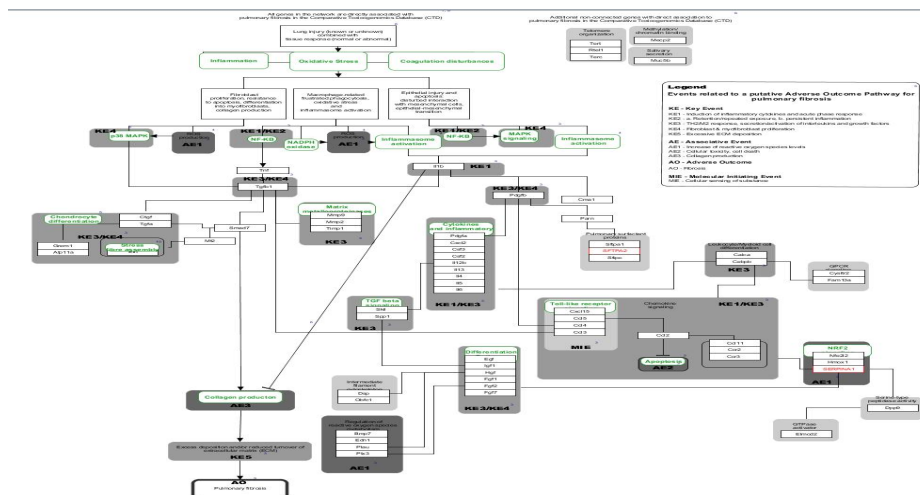


TimiRGeN - Pathvisio GRN creation guide:

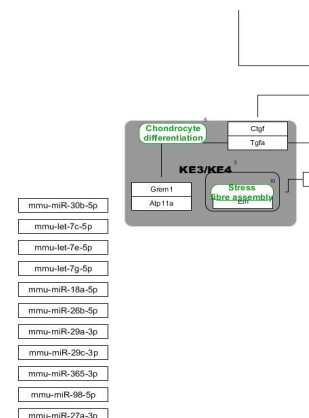
1) Open selected pathway in Pathvisio. (<https://pathvisio.github.io>)

Use the set up instructions found on the pathvisio website. You can download the pathway as a gpml file from [wikipathways](https://www.wikipathways.org/) or use the [wikipathways](https://www.wikipathways.org/) app in pathvisio to import the pathway (1, 2). Can download the [wikipathways](https://www.wikipathways.org/) app here <https://pathvisio.github.io/plugins/wikipathways.html>. Lung Fibrosis pathway is displayed here.



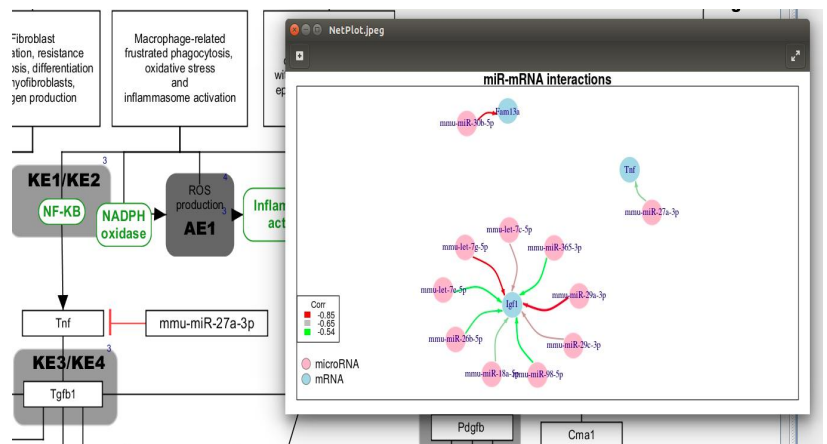
2) If microRNA entrezgene ID's/ ensembl ID's are missing, use MGI or ensembl/ NCBI to find these and manually insert them next to correct microRNA (3-5). For -5p and -3p clashes, add a .1 or .2 to differentiate.

3) Use the MAPP app on Pathvisio to import the MAPP.txt file created with TimiRGeN. (<https://github.com/PathVisio/mappbuilder>).



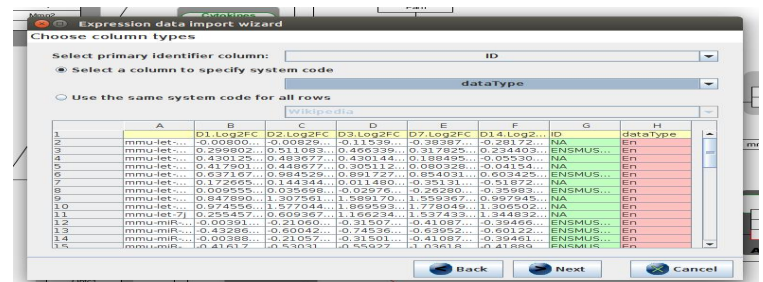
4) Manually place microRNAs where they should be on the wiki pathway.

5) Import the dynamics.csv file
(Data > Import expression data).
Select comma.

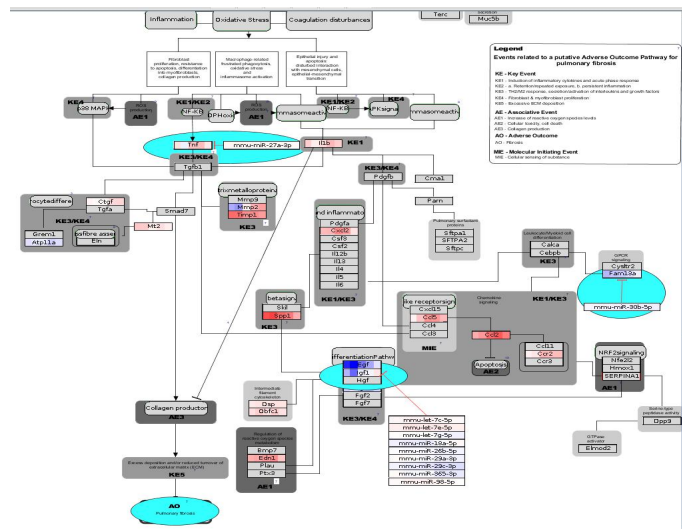


6) Choose Primary identifier column (Green) as ID and column to specify system code as dataType (red).

Do check if the loaded wiki pathway uses entrezgene IDs or ensembl gene IDs. Errors may occur if the incorrect ID type was used during the analysis.



8) Isolate key parts of the pathway for a targeted literature search and then bottom-up GRN construction.



References

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- 2) Kutmon M, van Iersel MP, Bohler A, et al. PathVisio 3: an extendable pathway analysis toolbox. *PLoS Comput Biol.* 2015;11(2):e1004085. Published 2015 Feb 23. doi:10.1371/journal.pcbi.1004085
- 3) Bult CJ, Blake JA, Smith CL, Kadin JA, Richardson JE; Mouse Genome Database Group. Mouse Genome Database (MGD) 2019. *Nucleic Acids Res.* 2019;47(D1):D801-D806. doi:10.1093/nar/gky1056
- 4) Sarah E Hunt, William McLaren, Laurent Gil, Anja Thormann, Helen Schuilenburg, Dan Sheppard, Andrew Parton, Irina M Armean, Stephen J Trevanion, Paul Flicek, Fiona Cunningham. Ensembl variation resources. *Database.* 2018. doi:10.1093/database/bay119
- 5) National Center for Biotechnology Information (NCBI)[Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; [1988] – [cited 2020 Sep 17]. Available from: <https://www.ncbi.nlm.nih.gov/>