Pathway analysis and signatures

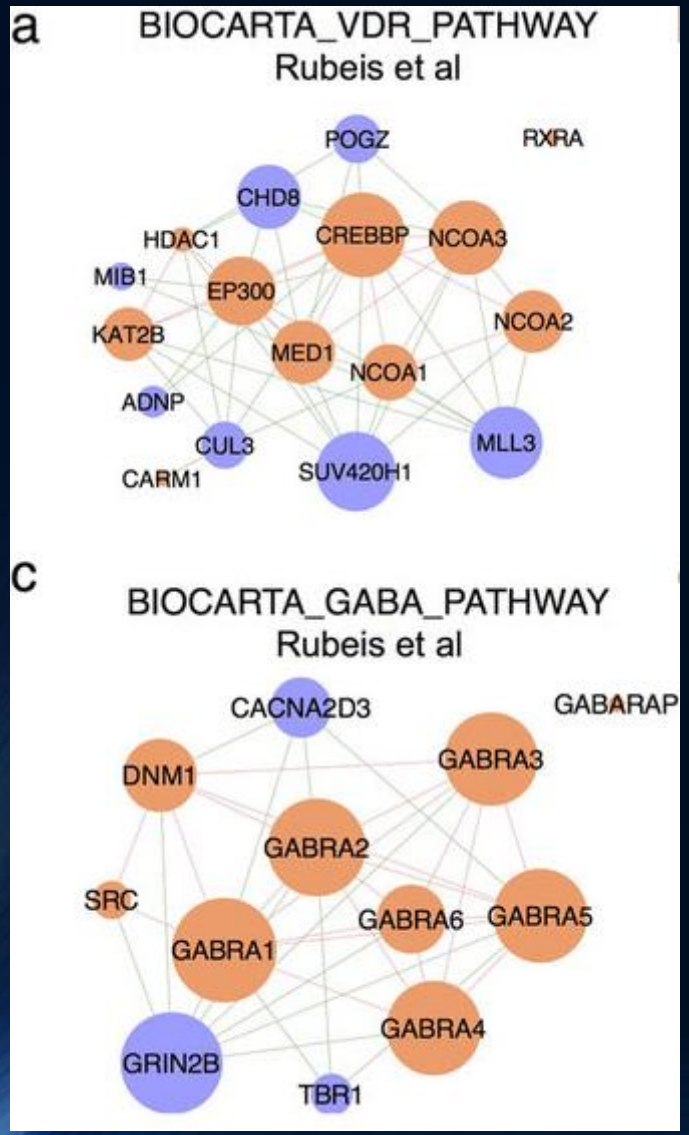
AN INTRODUCTION TO PATHWAY ANALYSIS AND SIGNATURES IN R

RADIA JOHNSON, PH.D.

