Supplementary data

S 1. Complementary bibliography

The bibliography included in this section was compiled aiming to provide additional examples on general resources and methodological articles to complement those cited in the main version of this tutorial review. It only represents a partial selection from the large amount of available literature, and it is expected to serve as a guide for young researchers that want to further explore the omics tools covered in this tutorial. For practical reasons, the bibliography is sort by date of publication within different topics.

S_1 Transcriptomics

General resources

- Z. Wang, M. Gerstein and M. Snyder, RNA-Seq: a revolutionary tool for transcriptomics, *Nat. Rev. Genet.*, 2009, **10**, 57–63.

This review article provides an overview of the functioning of RNA-seq technology, and discusses its challenges.

- S. Goodwin, J. D. Mcpherson and W. R. Mccombie, Coming of age: ten years of next-generation sequencing technologies, *Nat. Rev. Genet.*, 2016, **17**, 333–351.

- E. R. Mardis, DNA sequencing technologies: 2006–2016, *Nat. Protoc.*, 2017, **12**, 213–218.

These articles review the developments in DNA sequencing technologies over the past 10 years. They also discuss the benefits and drawbacks of different approaches used in next-generation sequencing (NGS), and emerging applications.

Library preparation

- E. L. Van Dijk, Y. Jaszczyszyn and C. Thermes, Library preparation methods for nextgeneration sequencing: Tone down the bias, *Exp. Cell Res.*, 2014, **322**, 12–20.

The authors review the occurrence of biases reported in literature in NGS library preparation protocols for DNA-seq and RNA-seq, and provide some suggestions on how to improve library quality.

Experimental design

- Robles, S. E. Qureshi, S. J. Stephen, S. R. Wilson, C. J. Burden and J. M. Taylor, Efficient experimental design and analysis strategies for the detection of differential expression using RNA-Sequencing, *BMC Genomics*, 2012, **13**, 484.

- N. J. Schurch, P. Schofield, M. Gierliński, C. Cole, A. Sherstnev, V. Singh, N. Wrobel, K. Gharbi, G. G. Simpson, T. Owen-Hughes, M. Blaxter and G. J. Barton, How many biological replicates are needed in an RNA-seq experiment and which differential expression tool should you use?, *RNA*, 2016, 1–13.

These articles examine in simulated (Robles and co-workers) and real (Schurch and co-workers) datasets the number of biological replicates needed in RNA-seq experiments for the detection of differential expression. Both articles compare the performance of different analytical tools to detect these differences.

- E. V. Todd, M. A. Black and N. J. Gemmell, Mol. Ecol., 2016, 25, 1224–1241.

This review discusses the trade-off between sequencing effort (sequencing depth) and replication (biological replicates) in RNA-seq experimental designs.

Pre-processing

- L. Wang, S. Wang and W. Li, RSeQC: quality control of RNA-seq experiments, *Bioinformatics*, 2012, **28**, 2184–5.

- C. Del Fabbro, S. Scalabrin, M. Morgante and F. M. Giorgi, An Extensive Evaluation of Read Trimming Effects on Illumina NGS Data Analysis, *PLoS One*, 2013, **8**, 1–13.

- A. M. Bolger, M. Lohse and B. Usadel, Trimmomatic: a flexible trimmer for Illumina sequence data, *Bioinformatics*, 2014, **30**, 2114–2120.

Description and performance evaluation of some of the tools used in pre-processing NGS reads.

Transcriptome assembly

- M. G. Grabherr, B. J. Haas, M. Yassour, J. Z. Levin, D. A. Thompson, I. Amit, X. Adiconis, L. Fan, R. Raychowdhury, Q. Zeng, Z. Chen, E. Mauceli, N. Hacohen, A. Gnirke, N. Rhind, F. di Palma, B. W. Birren, C. Nusbaum, K. Lindblad-Toh, N. Friedman and A. Regev, Full-length transcriptome assembly from RNA-Seq data without a reference genome, *Nat. Biotechnol.*, 2011, **29**, 644–652.

- B. J. Haas, A. Papanicolaou, M. Yassour, M. Grabherr, D. Philip, J. Bowden, M. B. Couger, D. Eccles, B. Li, M. D. Macmanes, M. Ott, J. Orvis and N. Pochet, De novo transcript sequence reconstruction from RNA-Seq: reference generation and analysis with Trinity, *Nat. Protoc.*, 2014, **8**, 1–43.

