1471-2105-9-399