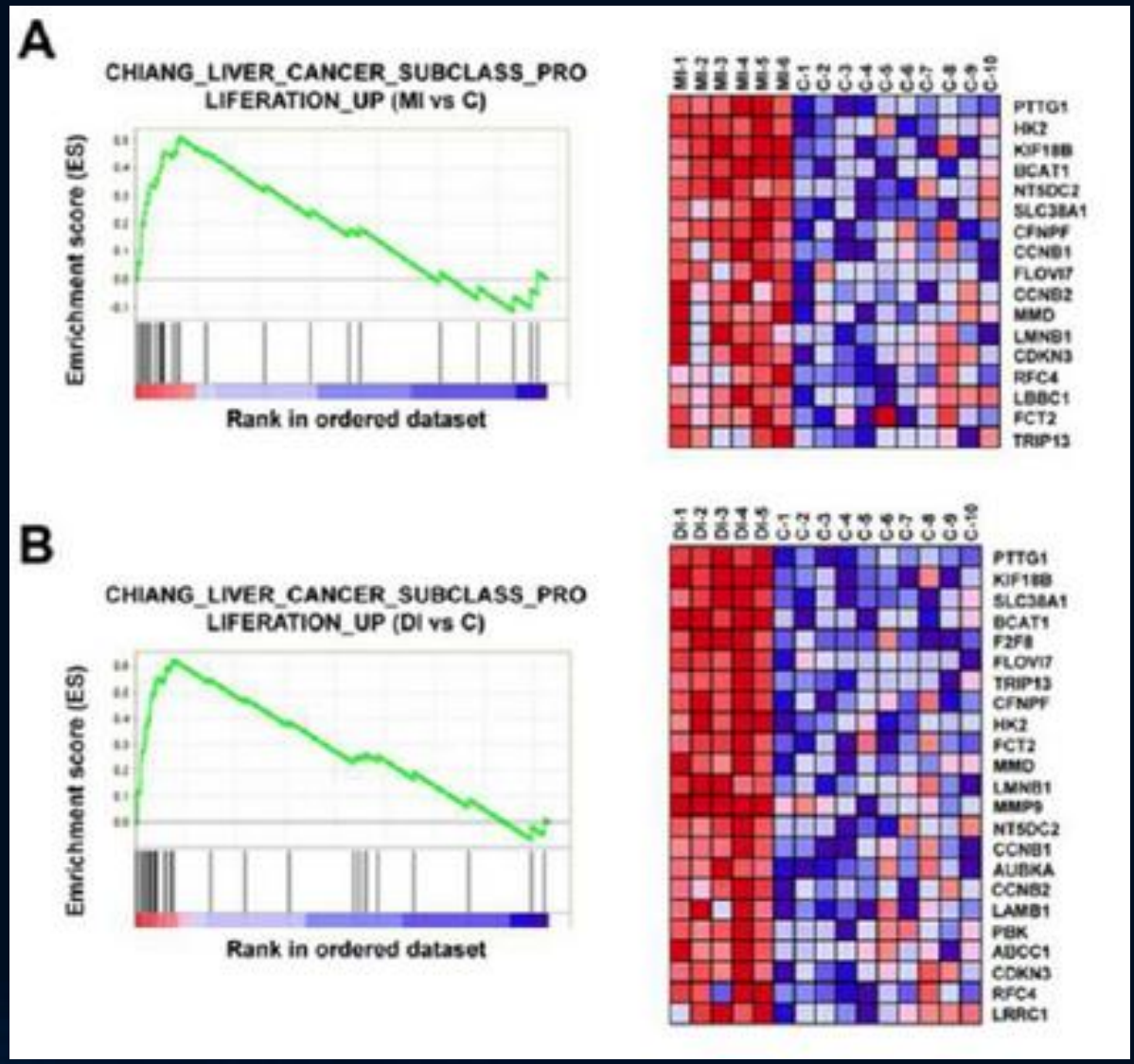
Outline

- Basics of pathway analysis
- Online tools for pathway analysis
- Run pathway & signature analysis in R using Bioconductor packages:
  - gage
  - ClusterProfiler
  - ReactomePA
  - fgsea
- Summarizing pathway analysis results

What is pathway analysis?



Dong *et al.*, 2016. Nature



Jung *et al.*, 2012. Env. Sci. & Tech.

Benefits of Pathway Analysis

- Improved statistical power
- Testing gene signatures are more reproducible than individual genes in different studies
- Potentially identify the mechanism
- Predict new roles for those genes

Steps for pathway analysis

- Normalization
- Generate your gene list by DEG analysis
- Visualize & identify interesting pathways and networks
- Hypothesize molecular mechanism

Online Tools for Gene Lists

- DAVID https://david.ncifcrf.gov/
- GSEA http://software.broadinstitute.org/gsea/index.jsp
- g:Profiler http://biit.cs.ut.ee/gprofiler/
- PANTHER http://www.pantherdb.org/
- LEGO http://lego.tianlab.cn/analysis

Running Pathway Analysis in R

- R & Bioconductor Packages:
  - GAGE
  - Cluster profiler
  - ReactomePA
  - fgsea