These articles describe the use of Trinity platform for *de novo* transcriptome assembly of RNA-Seq data. Transcriptome reconstruction is necessary in the absence of reference genome, which is the case for most non-model organisms.

Annotation

- M. Garber, M. G. Grabherr, M. Guttman and C. Trapnell, Computational methods for transcriptome annotation and quantification using RNA-seq, *Nat. Methods*, 2011, **8**, 469–477.

This review explains the most relevant computational challenges for transcriptome annotation, which the authors divide in three categories: (i) read mapping, (ii) transcriptome reconstruction and (iii) expression quantification.

Differential expression analysis

- C. Trapnell, A. Roberts, L. Goff, G. Pertea, D. Kim, D. R. Kelley, H. Pimentel, S. L. Salzberg, J. L. Rinn and L. Pachter, Differential gene and transcript expression analysis of RNA-seq experiments with TopHat and Cufflinks, *Nat. Protoc.*, 2012, **7**, 562–578.

- R. Patro, G. Duggal, M. I. Love, R. A. Irizarry and C. Kingsford, Salmon provides fast and bias-aware quantification of transcript expression, *Nat. Methods*, 2017, **14**, 417–419.

These articles present different open-source software tools to perform expression analysis

- M. Teng, M. I. Love, C. A. Davis, S. Djebali, A. Dobin, B. R. Graveley, S. Li, C. E. Mason, S. Olson, D. Pervouchine, C. A. Sloan, X. Wei, L. Zhan and R. A. Irizarry, A benchmark for RNA-seq quantification pipelines, *Genome Biol.*, 2016, **17**, 74. The authors evaluate the performance in terms of specificity and sensitivity of RNA-seq measurements from seven different pipelines.

Single cell transcriptomics

F. Tang, C. Barbacioru, Y. Wang, E. Nordman, C. Lee, N. Xu, X. Wang, J. Bodeau, B.
B. Tuch, A. Siddiqui, K. Lao and M. A. Surani, mRNA-Seq whole-transcriptome analysis of a single cell, *Nat. Methods*, 2009, 6, 377–382.

The article describes single-cell digital gene expression profiling assay, and discuss the importance of this type of analysis to examine transcriptome complexity in individual cells.

- R. Bacher and C. Kendziorski, Design and computational analysis of single-cell RNA-sequencing experiments, *Genome Biol.*, 2016, **17**, 63.

The authors review the computational methods, their benefits and drawbacks, for the design and analysis of single cell RNA-seq experiments.

General methodological considerations

- S. M. Brown, *Next-generation DNA Sequencing Informatics*, Cold Spring Harbor Laboratory Press, 2nd Ed. 2015.

This book serves as a general resource for a broad audience seeking to understand the bases of NGS as well as available sequencing platforms. It covers several aspects of the analysis of NGS data including genomics, transcriptomics, and metagenomics. It provides the tools to know how, to interpret, visualize and present this type of data.

- A. Conesa, P. Madrigal, S. Tarazona, D. Gomez-Cabrero, A. Cervera, A.

McPherson, M. W. Szczesniak, D. J. Gaffney, L. L. Elo, X. Zhang and A. Mortazavi, *Genome Biol.*, 2016, **17**, 13–19.

This review provides an overall picture of each of the major steps in RNA-seq data analysis. It may be very useful especially for beginners because it gives the overall map of the sequence processing with comments and suggestions that may help to improve the experimental design and analysis.

S_2 Proteomics

General resources in MS-based Proteomics

- N. L. Anderson and N. G. Anderson, Proteome and proteomics: new technologies, new concepts, and new words, *Electrophoresis*, 1998, **19**, 1853–1861.

It represents the first attempt to generate proteomics data and gene annotation from proteomics-derived information.

- R. Aebersold and M. Mann, Mass spectrometry-based proteomics, *Nature*, 2003, **422**, 198–207.

This article describes the standard protocol used in MS-based proteomics, including experimental design, data collection, data analysis and visualization. The authors discuss the advantages of MS-based protein identification over traditional biochemical approaches.

Protein enrichment and isolation steps

- T. E. Angel, U. K. Aryal, S. M. Hengel, E. S. Baker, R. T. Kelly, E. W. Robinson and R. D. Smith, Mass spectrometry-based proteomics: existing capabilities and future directions, *Chem. Soc. Rev.*, 2012, **41**, 3912–3928.

The authors review some of the workflows used in classical proteomics analyses, either from digestion or LC separation steps. They also provide a clear description of MS and MS/MS concepts.

Identification of peptides with tandem mass spectrometry

- R. G. Sadygov, D. Cociorva and J. R. Yates, Large-scale database searching using tandem mass spectra: looking up the answer in the back of the book, *Nat. Methods*, 2004, **1**, 195–202.

A comprehensive review of database searching algorithms. It presents the basic concepts used by most algorithms such as Mascot, SEQUEST, PeptideSearch or X!Tandem, in order to understand how the rationale behind them.

De novo sequencing and homology-based database search for organisms with unsequenced genomes

- B. Ma and R. Johnson, *De novo* sequencing and homology searching, *Mol. Cell. Proteomics*, 2012, **11**, O111.014902.

The authors review computer algorithms and programs for automated sequencing such as PEAKS, Lutefisk and PepNovo. They also provide guidelines for homology-based database search for organisms with unsequenced genomes using tools such as MS-BLAST and FASTS.

Quantification

- S. P. Gygi, B. Rist, S. A. Gerber, F. Turecek, M. H. Gelb and R. Aebersold, Quantitative analysis of complex protein mixtures using isotope-coded affinity tags, *Nat. Biotechnol.*, 1999, **17**, 994–999. - S. E. Ong, B. Blagoev, I. Kratchmarova, D. B. Kristensen, H. Steen, A. Pandey and M. Mann, Stable isotope labeling by amino acids in cell culture, SILAC, as a simple and accurate approach to expression proteomics, *Mol. Cell. Proteomics*, 2002, **1**, 376–386. These two articles are seminal papers at the beginning of labelling quantification proteomics.

- J. Cox and M. Mann, MaxQuant enables high peptide identification rates, individualized ppb-range mass accuracies and proteome-wide protein quantification, *Nat. Biotechnol.*, 2008, **26**, 1367–1372.

This article describes MaxQuant, an integrated suite of algorithms specifically developed for high-resolution, quantitative MS data, which allow the identification of peptides in large amount of raw data.

- P. J. Boersema, R. Raijmakers, S. Lemeer, S. Mohammed and A. J. Heck, Multiplex peptide stable isotope dimethyl labeling for quantitative proteomics, *Nat. Protoc.*, 2009, 4, 484–494.

A step-by-step instruction for a quantitative derivatization method.

- M. Kandiah and P. L. Urban, Advances in ultrasensitive mass spectrometry of organic molecules, *Chem. Soc. Rev.*, 2013, **42**, 5299–5322.

The authors review the state-of-the-art of ionization interfaces in MS. They explain and discuss some of the organic-free-matrix MS that would be able to achieve yoctomoles scales, such as nanostructureinitiator mass spectrometry (NIMS) and laser-induced silicon microcolumn arrays (LISMA).

- S. Surinova, R. Hüttenhain, C. Y. Chang, L. Espona, O. Vitek and R. Aebersold, Automated selected reaction monitoring data analysis workflow for large-scale targeted proteomic studies, *Nat. Protoc.*, 2013, **8**, 1602–1619.

The authors present a protocol for hypothesis-driven studies in MS-Based Proteomics.

- O. T. Schubert, H. L. Röst, B. C. Collins, G. Rosenberger and R. Aebersold, Quantitative proteomics: challenges and opportunities in basic and applied research, *Nat. Protoc.*, 2017, **12**, 1289–1294. The author review most of the recent technical updates from the last 10 years, and provide some descriptions and advises on the workflows used in targeted proteomics.

Top-Down Proteomics

- J. C. Tran, L. Zamdborg, D. R. Ahlf, J. E. Lee, A. D. Catherman, K. R. Durbin, J. D. Tipton, A. Vellaichamy, J. F. Kellie, M. Li, C. Wu, S. M. Sweet, B. P. Early, N. Siuti, R. D. LeDuc, P. D. Compton, P. M. Thomas and N. L. Kelleher, Mapping Intact Protein Isoforms in Discovery Mode Using Top Down Proteomics, *Nature*, 2011, **480**, 254–258.