Gene sets/Pathways

- GO terms
- KEGG pathways
- MSigDB
- Reactome

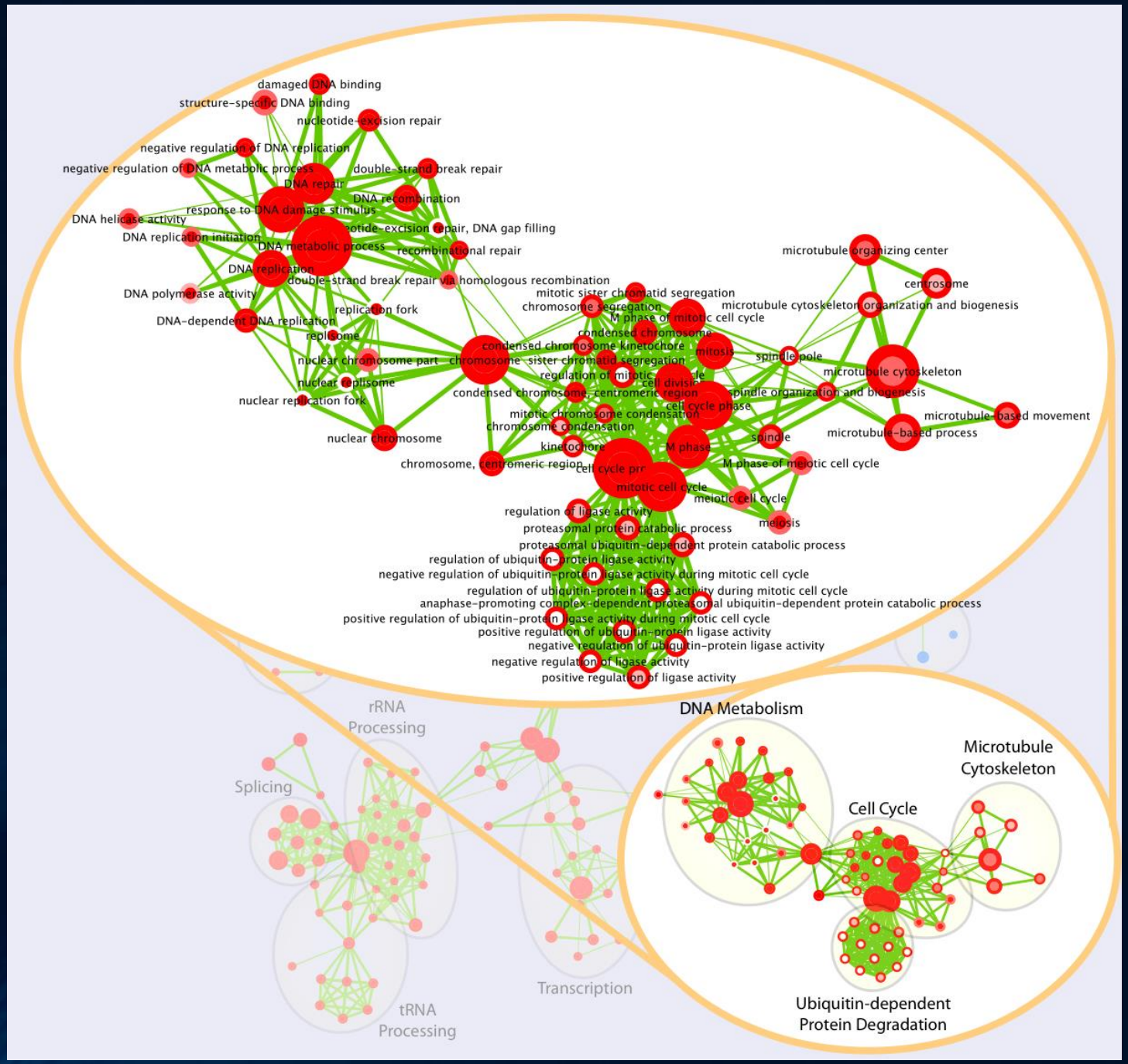
Summarizing Pathway Analysis Results

Network visualization techniques to summarize results

- REVIGO to reduce and visualize GO terms http://revigo.irb.hr/
- Enrichment Map Cytoscape Plugin http://baderlab.org/Software/EnrichmentMap/Description
- R/Bioconductor Packages:
  - Pathview
  - clusterProfiler