The authors describe the functioning of top down proteomics, and describe how this approach can overcome some of the ambiguous or incomplete protein characterization derived from bottom up process.

A general guide for proteomics workflows

- B. T. Chait, Mass spectrometry: bottom-up or top-down?, Science, 2006, 314, 65-66.

- Y. Zhang, B. R. Fonslow, B. Shan, M. C. Baek and J. R. Yates III, Protein analysis by shotgun/bottom-up proteomics, *Chem. Rev.*, 2013, **113**, 2343–2394.

These review articles discuss benefits and drawbacks of some of the protocols used in proteomics

Pipelines of data collection and analysis

- J. A. Vizcaíno, R. G. Côté, A. Csordas, J. A. Dianes, A. Fabregat, J. M. Foster, J. Griss, E. Alpi, M. Birim, J. C. G. O'Kelly, A. Schoenegger, D. Ovelleiro, Y. Pérez-Riverol, F. Reisinger, D. Ríos, R. Wang and H. Hermjakob, The PRoteomics IDEntifications (PRIDE) database and associated tools: status in 2013, *Nucleic acids research*. 2012, **41**, D1063–D1069.

Summarizes recent developments in the PRIDE database and related tools, which represents a great effort in public repositories and integrative data analysis.

S 1.3 Metabolomics

General resources

- M. R. Viant, Improved methods for the acquisition and interpretation of NMR metabolomic data, *Biochem. Biophys. Res. Commun.*, 2003, **310**, 943–948.

- P. Jonsson, A. I. Johansson, J. Gullberg, J. Trygg, B. Grung, S. Marklund, M. Sjöström, H. Antti and T. Moritz, High-throughput data analysis for detecting and identifying differences between samples in GC/MS-based metabolomic analyses, *Anal. Chem.*, 2005, **77**, 5635–5642.R.

- R. Steuer, On the analysis and interpretation of correlations in metabolomic data, *Brief. Bioinform.*, 2006, 7, 151–158.

M. Wang, J. J. Carver, V. V. Phelan, L. M. Sanchez, N. Garg, Y. Peng, D. D. Nguyen,J. Watrous, C. A. Kapono and T. Luzzatto-Knaan, Sharing and community curation of

mass spectrometry data with GNPS, Nat. Biotech., 2016, 34, 828.

These articles present and discuss how to treat the large-scale data obtained from metabolomic analysis, from MS and NMR, including statistical tools that can improve data visualization.

Separation techniques

- L. R. Snyder, Role of the solvent in liquid-solid chromatography, Review. Anal. Chem., 1974, 46, 1384–1393.

- N. G. Agelopoulos and J. A. Pickett, Headspace analysis in chemical ecology: effects of different sampling methods on ratios of volatile compounds present in headspace samples, *J. Chem. Ecol.*, 1998, **24**, 1161–1172.

- R. C. De Vos, S. Moco, A. Lommen, J. J. Keurentjes, R. J. Bino and R. D. Hall, Untargeted large-scale plant metabolomics using liquid chromatography coupled to mass spectrometry, *Nat. Protoc.*, 2007, **2**, 778. - J. L. Wolfender, G. Marti, A. Thomas and S. Bertrand, Current approaches and challenges for the metabolite profiling of complex natural extracts, *J. Chromat. A*, 2015, **1382**, 136–164.

These articles present detailed chromatographic concepts, including different separation techniques and when and how to apply them.

MS-based metabolomics

- K. Dettmer, P. A. Aronov and B. D. Hammock, Mass spectrometry-based metabolomics, *Mass Spec. Rev.*, 2007, **26**, 51–78.

- K. Ralston-Hooper, A. Hopf, C. Oh, X. Zhang, J. Adamec and M. S. Sepúlveda, Development of GCxGC/TOF-MS metabolomics for use in ecotoxicological studies with invertebrates, *Aquat. Toxicol.*, 2008, **88**, 48–52.

- P. M. Allard, T. Peresse, J. Bisson, K. Gindro, L. Marcourt, V. C. Pham, F. Roussi, M. Litaudon and J. L. Wolfender, Integration of Molecular Networking and *In-Silico* MS/MS Fragmentation for Natural Products Dereplication, *Anal. Chem.*, 2016, **88**, 3317–3323.

These articles show how to develop metabolomics studies using mass spectrometry approaches, including direct-infusion, GC-MS, LC-MS/MS among others.

MS-based imaging

D. S. Cornett, M. L. Reyzer, P. Chaurand and R. M. Caprioli, MALDI imaging mass spectrometry: molecular snapshots of biochemical systems *Nat. Methods*, 2007, 4, 828–833.

- J. D. Watrous and P. C. Dorrestein, Imaging mass spectrometry in microbiology, *Nat. Rev. Microbiol.*, 2011, **9**, 683–694.

A. Bouslimani, C. Porto, C. M. Rath, M. Wang, Y. Guo, A. Gonzalez, D. Berg-Lyon,
G. Ackermann, G. J. Moeller Christensen, T. Nakatsuji, L. Zhang, A. W. Borkowski,
M. J. Meehan, K. Dorrestein, R. L. Gallo, N. Bandeira, R. Knight, T. Alexandrov and P.
C. Dorrestein, Molecular cartography of the human skin surface in 3D, *Proc. Natl. Acad. Sci.*, 2015, **112**, E2120–E2129.

P. Ràfols, D. Vilalta, J. Brezmes, N. Cañellas, E. del Castillo, O. Yanes, N. Ramírez and X. Correig, Signal preprocessing, multivariate analysis and software tools for MA(LDI)-TOF mass spectrometry imaging for biological applications, *Mass Spectrom. Rev.*, 2016, 2016, 1–26.

These articles present and discuss the use of different strategies, such as MALDI-IMS and LC-MS, to investigate the distribution of molecules within biological systems through direct analysis from tissue sections and through 3D molecular mapping.

NMR-based metabolomics

- H. K. Kim, Y. H. Choi and R. Verpoorte, NMR-based metabolomic analysis of plants, *Nat. Protoc.*, 2010, **5**, 536.

- K. A. Leiss, Y. H. Choi, I. B. Abdel-Farid, R. Verpoorte and P. G. Klinkhamer, NMR metabolomics of thrips (*Frankliniella occidentalis*) resistance in Senecio hybrids, *J. Chem. Ecol.*, 2009, **35**, 219–229.

These articles discuss the advantages and disadvantages of using NMR technique for metabolomics analyses.

General approaches for studying chemical interactions using metabolomics

- J. G. Bundy, M. P. Davey and M. R. Viant, Environmental metabolomics: a critical review and future perspectives, *Metabol.*, 2009, **5**, 3.

- E. K. Prince and G. Pohnert, Searching for signals in the noise: metabolomics in chemical ecology, *Anal. Bioanal. Chem.*, 2010, **396**, 193–197.

- P. J. Apps, P. J. Weldon and M. Kramer, Chemical signals in terrestrial vertebrates: search for design features, *Nat. Prod. Rep.*, 2015, **32**, 1131–1153.

- C. Kuhlisch and G. Pohnert, Metabolomics in chemical ecology, *Nat. Prod. Rep.*, 2015, **32**, 937–955.

- L. Nunez-Pons and C. Avila, Natural products mediating ecological interactions in Antarctic benthic communities: a mini-review of the known molecules, *Nat. Prod. Rep.*, 2015, **32**, 1114–1130.

These articles present some strategies commonly used to identify/investigate chemical molecules that mediate ecological interactions between different organisms. They also report the main analytical tools employed in such investigations considering metabolomics approaches.

S 1.4 Hologenomics

General resources

The bibliography suggested for transcriptomics may also be useful in hologenomic analysis. For instance see chapter 14 in the book "Next-generation DNA Sequencing Informatics"

Identification of uncultured microorganisms

- Amann, R. I., Ludwig, W., & Schleifer, K. H., Phylogenetic identification and *in situ* detection of individual microbial cells without cultivation, *Microbiol. Mol. Biol. Rev.*, 1995, **59**, 143-169.

This article describe for the first time how rRNA sequence can be used to identify uncultured bacteria from natural samples.

- J. Handelsman, Metagenomics: application of genomics to uncultured microorganisms, *Microbiol. Mol. Biol. Rev.*, 2004, **68**, 669–685.

- C. S. Riesenfeld, P. D. Schloss and J. Handelsman, Metagenomics: genomic analysis of microbial communities *Annu. Rev. Genet.*, 2004, **38**, 525–552.

These review describe the origin and progresses made in the analysis of genetic content from uncultured microorganism after 10 years of the seminal paper of Amman and co-workers.

DNA barcode: analytical considerations

- M. Blaxter, J. Mann, T. Chapman, F. Thomas, C. Whitton, R. Floyd and E.

Abebe, Defining operational taxonomic units using DNA barcode data, *Philos. Trans. R. Soc. Lond. B. Biol. Sci.*, 2005, **360**, 1935–1943.

This article may be particularly useful for those researchers that are not so familiar with taxonomic classification of bacteria using DNA barcode data.

- Y. Wang and P. Y. Qian, Conservative fragments in bacterial 16S rRNA genes and primer design for 16S ribosomal DNA amplicons in metagenomic studies, *PLoS One*, 2009, **4**, e7401.

The authors describe conservative fragments in 16S rRNA genes that have average coverage rate of 96%, and discuss potential application for metagenomic studies.

Analysis of metagenomic DNA sequences

- J. G. Caporaso, C. L. Lauber, W. A. Walters, D. Berg-Lyons, C. A. Lozupone, P.

J. Turnbaugh, N. Fierer and R. Knight, Global patterns of 16S rRNA diversity at a depth of millions of sequences per sample, *Proc. Natl. Acad. Sci. U. S. A.*, 2011, **108**, 4516–4522.

The authors demonstrate that single-end Illumina reads, between 75 and 100 bases, enable to have an excellent consistency in taxonomic recovery and recapture the diversity patterns observed with longer

reads. These results have opened the possibility of conducting large-scale studies of microbial communities analysing thousands of samples simultaneously.

- D. E. Wood and S. L. Salzberg, Kraken: ultrafast metagenomic sequence classification using exact alignments, *Genome Biol.*, 2014, **15**, R46

Kraken is classification programme based on exact alignment of *k*-mers that allows assigning taxonomic labels to metagenomic DNA sequences.

- D. H. Huson, S. Beier, I. Flade, A. Górska, M. El-Hadidi, S. Mitra, H. J. Ruscheweyh and R. Tappu, MEGAN Community Edition - Interactive Exploration and Analysis of Large-Scale Microbiome Sequencing Data, *PLoS Comput. Biol.*, 2016, **12**, 1–12.

The authors introduce MEGAN Community Edition (CE), which is an open source program that provides a straightforward and complete pipeline for the analysis of metagenome shotgun sequences.

- A. Amir, D. McDonald, J. A. Navas-Molina, E. Kopylova, J. T. Morton, Z. Z. Xu, E.

P. Kightley, L. R. Thompson, E. R. Hyde, A. Gonzalez and R. Knight, Deblur Rapidly Resolves Single- Nucleotide Community Sequence Patterns, 2017, **2**, e00191–16.

Deblur is an open source platform that allows identification of real ecological differences between taxa whose amplicons differ by a single base pair. It is based on a novel sub-operational-taxonomic-unit (sOTU) approach that takes into account putative sequences errors from Illumina MiSeq and HiSeq sequencing platforms.

Prokaryiotic genome annotation

- T. Seemann, Prokka: rapid prokaryotic genome annotation, *Bioinformatics*, 2014, **30**, 2068–2069.

The author introduces Prokka, a command line software tool that allows full bacterial genome annotation on a typical desktop computer. Prokka is freely available.

Databases

- I. B. Zhulin, J. Bacteriol., Databases for microbiologists, 2015, 197, 2458–2467.

The author provides a survey of key databases on microorganisms. It includes databases with different scopes, such as SILVA and GREENGENS for characterization of microbial diversity, and SEED and IMG for annotation and analysis of microbial genomes.

S 1.6 Omics integration

- M. Dicke, in *Chemical Ecology: From Gene to Ecosystem*, eds. M. Dicke and W.

Takken, Springer, Dordrecht, Netherlands, 2006, pp. 175–189.

A very inspiring book section that discuss how the developments from different omics could be integrated by chemical ecologist to investigate the role of infochemicals in populations and communities.

- K. Yugi, H. Kubota, A. Hatano and S. Kuroda, Trans-Omics: How To Reconstruct Biochemical Networks Across Multiple 'Omic' Layers*Trends Biotechnol.*, 2016, **34**, 276–290.

In this review the authors present an overview of the recent emergence of trans-omic studies from a biochemical perspective using a reconstruction approach of a biochemical trans-omic network through prior knowledge of interactions.