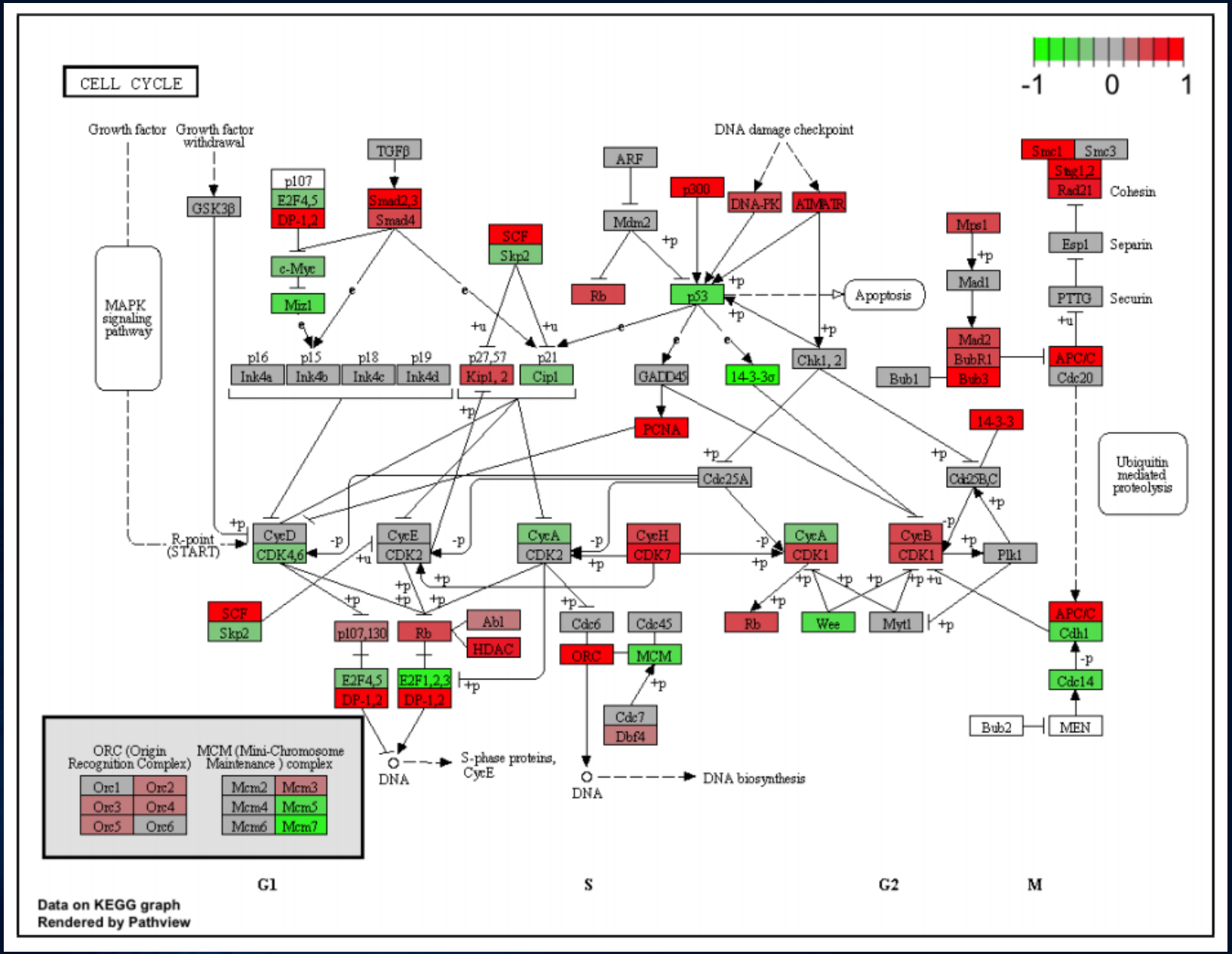
Enrichment Map

Relationship between the different pathway terms



Pathview

KEGG Cell Cycle Example



R code examples

HTTPS://GITHUB.COM/RADIAJ/GCRC_SESSION4

R packages for pathway analysis

- clusterProfiler: https://bioconductor.org/packages/release/bioc/html/clusterProfiler.html
- gage: https://bioconductor.org/packages/release/bioc/html/gage.html
- ReactomePA: https://www.bioconductor.org/packages/release/bioc/html/ReactomePA.html

Other resources

- R programming Blogs:
  - https://rjbioinformatics.com/
  - https://www.r-bloggers.com/
- R programming Books: