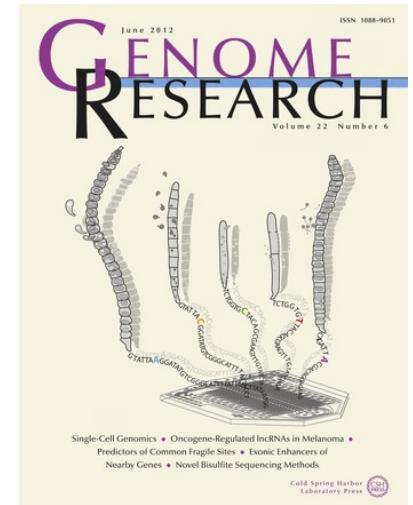




Un vistazo a los microorganismos desde las omicas

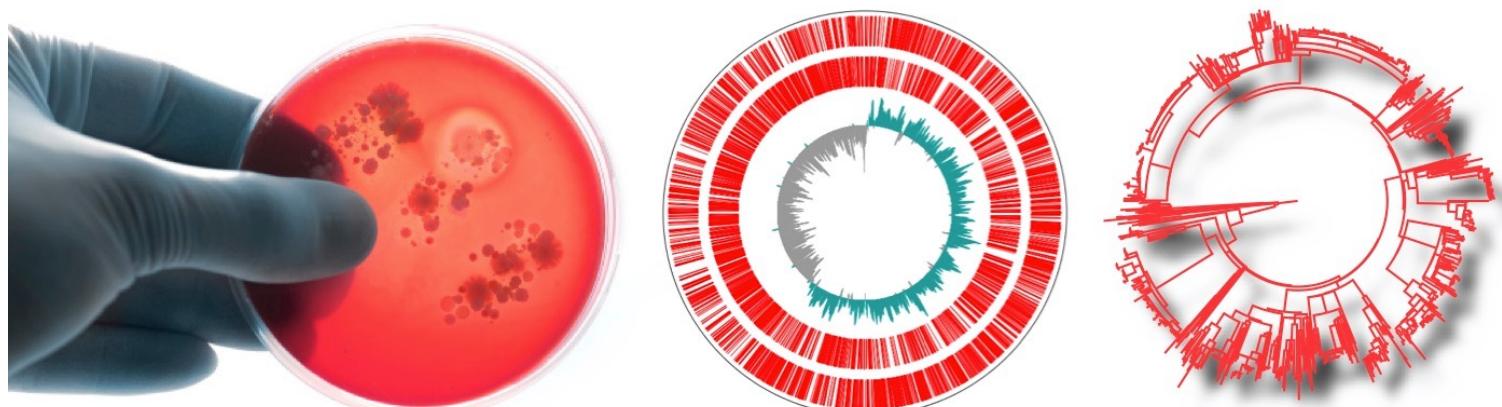
Yesid Cuesta-Astroz

yesid.cuesta@gmail.com



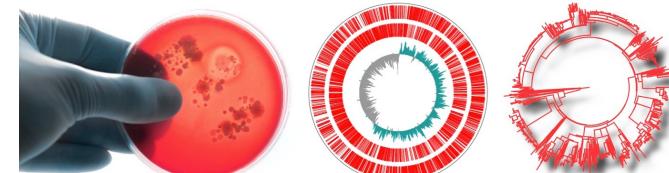
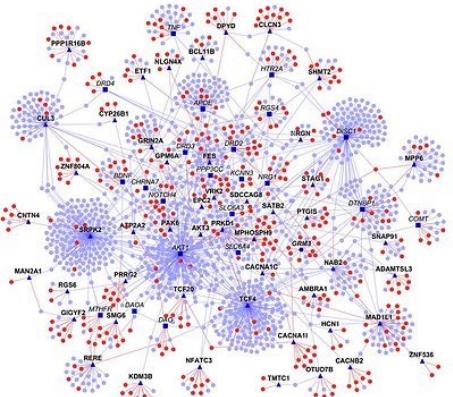
Single-Cell Genomics • Oncogene-Regulated lncRNAs in Melanoma •
Predictors of Common Fragile Sites • Exonic Enhancers of
Nearby Genes • Novel Bisulfite Sequencing Methods

Cold Spring Harbor Laboratory Press

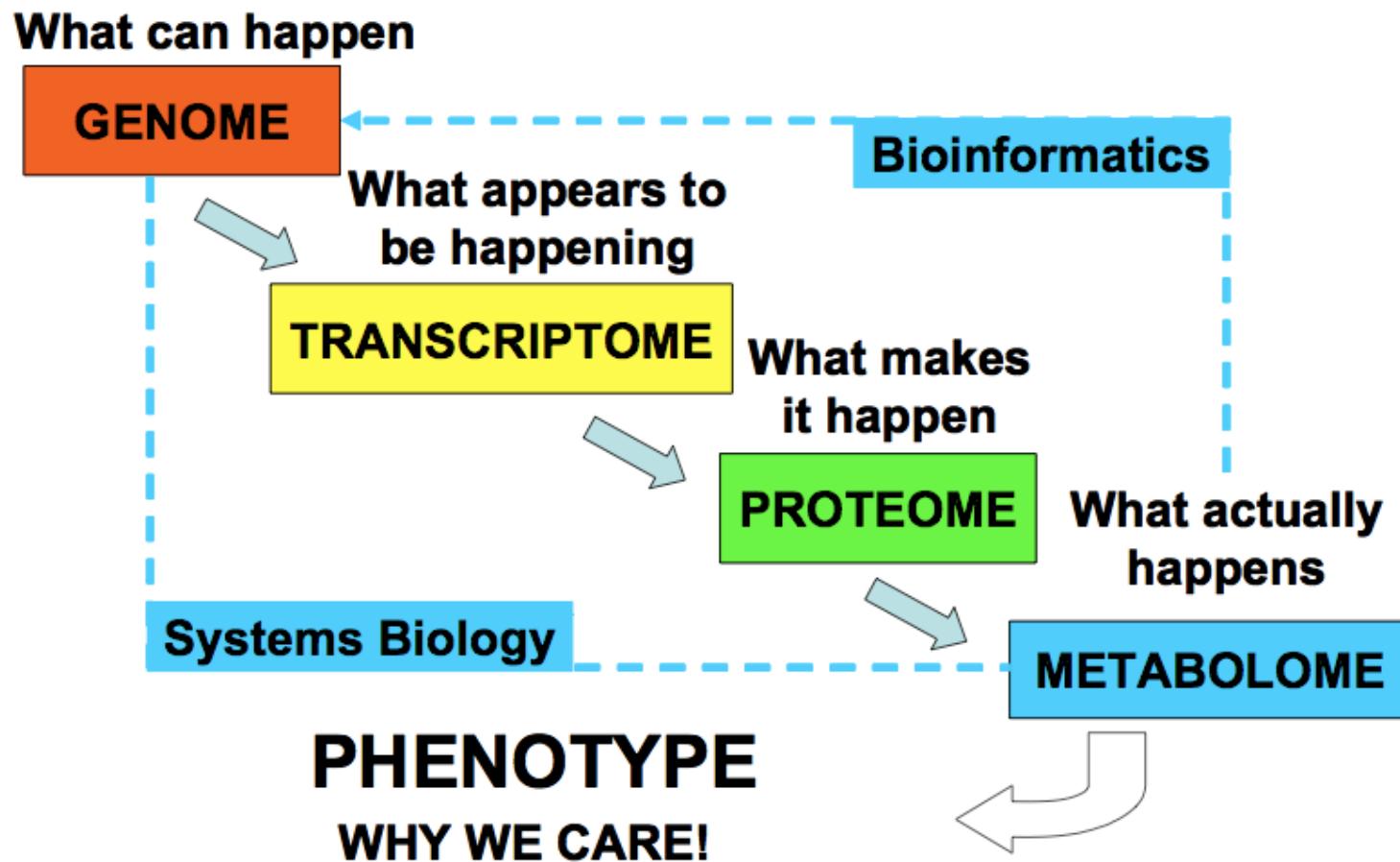


Contenido

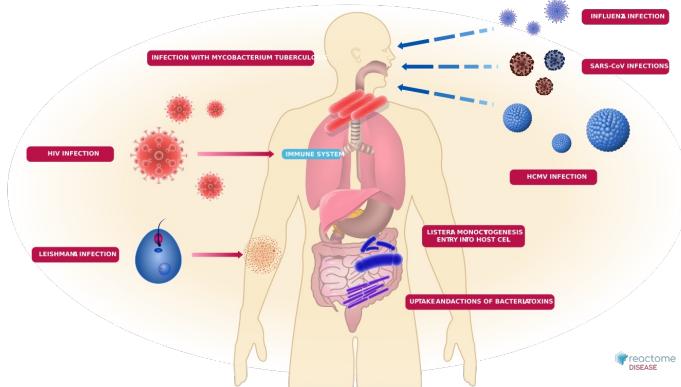
1. Introducción a las omicas y aplicaciones
2. Meta - omicas
2. Metagenómica
3. Metatranscriptómica
4. Metaproteómica
5. Metabolómica
6. Aplicaciones en “network medicine”



The Omics-Cascade



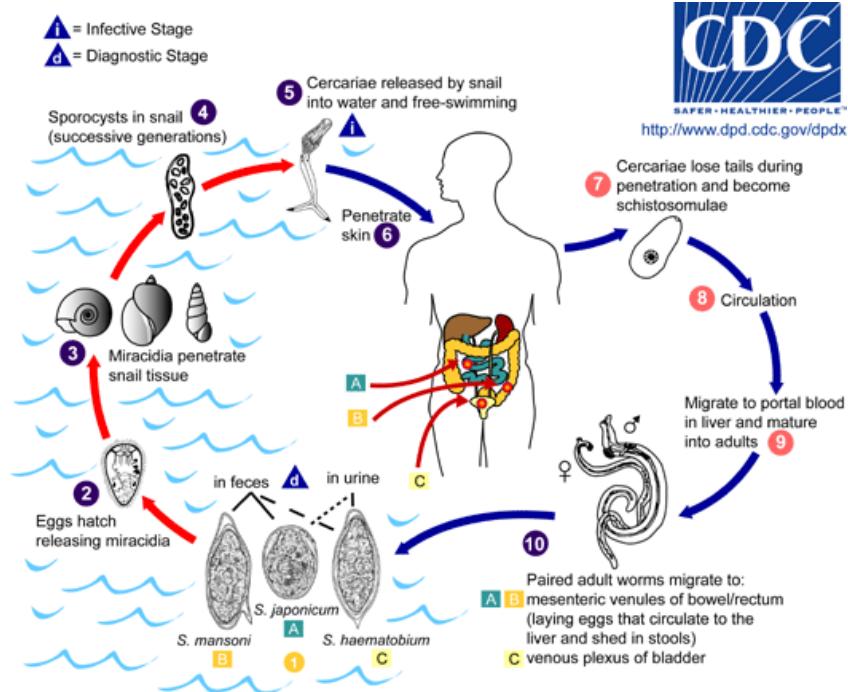
Infectious Diseases - Challenges



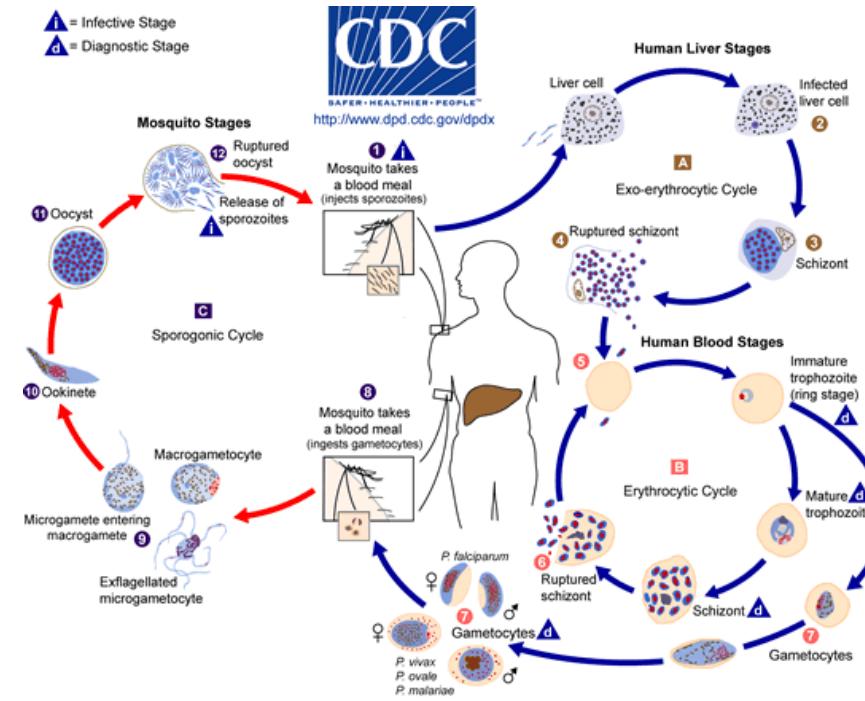
- Annually 15% of all deaths in the world are directly associated with infectious diseases (WHO, 2018).
- Multi-drug resistant pathogens.
- Rapid spread of emerging diseases and the wide scope of tropical and vector-borne diseases due to climate change.
- Greater number of people at risk of chronic or acute infectious diseases.

The complexity of parasites life cycles

Schistosoma mansoni



Plasmodium falciparum

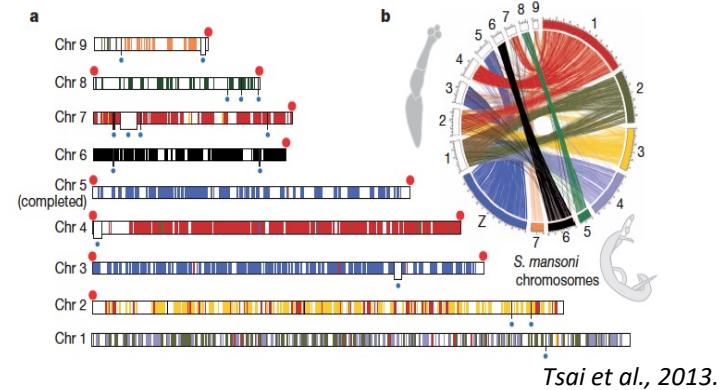


Protein diversity based on genomics data

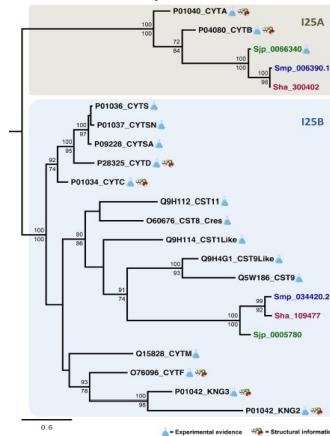
Comparative Genomics

By comparing the genomes of different organisms, it is possible to understand, at the molecular level, the differences between organisms / cells.

- Gene **function** prediction
- Evolutionary relationships
- Evolution of gene families
- Prediction of horizontal gene transfer
- Identify common / specific genes related to the **pathogen's lifestyle**
- Propose promising vaccines and treatment targets



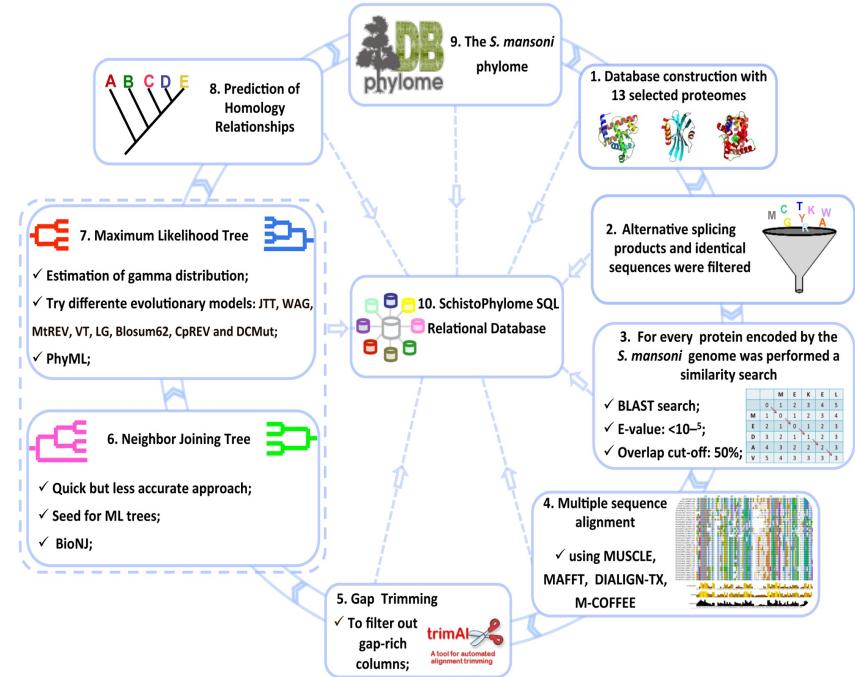
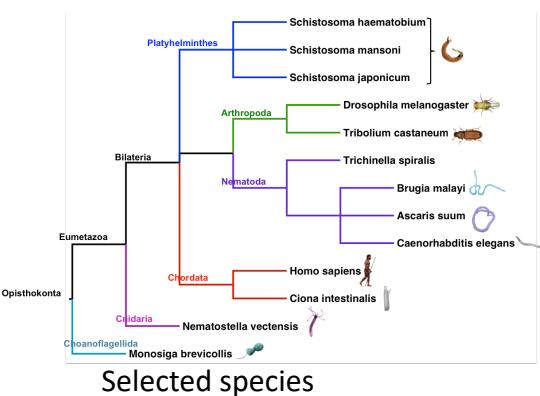
Tsai et al., 2013.



Cuesta-Astroz et al., 2014.

Phylogenomics

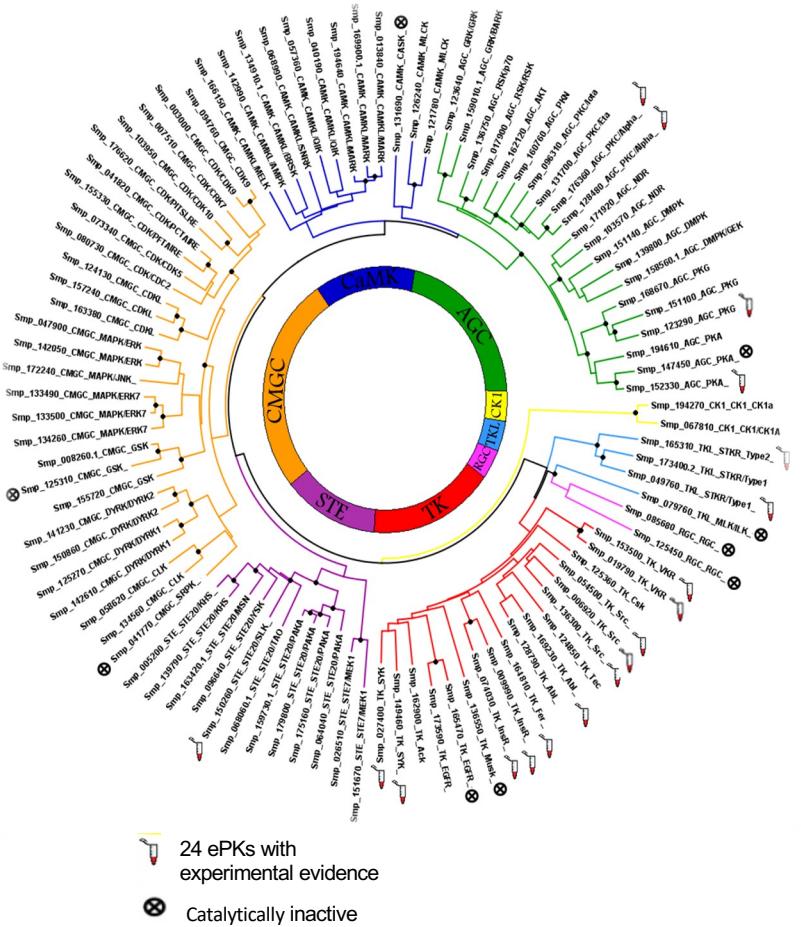
- Reconstruct the **evolutionary history** of each protein encoded in the pathogen genome.
- Improving the **functional annotation** of the genome/proteome.
- Gaining insight into **lineage-specific** evolutionary events potentially related to the pathogen lifestyle.



Pipeline used to reconstruct and analyze the *Schistosoma mansoni* phylome.

Lopes-Silva et al., 2012.

Schistosoma mansoni kinome



- 252 ePKs identified (2% of the predicted proteome).
- By reconstructing the evolutionary history of ePKs was possible to classify them into groups, families.
- Improving the functional annotation of 40% of *S. mansoni* ePKs.

Andrade et al., 2011.

Closing the gap using comparative genomics

In pathogens, **few genes** and **gene products** have been experimentally characterized so far. In this context, **comparative analysis** of partially or completely sequenced genes and genomes and **phylogenetic reconstruction** allow the identification of functional elements.

WormBase ParaSite

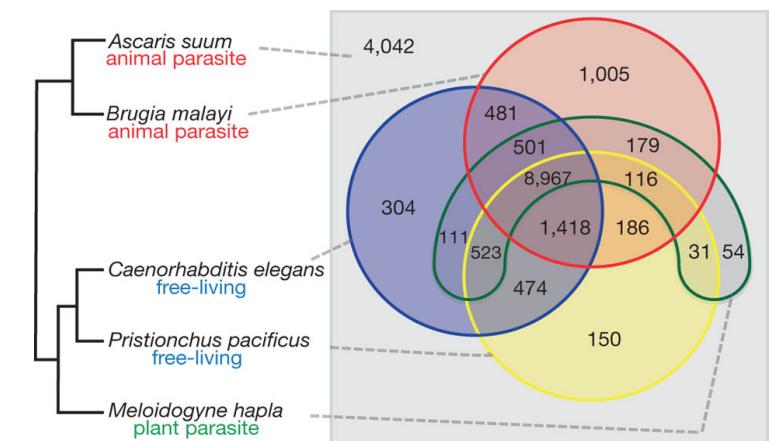
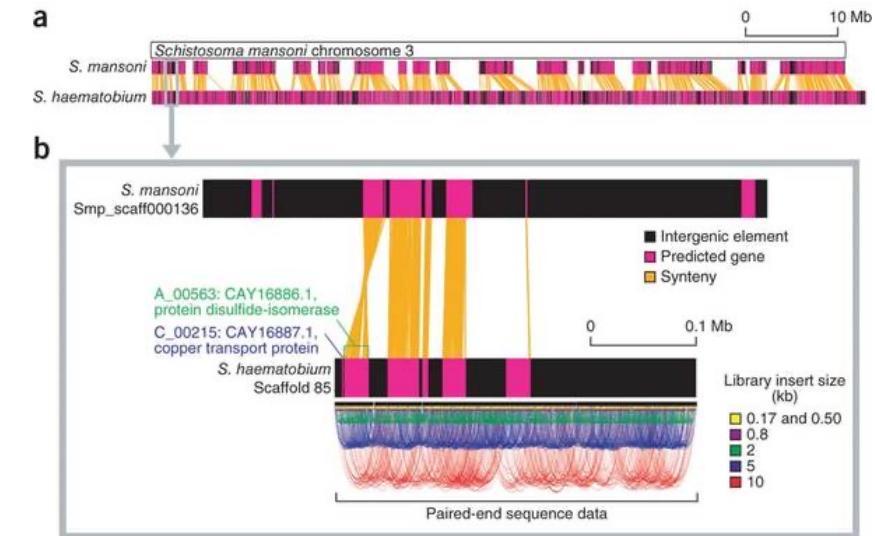
<https://parasite.wormbase.org/>



VEuPathDB
Eukaryotic Pathogen, Vector & Host
Informatics Resources



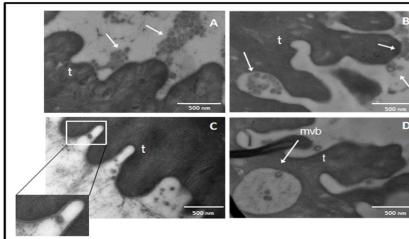
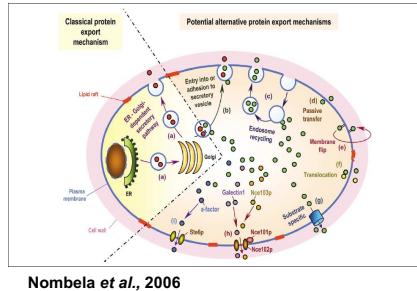
<https://veupathdb.org/>



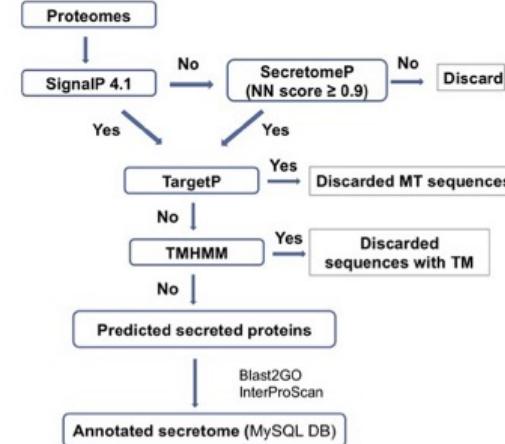
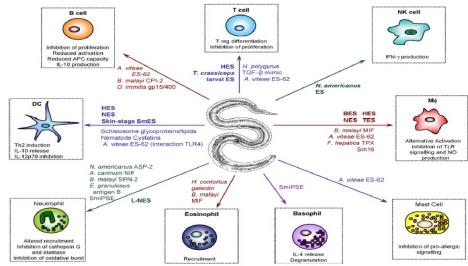
Jex et al., 2011

Worm's secretome: another diversity story

Do the secretome reflect different lifestyles and parasitized hosts?



Marcilla et al., 2012
(*Echinostoma caproni*)



The **comparative study** of the secretome will contribute to the understanding of the **evolution of parasitism** and the host-parasite interaction.



Contents lists available at ScienceDirect

International Journal for Parasitology

journal homepage: www.elsevier.com/locate/ijpara



Helminth secretomes reflect different lifestyles and parasitized hosts

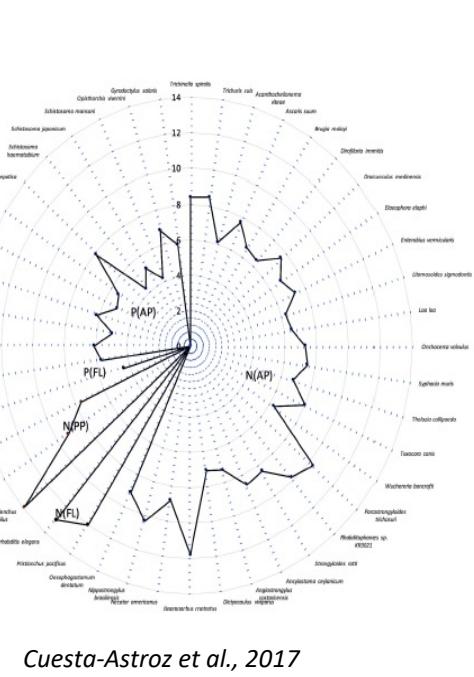
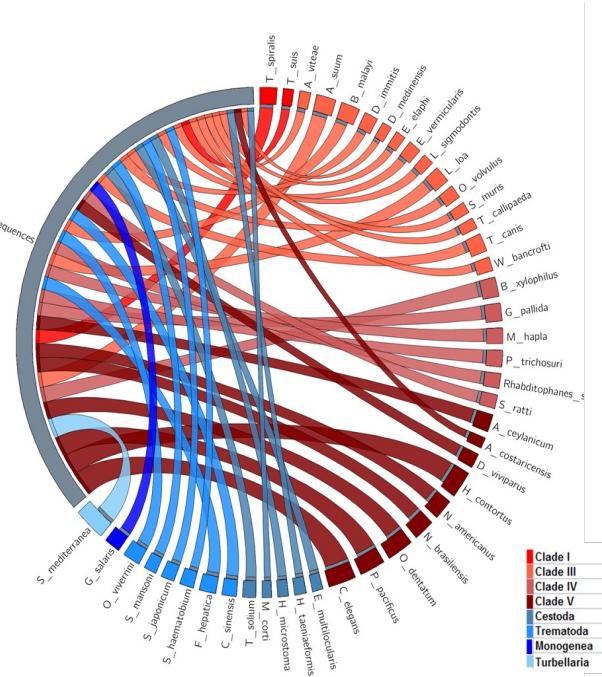
Yesid Cuesta-Astroz ^{a,c}, Francilson Silva de Oliveira ^{a,c}, Laila Alves Nahum ^{a,d}, Guilherme Oliveira ^{a,b,*}

^aCentro de Pesquisas René Rachou (CPRR), Fundação Oswaldo Cruz (FIOCRUZ), Belo Horizonte, MG 30190-002, Brazil

Protein domains diversity

Pfam

5.429 Secreted domains
2.345 Non- secreted



• Protein interaction

- PF02839 (Carbohydrate binding domain)
- PF03173 (Putative Carbohydrate binding domain)
- PF07462 (Surface protein)

• Degradation

- PF06951 (Phospholipase A2)
- PF08192 (Peptidase family S64)
- PF00295 (Glycosyl hydrolases family 28)

• Protection (antibacterial)

- PF03815 (LCCL domain)
- PF15291 (Dermcidin, antibiotic peptide)

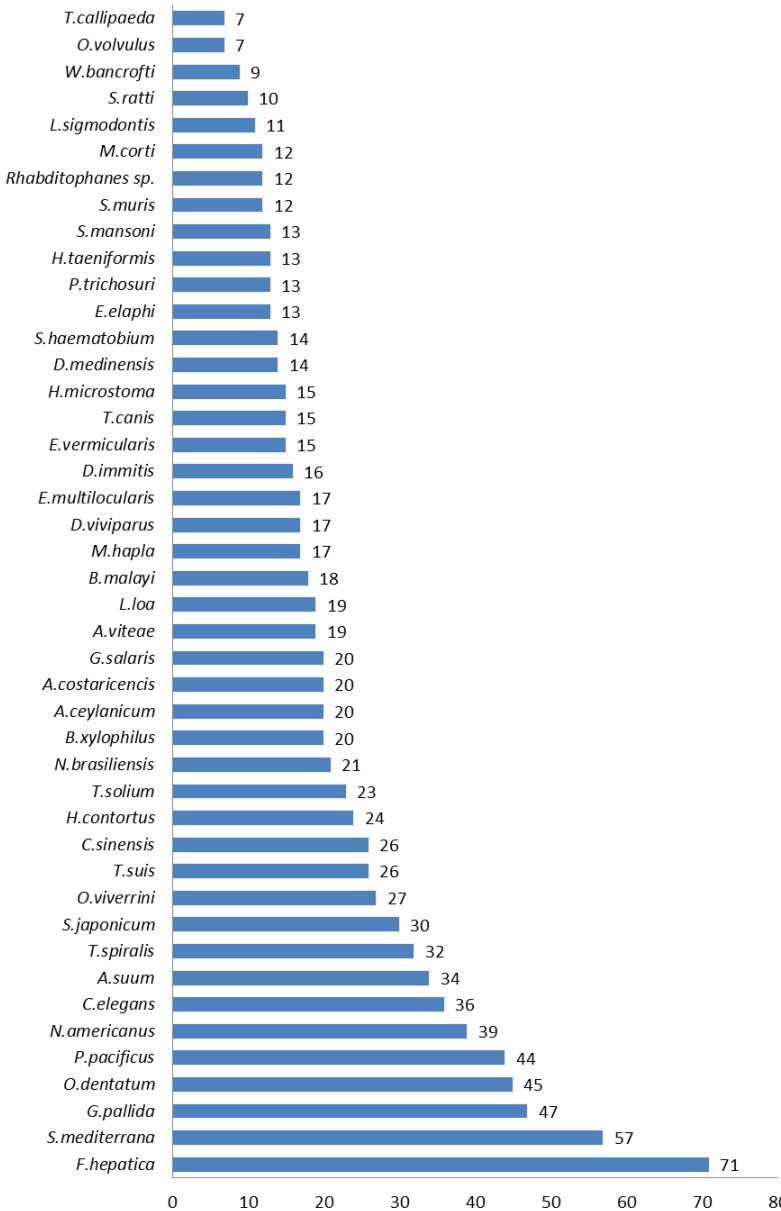
• Pathogenesis

- PF04203 (Sortase)
- PF05596 (Taeniidae antigen)
- PF05630 (Necrosis inducing protein)
- PF07740 (Spider toxin)

• Adhesion

- PF04203 (Sortase)

Specie-specific protein domains



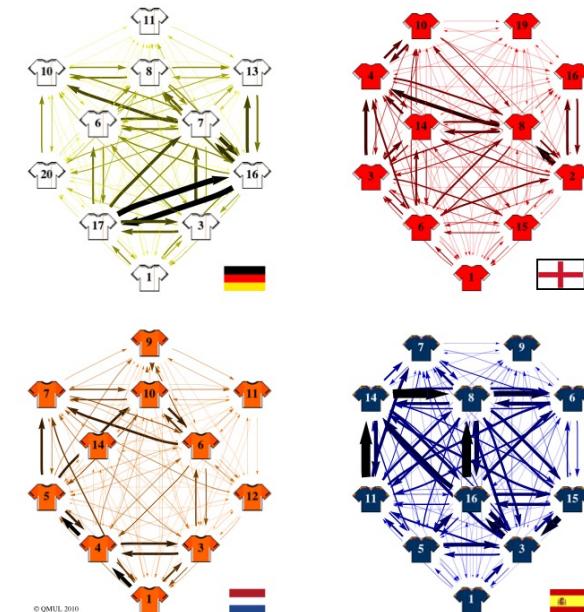
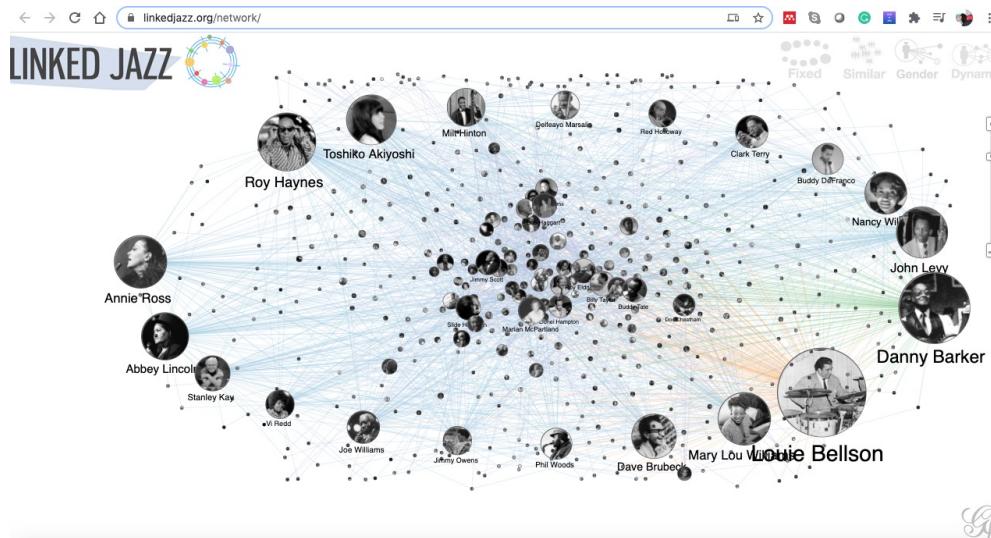
- Particular parasite **adaptations** to specific niches and mechanisms implemented by parasites to establish infection and survival in the host.
- Secretomes from **plant parasites** and **free-living helminths** are larger than animal parasites.
- Secreted proteins associated with invasion, infection, adhesion and immunoregulation processes were identified.
- Secreted proteins have higher architecture diversity compared with non-secreted proteins.
- The secretome is not conserved across species and the differences suggest possible **evolutionary adaptations**.

Biological Networks

Non - biological networks



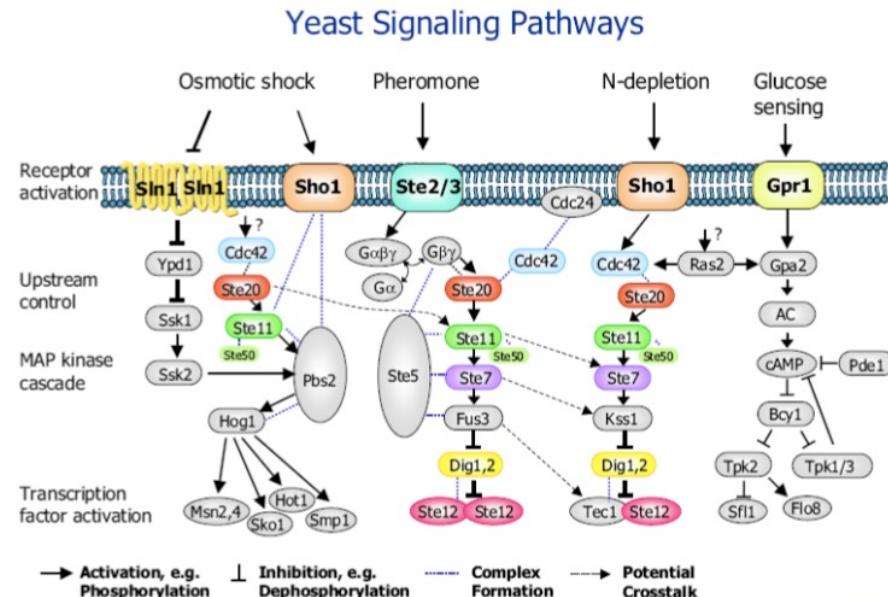
<https://associationsnow.com/wp-content/uploads/2018/04/GettyImages-547533236-800x480.jpg>



© QMUL, 2010

Cellular networks

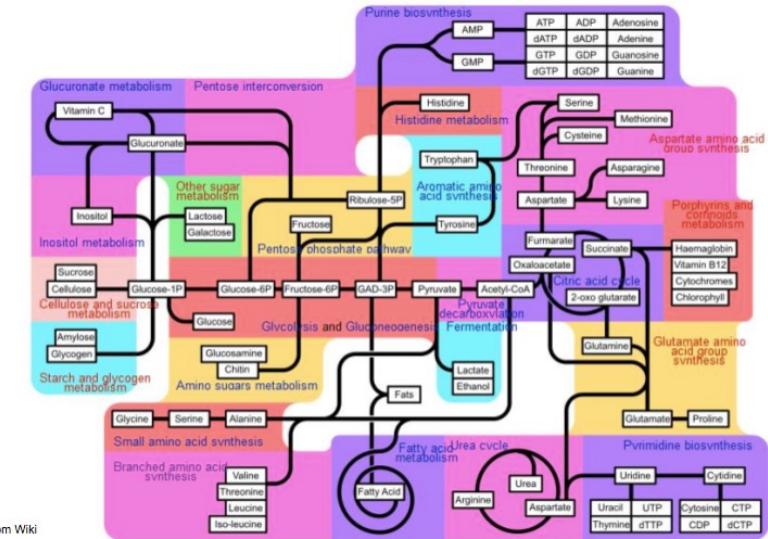
A graphical representation of a complex system



from BMC Neuroscience 2006, 7:S10

40

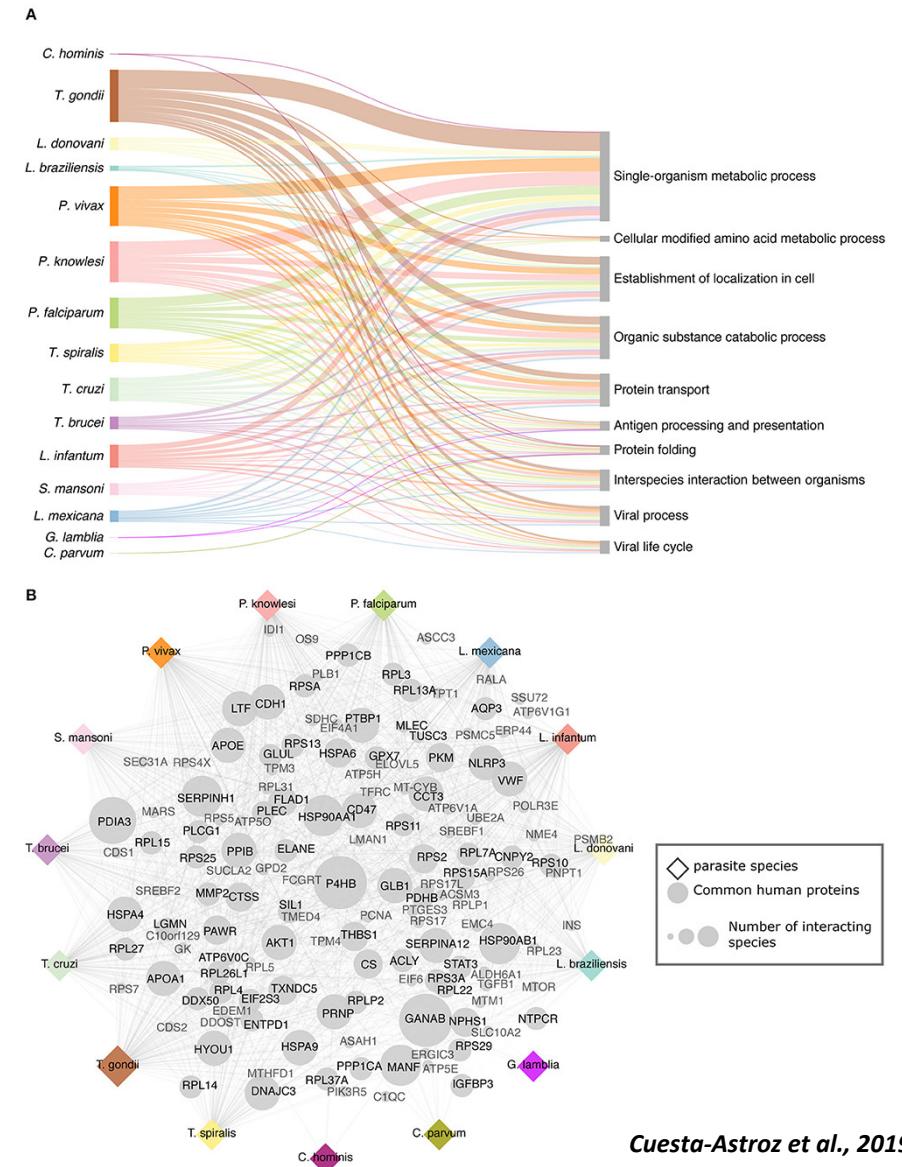
Metabolic networks



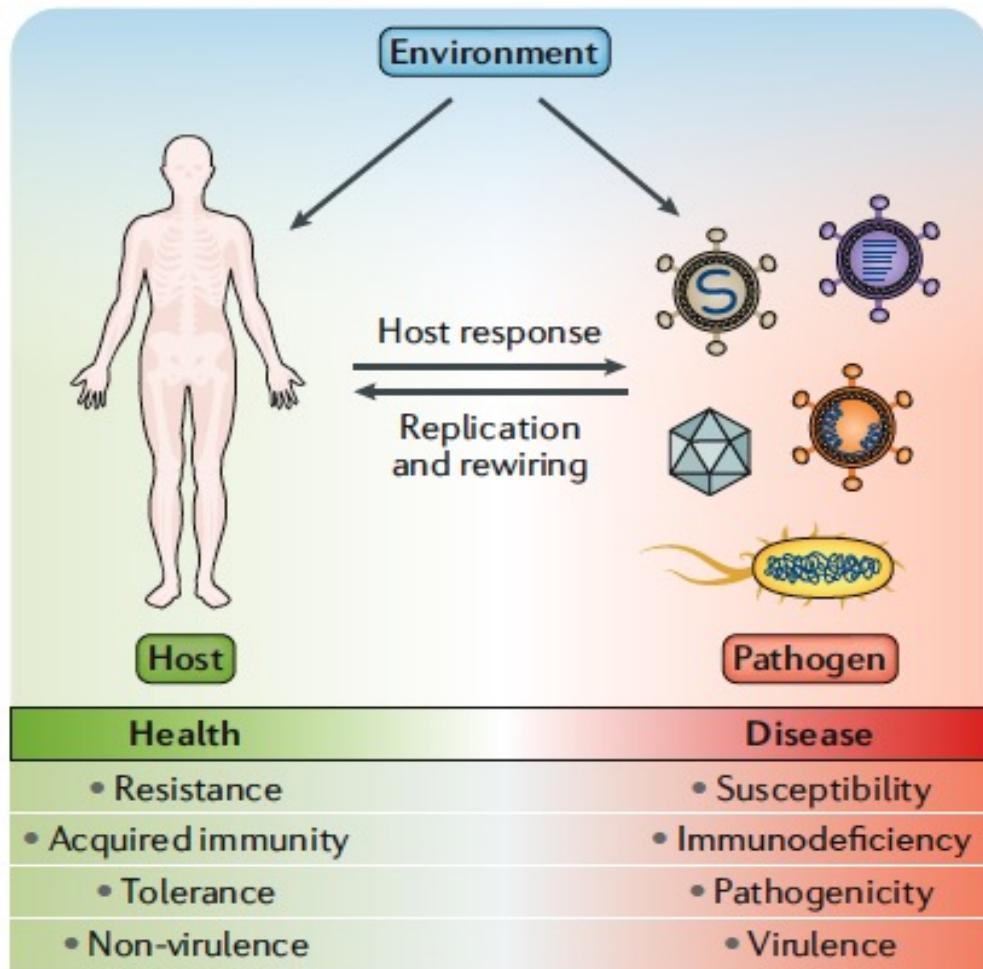
Biological networks in infectious diseases

- The development of **vaccines or treatments** has been impeded by the lack of understanding of the pathogens infection and survival mechanisms.
 - The study of host-parasite **molecular interactions** is essential for understanding infection, local adaptation within the host, and pathogenesis.

These complex interactions can be described as a network.



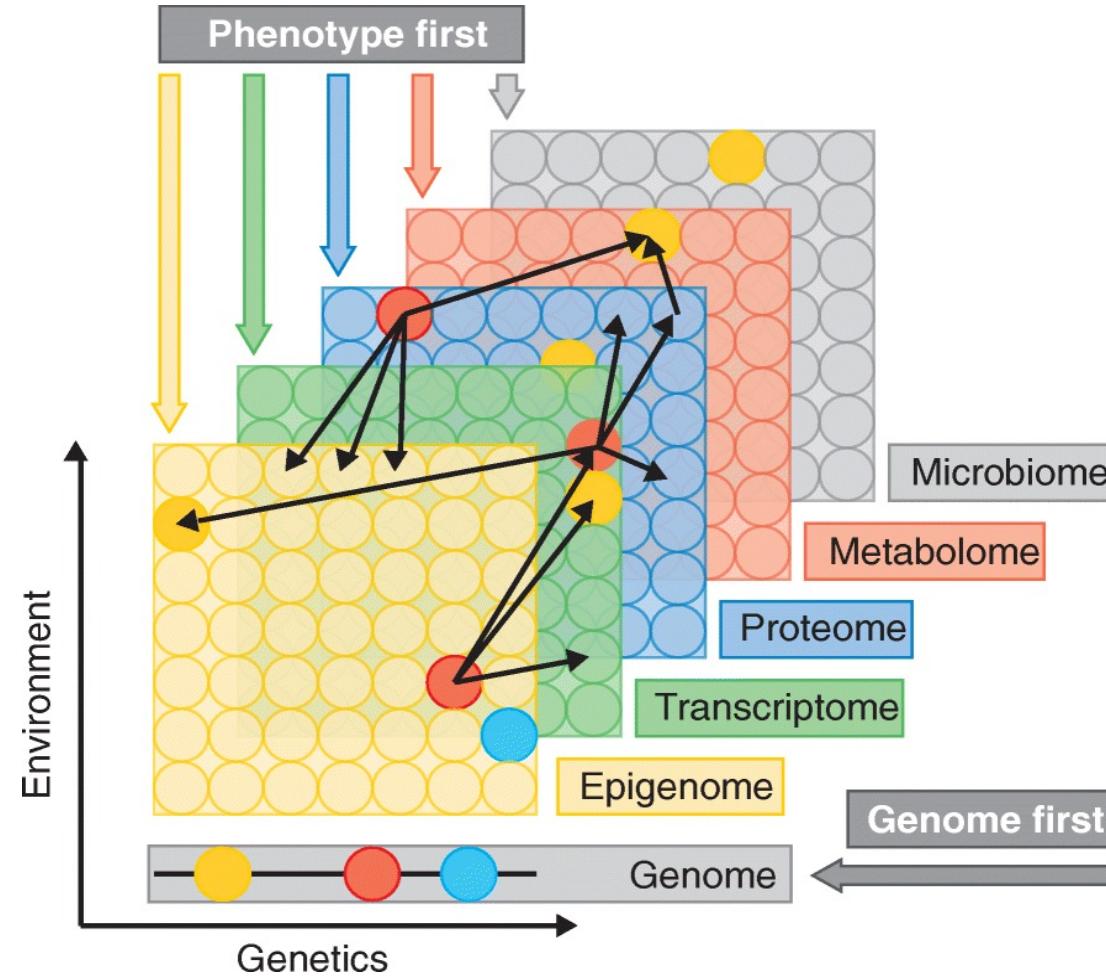
Systems biology and infectious diseases



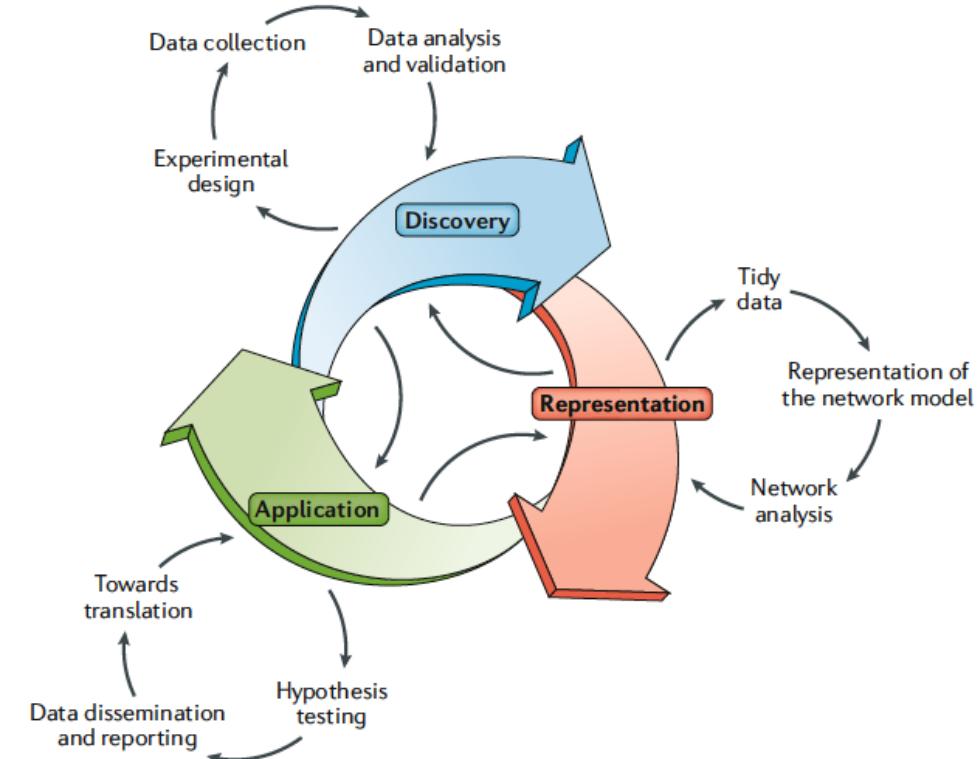
Systems biology is a holistic and modeled characterization of a living system and can be represented as a biological network.

The systems biology approach to infectious diseases involves consideration of two components:
The host, the pathogen and vectors.

Multi-omics data types in disease research



Relevant questions before integrating omics data



Eckhardt et al., 2020

- What are the **goals** of the experiments?
- What model system is being used and what components (**biomolecules**) are being measured?
- What types of data are valuable in answering the **biological questions**?
- What computational steps are necessary for the **interpretation** and **analysis** of the data?
- After data collection, statistical analysis and validation of primary data. The next step is the **construction of the model**.

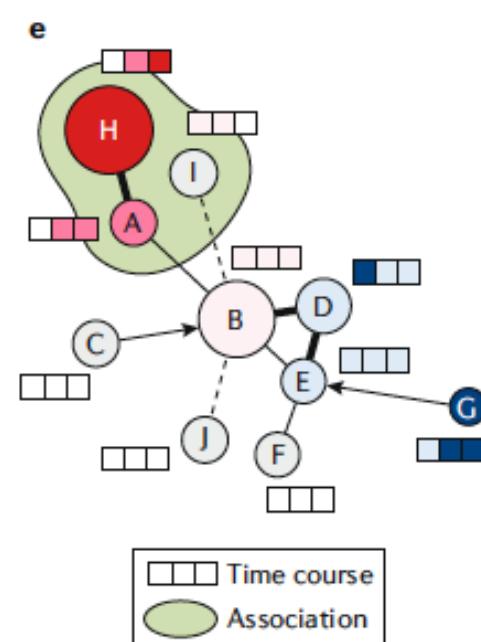
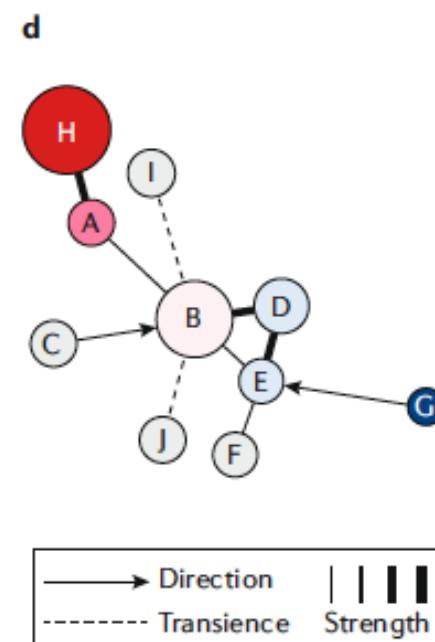
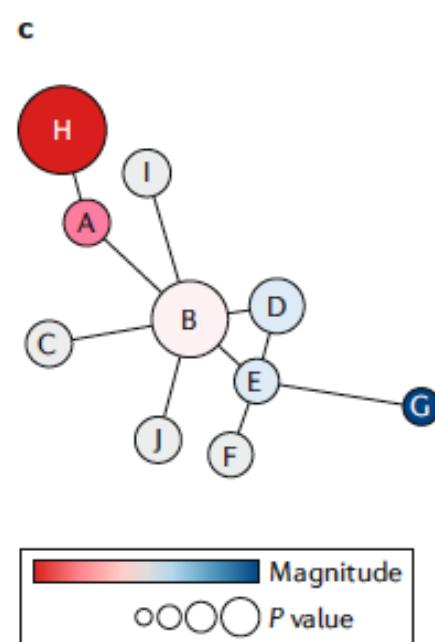
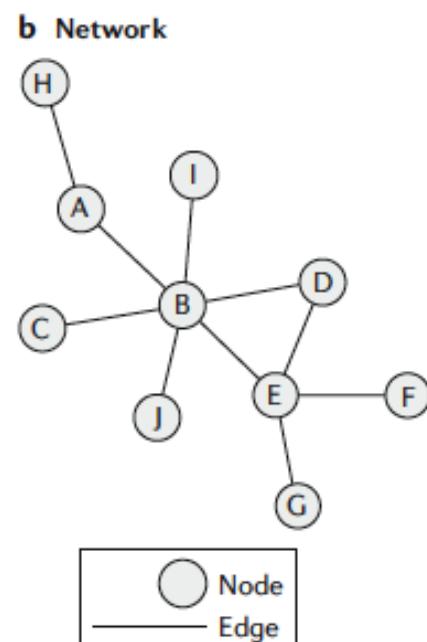
These models can be represented as a network.

Network-based modelling

Network models can be dynamic or static depending on a variety of variables, and can include weights, directionality, groupings to convey additional information.

a

Variables							Independent data sets	
Identifier	Descriptor	Magnitude	P value	etc.				
Gene A		Identifier	Descriptor	Magnitude	P value	etc.		
Gene B		Gene A						
Gene C		Gene B		Identifier	Descriptor	Magnitude	P value	etc.
Gene D		Gene C		Gene A				
etc.		Gene D		Gene B				
		etc.		Gene C				
				Gene D				
				etc.				



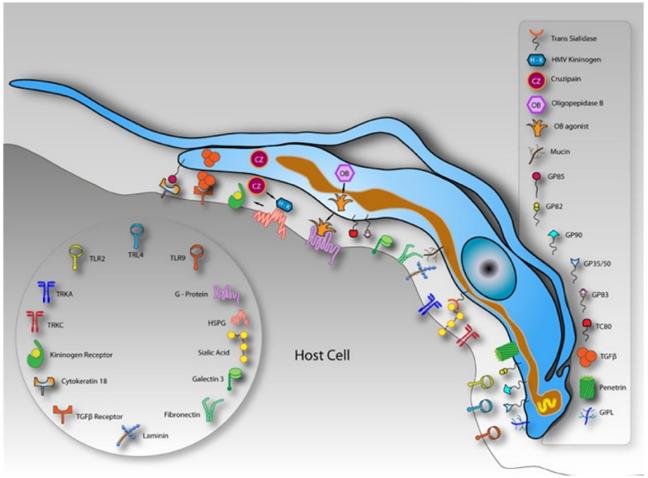
Network-based approaches applied to host-pathogen interactions

Computational systems biology of Host-Pathogen networks includes:

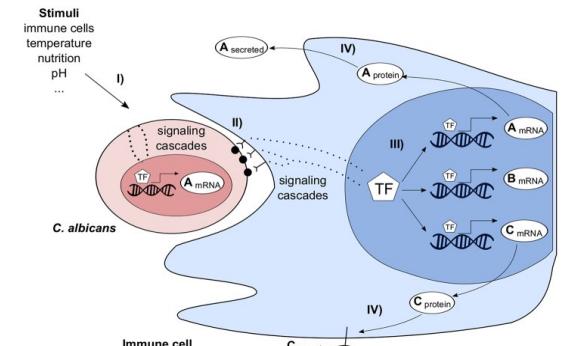
- **Modeling** of molecular mechanisms of infections
- Modeling of **defense mechanisms** against of pathogens to generate information for possible immune therapies.
- Modeling of HPI dynamics and identification of **biomarkers for diagnosis** and to individualize the anti-infection therapy.
- Identify essential **virulence determinants** and predict potential therapeutic targets.
- Understanding the **host immune response and immune evasion of pathogens**, as a result of long-term evolutionary adaptation and selection.

Host-pathogen protein-protein interactions

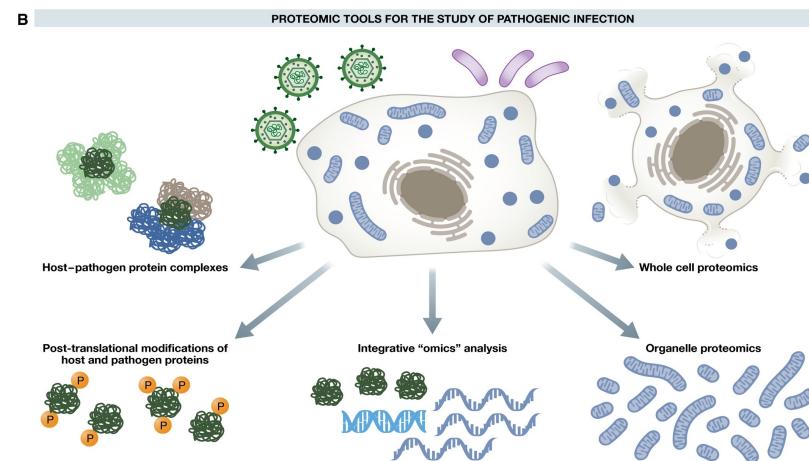
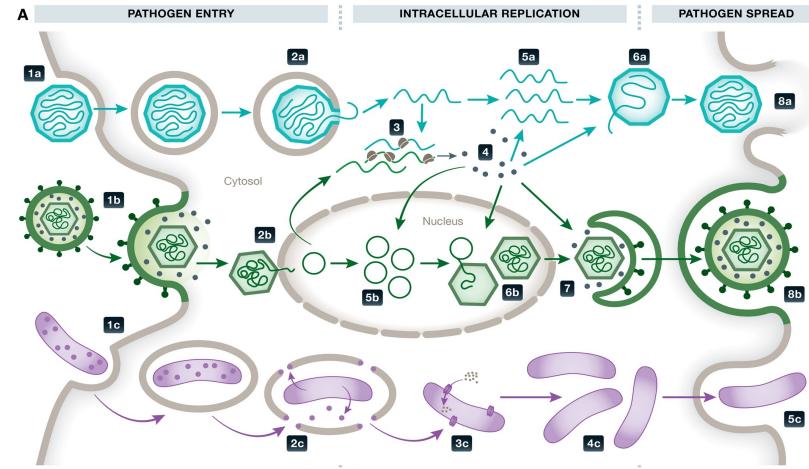
Interactions among different social networks



Santos et al., 2013. (*T. cruzi*)

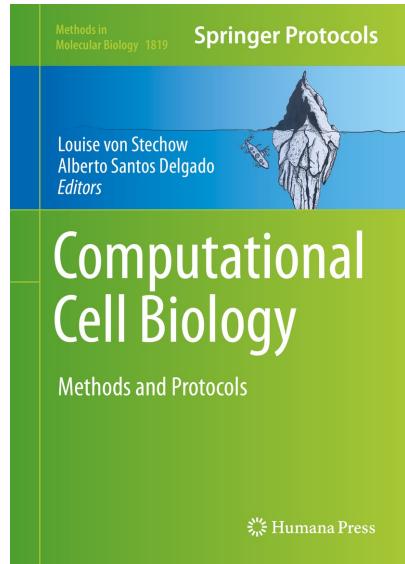


Schulze et al., 2016. (*C. albicans*)



Beltran et al., 2017

Computational methods for inferring host-parasite interactions



Chapter 7

Computational and Experimental Approaches to Predict Host–Parasite Protein–Protein Interactions

Yesid Cuesta-Astroz and Guilherme Oliveira

Computational methods for inferring host-parasite interactions

Data sources: experimental and computational

Table 1
Summary of human–parasite PPIs detection methods reviewed in this chapter

Approach	Technique	Parasites	Reference
Experimental	Y2H ^G	<i>T. gondii</i>	[40]
	Phage display ^G	<i>C. parvum</i>	[48]
	Coimmunoprecipitation ^B	<i>F. hepatica</i>	[52]
	Affinity purification ^B	<i>T. cruzi</i>	[60]
	Cross-linking ^B	<i>P. falciparum</i>	[63]
	Protein arrays ^B	<i>S. mansoni</i>	[65]
Computational	Homology	<i>P. falciparum</i>	[74]
	Domains and motifs	<i>P. falciparum</i>	[85]
	Structure-based	<i>L. major</i> , <i>T. brucei</i> , <i>T. cruzi</i> , <i>C. hominis</i> , <i>C. parvum</i> , <i>P. falciparum</i> , <i>P. vivax</i> , <i>T. gondii</i>	[88]
	Machine learning	<i>P. falciparum</i>	[97]
	Coexpression	<i>P. falciparum</i>	[101]

G genetic, *B* biochemical method

Table 3
Intraspecies PPIs databases

Database name	Total number of interactions	Source link	Number of organisms
IntAct 4.2.7	506,367	http://www.ebi.ac.uk/intact/	8
STRING	1,380,838,440	https://string-db.org/	2031
APID	678,441	http://apid.dep.usal.es	25
DIP	81,766	http://dip.doe-mbi.ucla.edu/dip/	834
HitPredict	547,879	http://hitdb.hgc.jp/htp/	115
MINT	125,464	http://mint.bio.uniroma2.it/	611
BioGrid 3.4	1,495,320	https://thebiogrid.org/	61

Table 2
Human and parasite databases/tools used to support or context experimental and computational predictions of host-parasite PPIs

Organism (human/parasite)	Database/tool	Summary	Source link
HP	iPfam	A database of protein family and domain interactions calculated from known structures.	http://ipfam.org/
HP	3did	A database of three-dimensional interacting domains	http://3did.irbbarcelona.org/
HP	ELM	This resource focuses on annotation and detection of eukaryotic linear motifs	http://elm.eu.org/
HP	Pfam	Protein families database	http://pfam.xfam.org/
HP	Reactome	Pathways database	http://reactome.org/
HP	KEGG	Pathways database	http://www.genome.jp/kegg/
HP	Gene Ontology	Gene annotations.	http://geneontology.org/
HP	SignalP	Prediction of signal peptides from amino acid sequences. Proteins with signal peptides are targeted to the secretory pathway	http://www.cbs.dtu.dk/services/SignalP/
H	COMPARTMENTS	Subcellular localization database	https://compartment.jenlab.org/
H	TISSUES	Tissue expression database	https://tissues.jenlab.org/
H	TissueNet v.2	A database of protein–protein interactions across human tissues	http://netbio.bgu.ac.il/tissuenet/
P	GeneDB	Sequence data and annotation/curation for some parasites species	http://genedb.org/
P	EupathDB	Integrative database of eukaryotic pathogens include: sequencing, expression, proteomics, metabolic and phenotype data	http://eupathdb.org/

HP human/parasite, H human, P parasites

Human-parasite interactomes



ORIGINAL RESEARCH
published: 13 February 2019
doi: 10.3389/fimmu.2019.00212



Analysis of Predicted Host-Parasite Interactomes Reveals Commonalities and Specificities Related to Parasitic Lifestyle and Tissues Tropism

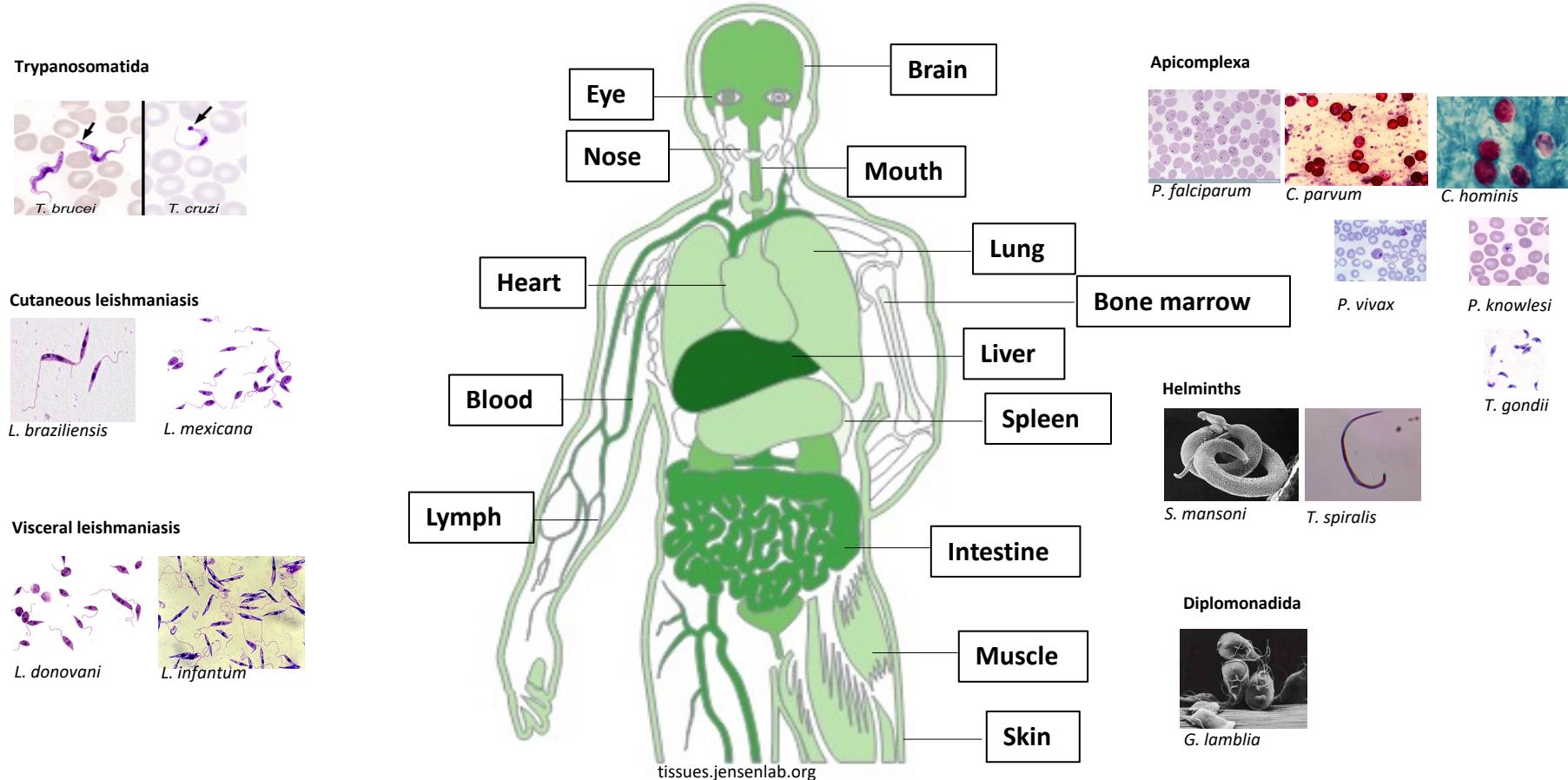
Yesid Cuesta-Astroz^{1†}, Alberto Santos^{2†}, Guilherme Oliveira^{3*} and Lars J. Jensen^{2*}

¹ Instituto René Rachou, Fundação Oswaldo Cruz - FIOCRUZ, Belo Horizonte, Brazil, ² Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark,

³ Environmental Genomics, Instituto Tecnológico Vale, Belém, Brazil

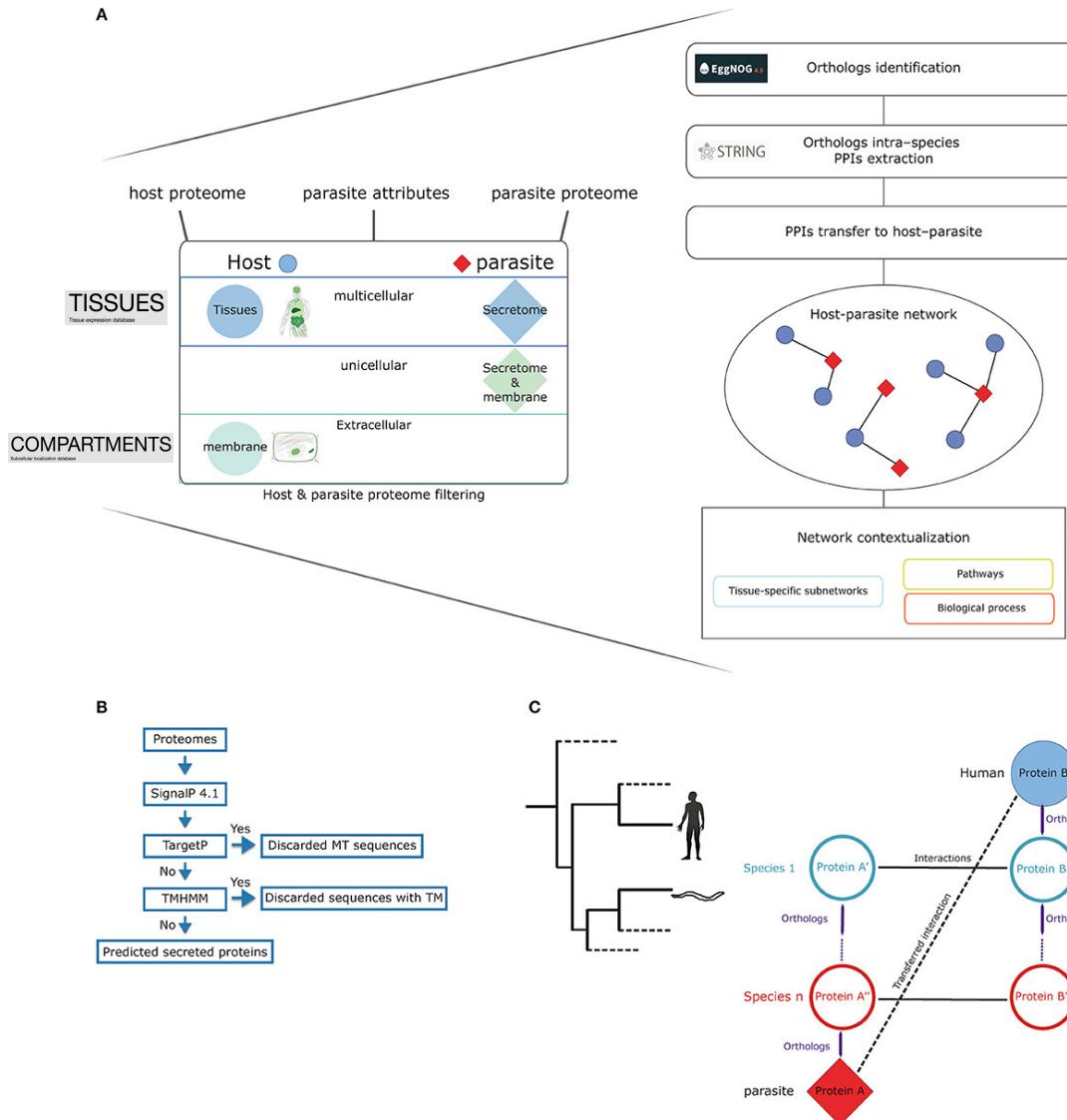
Keywords: computational biology, systems biology, biological networks, parasitology, schistosomiasis, host-parasite interactions

Host-parasite interactions: 15 parasites vs 14 tissues



We propose an **integrative approach** that gives **context** to the interactions according to the **parasite's life cycle** and **subcellular localization** of the proteins. To understand molecular **similarities** and **differences** in host response to diverse sets of parasites. These interactions are also essential to understand **parasite infection** and **local adaptation** within the host and vector.

Proteome filtering: adding parasite-specific biological context



- We used an **orthology-based** approach to transfer high-confidence intraspecies interactions obtained from the **STRING database** to the corresponding interspecies homolog protein pairs in the host–parasite system.
- The resulting PPI networks were compared across parasites to identify common mechanisms that may define a **global pathogenic hallmark**.

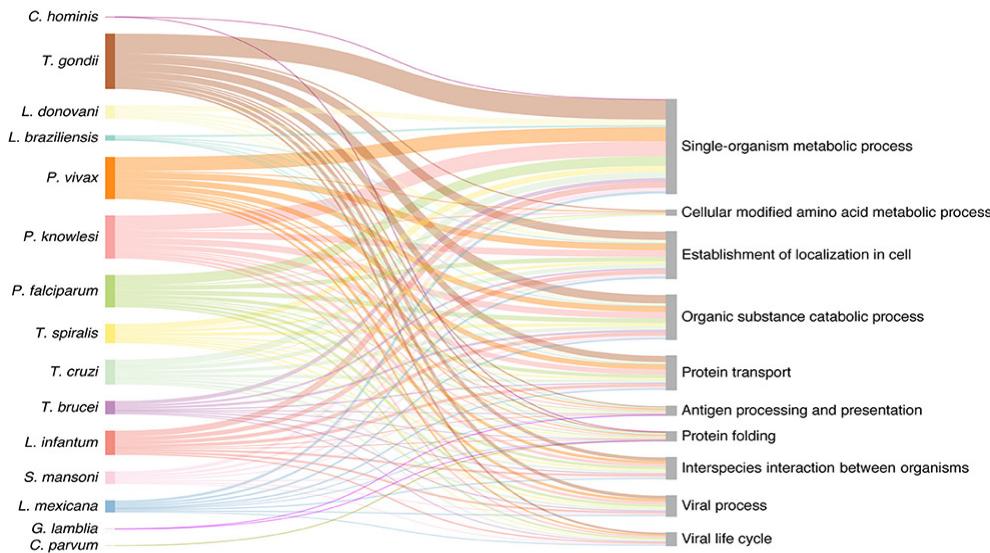
Human parasites analyzed

Tax_id	Species	E/I	U/M	Tissues	Proteome size	SS (%)	MP (%)	Input
5691	<i>Trypanosoma brucei</i>	E	U	Skin, blood, brain, lymph node, spinal cord	8,747	708 (8, 1)	1,439 (16, 4)	SS+MP
353153	<i>Trypanosoma cruzi</i>	I	U	Skin, heart, blood, eye,	19,602	2,633 (13, 4)	3,373 (17, 2)	SS+MP
6334	<i>Trichinella spiralis</i>	E	M	Intestine, brain, heart, muscle, lung	16,380	705 (4, 3)	N/A	SS
6183	<i>Schistosoma mansoni</i>	E	M	Skin, liver, intestine, lung, blood	11,770	318 (2, 7)	N/A	SS
184922	<i>Giardia lamblia</i>	E	U	Intestine	6,502	407 (6, 2)	727 (11, 2)	SS+MP
5833	<i>Plasmodium falciparum</i>	I	U	Skin, blood, liver	5,429	619 (11, 4)	1,355 (25, 0)	SS+MP
5855	<i>Plasmodium vivax</i>	I	U	Skin, blood, liver	5,050	553 (11, 0)	900 (17, 8)	SS+MP
5850	<i>Plasmodium knowlesi</i>	I	U	Skin, blood, liver	5,102	565 (11, 0)	890 (17, 4)	SS+MP
353151	<i>Cryptosporidium hominis</i>	E	U	Intestine	3,885	324 (8, 3)	641 (16, 5)	SS+MP
353152	<i>Cryptosporidium parvum</i>	E	U	Intestine	3,805	397 (10, 4)	678 (17, 8)	SS+MP
5811	<i>Toxoplasma gondii</i>	I	U	Blood, brain, eye, heart, muscle, placenta	7,988	658 (8, 2)	1,188 (14, 8)	SS+MP
420245	<i>Leishmania braziliensis</i>	I	U	Skin, nose, mouth, blood	8,160	294 (3, 6)	1,152 (14, 1)	SS+MP
929439	<i>Leishmania mexicana</i>	I	U	Skin, nose, mouth, blood	8,147	305 (3, 7)	1,186 (14, 5)	SS+MP
5661	<i>Leishmania donovani</i>	I	U	Skin, liver, spleen, blood, bone marrow	8,032	310 (3, 8)	1,104 (13, 7)	SS+MP
435258	<i>Leishmania infantum</i>	I	U	Skin, liver, spleen, blood, bone marrow	8,150	325 (3, 9)	1,159 (14, 2)	SS+MP

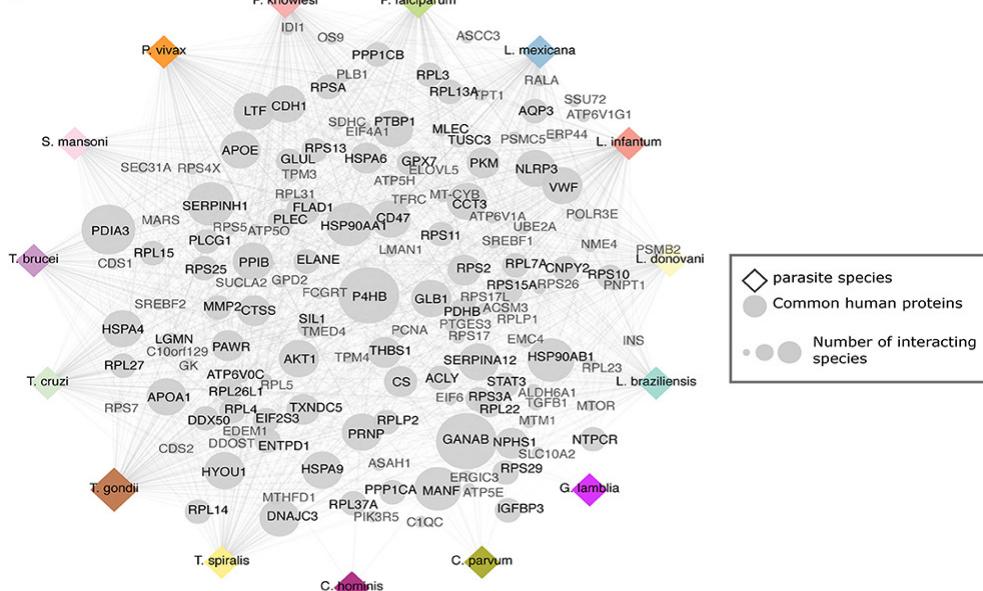
E, Extracellular; I, intracellular. U, Unicellular; M, Multicellular. Tissues: different tissues associated with the parasite's tropism (information retrieved from: <https://www.cdc.gov/parasites/>). Proteome size: sequences in the predicted proteome. SS, Soluble secretome; MP, Membrane proteins (%: is the percentage in relation to the overall proteome); N/A, Not applicable.

Common and specific mechanisms targeted by the studied parasites

A



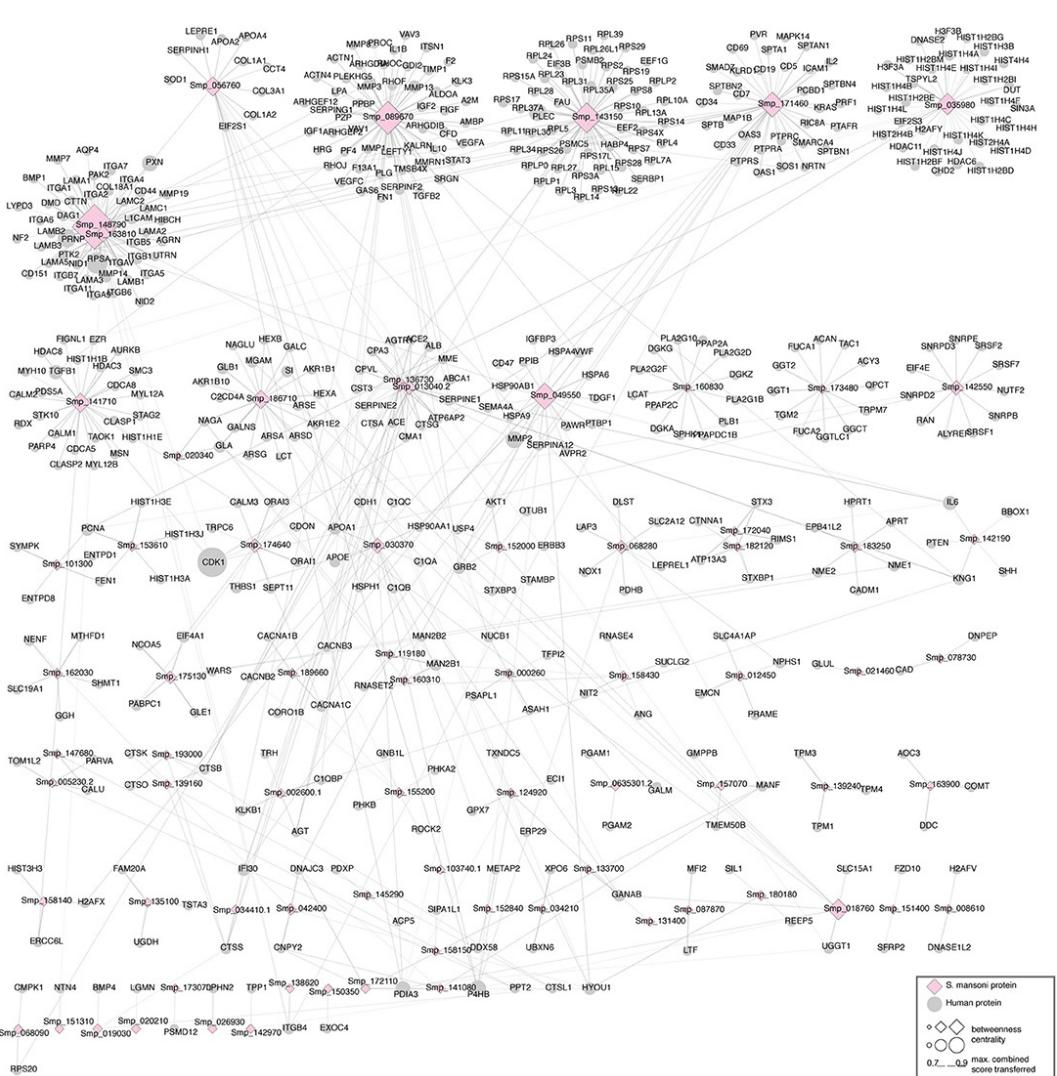
B



- We used annotations from both **biological processes** GO terms and Reactome pathways in human to get an overview of the shared pathways targeted by the studied parasites. In total, **1,910 GO terms** (biological process) were identified in human proteins targeted by parasites across all the interactomes.

- In all the inferred interactomes, **GANAB** (neutral alpha glucosidase AB) and **P4HB** (protein disulfide isomerase) proteins were predicted to interact with parasite proteins. GANAB protein is related to the **host defense mechanisms** and P4HB is relevant in the internalization of **broad spectrum of pathogens** such as *Leishmania*, HIV, dengue virus, and rotavirus.

S. mansoni – *H. sapiens* interactome

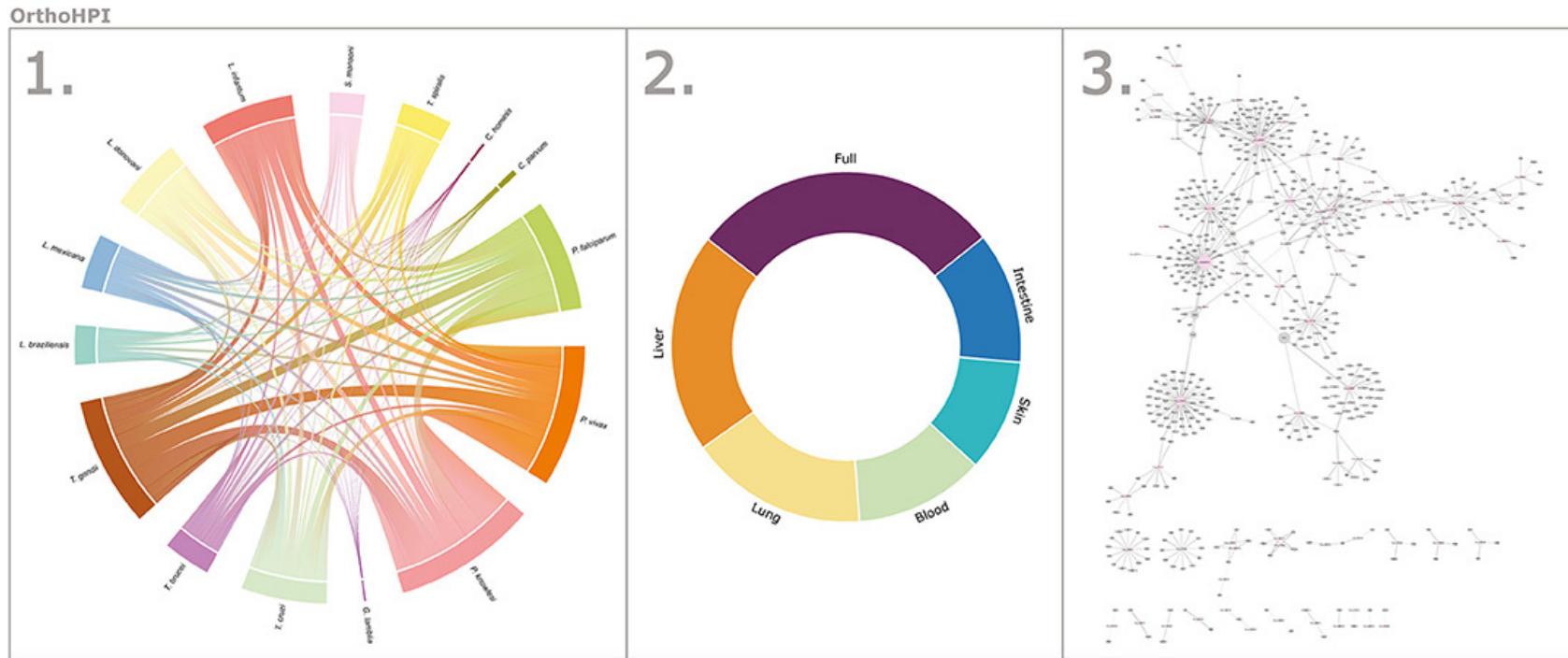


Protein ID	Description
Human proteins with the highest centrality	
ENSP00000346067	Ribosomal protein SA
ENSP00000378699	Cyclin-dependent kinase 1
<i>S. mansoni</i> proteins with the highest centrality	
Smp_056760	Protein disulfide-isomerase
Smp_018760	Neutral alpha-glucosidase ab
Smp_035980	Histone H2A
Smp_171460	Cell adhesion molecule
Smp_049550	Heat shock protein 70 (Hsp70)
Smp_143150	Eukaryotic translation elongation factor
Smp_089670	Alpha-2 macroglobulin
Smp_148790	Laminin subunit beta 1

- The nodes in these networks represent parasite and human proteins and their sizes correspond to their **betweenness centrality** in the network.
 - Network centrality helped to **prioritize proteins** by identifying nodes with a relevant role in the **communication flow** in the network, which may translate into **biological relevant essentiality**

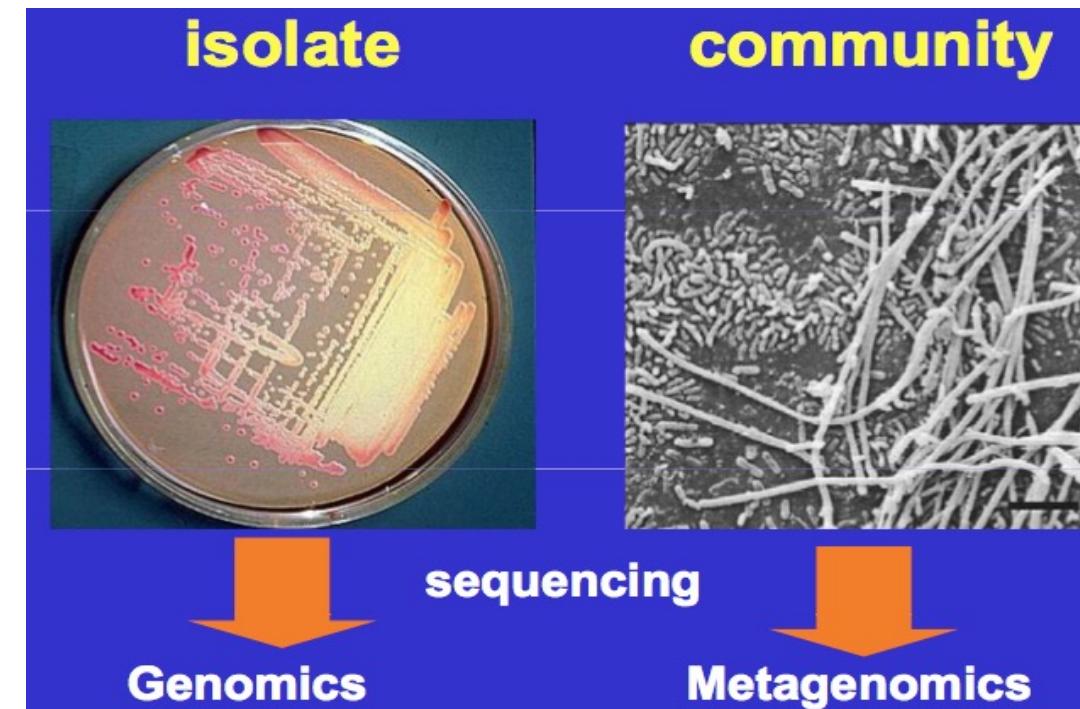
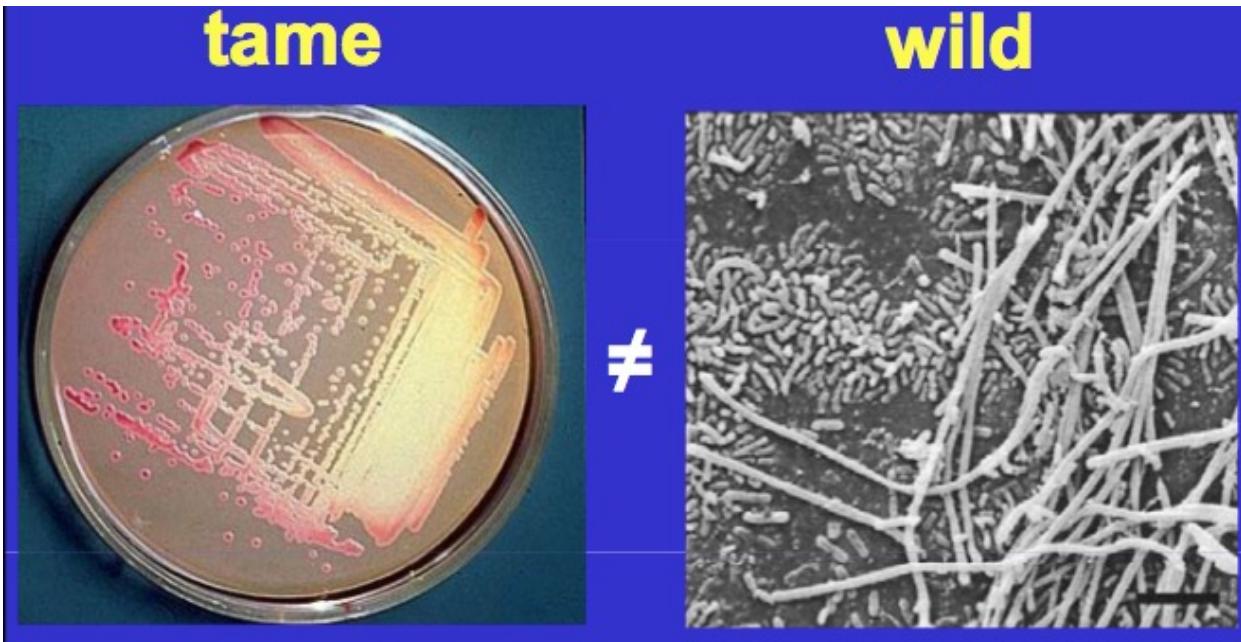
This method is available as a **web-interface** to allow **visualization** and **comparison** of interactomes across parasites. **OrthoHPI** (**O**rchology-based method to predict **H**uman-**P**arasite **I**nteractions).

<http://orthohpi.jensenlab.org/>



Meta - omicas

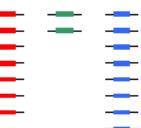
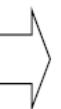
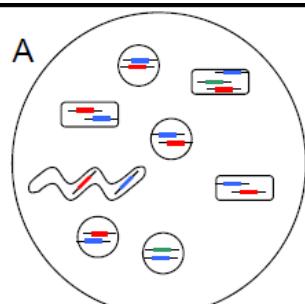
Objetivo de los estudios (meta) omicos



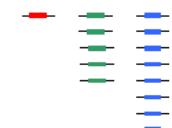
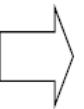
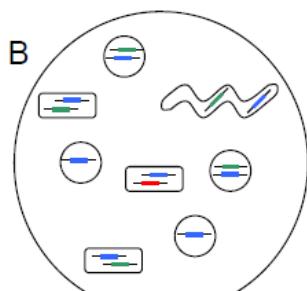
Metagenómica

Objetivos general de la metagenómica

Obtener una visión imparcial de la composición de la diversidad desde un punto de vista filogenético y funcional dentro de una comunidad microbiana.



Environmental Gene Tags
(EGTs)



Basic Computational Tasks of Metagenomics



- Taxonomic analysis (who is out there?)
- Functional analysis (what are they doing?)
- Comparative analysis (how do they compare?)

Meta-Genómica



The New Science of Metagenomics

Revealing the Secrets of Our Microbial Planet

National Research Council (US) Committee on
Metagenomics: Challenges and Functional Applications.

Washington (DC): [National Academies Press \(US\)](#); 2007.
ISBN-13: 978-0-309-10676-4 ISBN-10: 0-309-10676-1

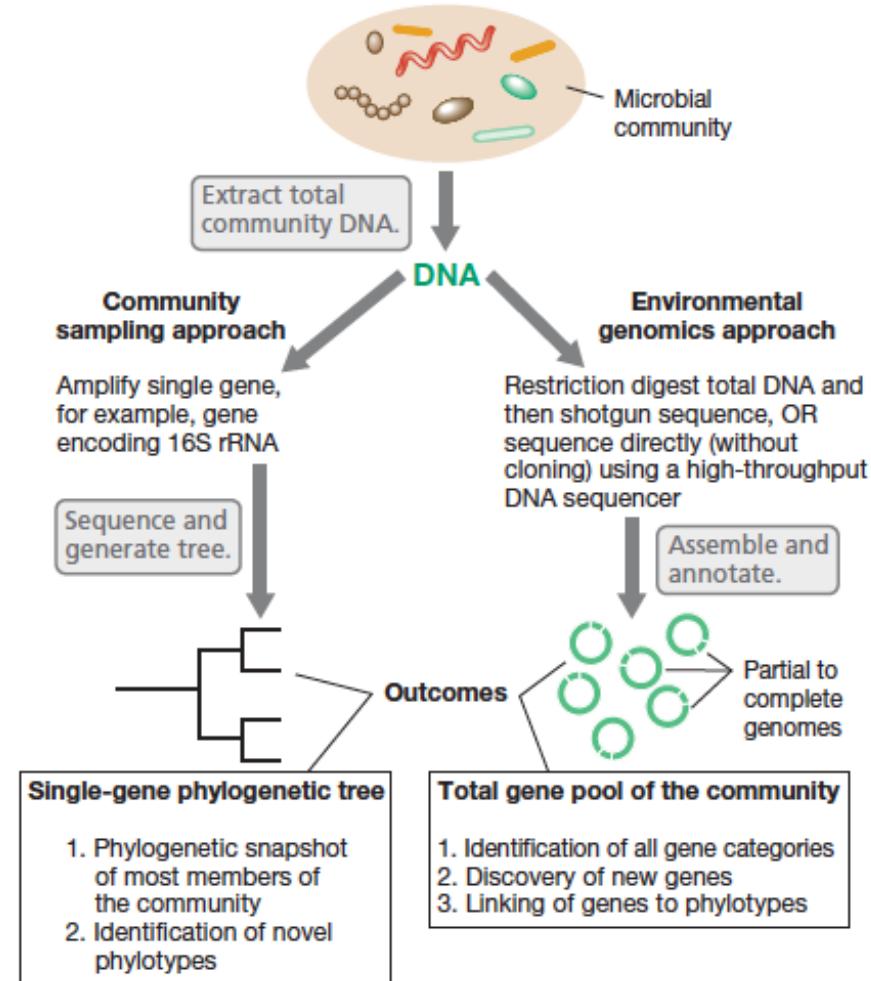
[Copyright and Permissions](#)

[Hardcopy Version at National Academies Press](#)

- Qué son y porqué estudiamos a los microbios?
- Qué entendemos por “meta”?
- El término “omicas” es reciente? (Hans Winkler)
- Qué proporción de biomasa representan las bacterias en un ser humano?

- The *proteome*, the total set of proteins in an organism, tissue, or cell type; **proteomics** is the associated field of study.
- The *transcriptome*, the total set of RNAs found in an organism, tissue, or cell type.
- The *metabolome*, the entire complement of metabolites that are generated in an organism, tissue, or cell type.
- The *interactome*, the entire set of molecular interactions in an organism.

Meta^genómica: técnica y campo de investigación.



(Madigan et al., 2015)

Metagenómica (definición)

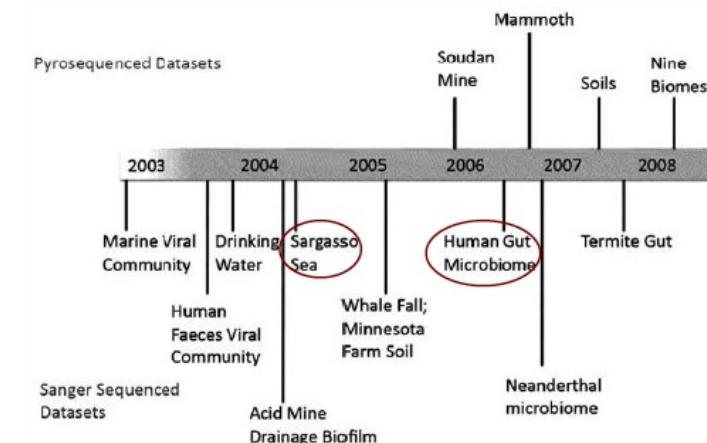
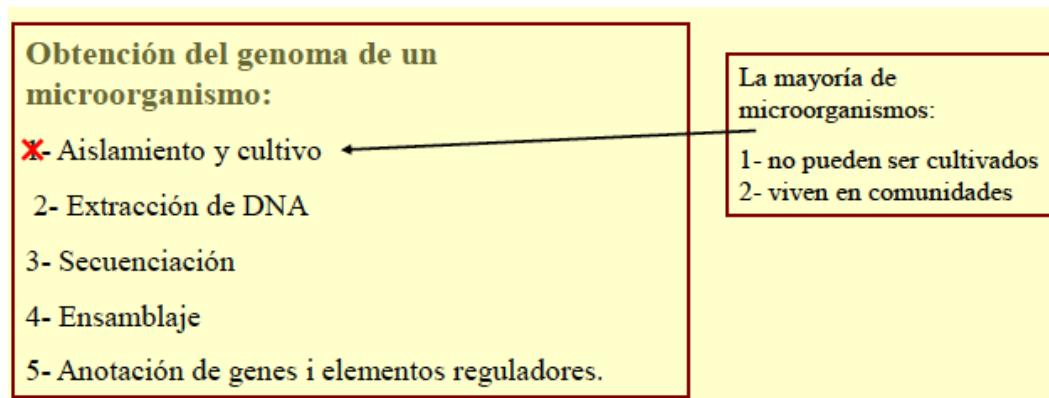
- Un metagenoma se refiere a una colección de ADN genómico a partir de un ambiente y podría ser analizado de manera análoga al estudio de un genoma único.
- Aplicación de técnicas al estudio de comunidades de organismos microbianos directamente en su ambiente natural.
- Metagenómica (Environmental Genomics or Community Genomics) es el estudio de genomas parciales recuperados de muestras del medioambiente sin la necesidad de cultivarlas.
- La metagenómica procesa los datos usando herramientas bioinformáticas.

Objetivos específicos de la metagenómica

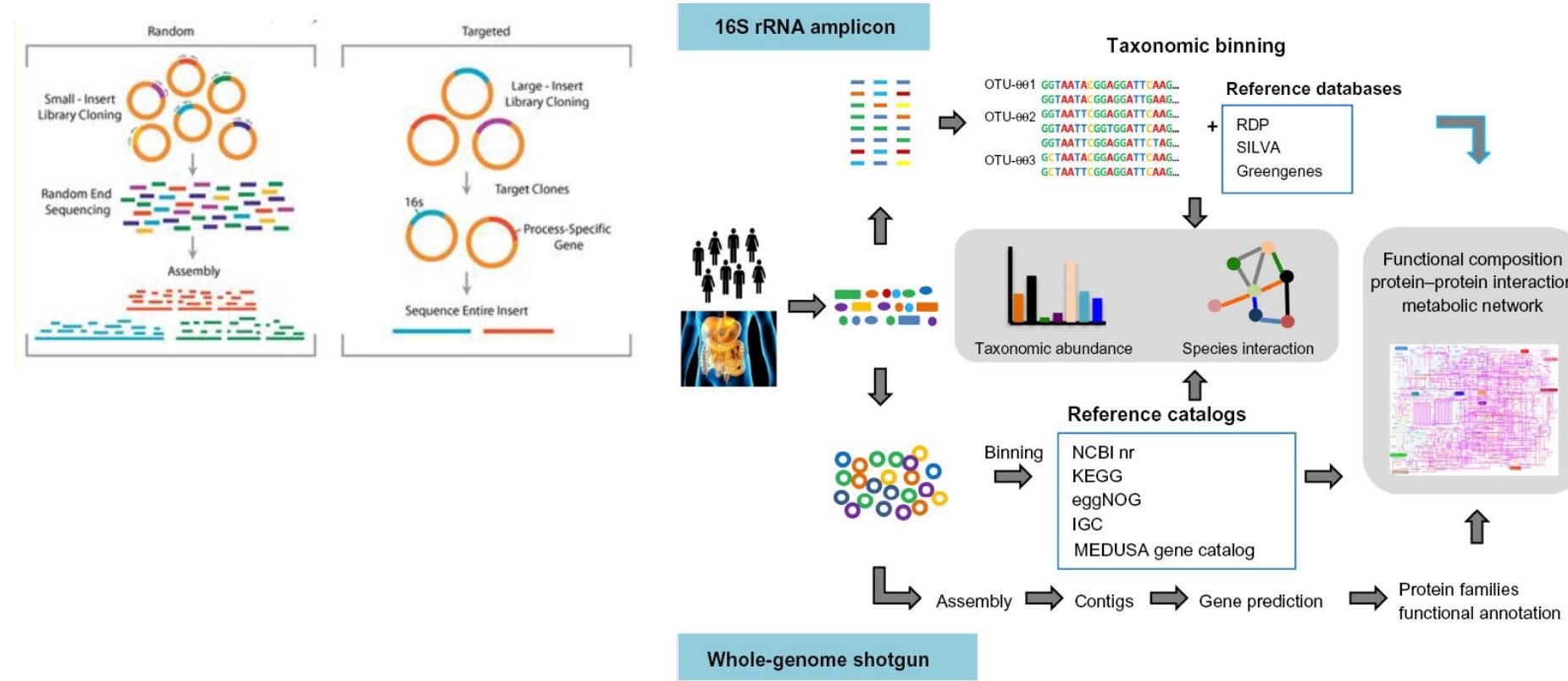
- Examinar la diversidad filogenética usando 16S rRNA y/o shotgun.
- Patrones de diversidad de microorganismos pueden ser usados para monitorear y predecir condiciones medioambientales y de cambio.
- Examinar rutas metabólicas.
- Investigar genes que predominan en un ambiente dado comparado con otros.
- Aportar en el entendimiento de la dinámica en una comunidad microbiana.

Por que es importante la metagenómica?

- Papel de los microorganismos en la biosfera.
- Como los ecosistemas microbianos responden a las perturbaciones medioambientales.
- Los organismos pueden ser estudiados directamente sin necesidad de aislar cada especie.
- Hay grandes ventajas para metagenómica viral debido a la dificultad de cultivar virus en su hospedero apropiado.



Metagenómica (dos enfoques: “random” y “targeted”)



Ji et al., 2014

- 16 rRNA genes do not provide direct evidence of the community's functional capabilities.
- Shotgun metagenomic analysis explore the taxonomic composition and biomolecular functions in microbial communities at the gene level.

Metagenómica (análisis e interpretación)

An introduction to the analysis of shotgun metagenomic data

Thomas J. Sharpton*

Department of Microbiology and Department of Statistics, Oregon State University, Corvallis, OR, USA

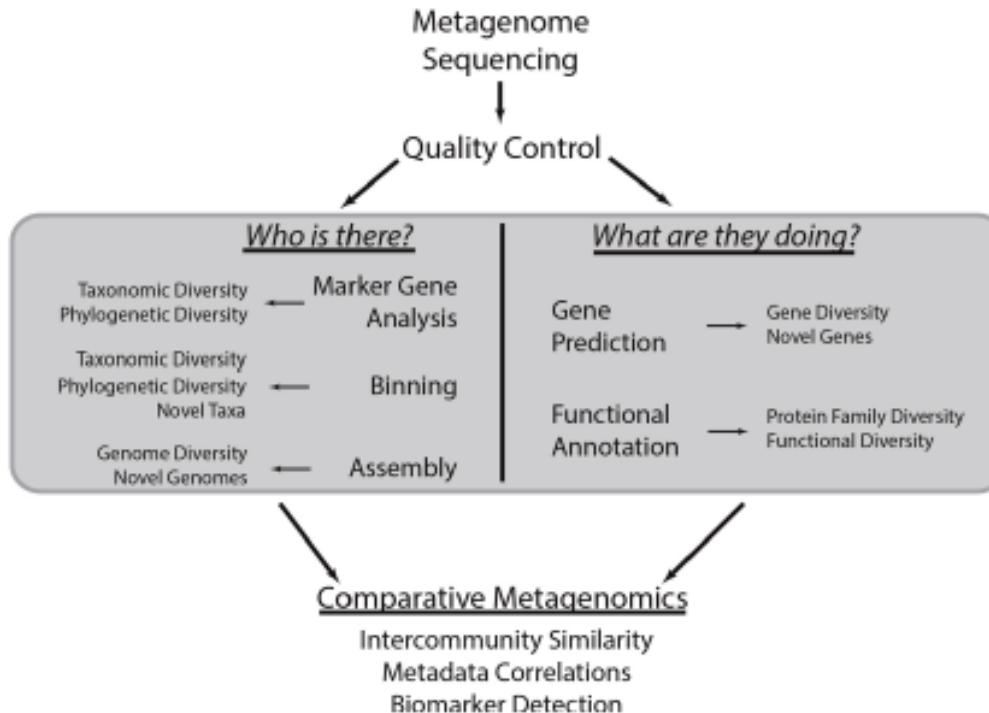


FIGURE 1 | Common metagenomic analytical strategies. This methodological workflow illustrates a typical metagenomic analysis. First, shotgun metagenomic data is generated from a microbial community of interest. After conducting quality control procedures, metagenomic sequences can be subject to various analyses centered on the taxonomic and functional characterization of the community (gray box). These procedures are the focus of this review. Briefly, marker gene, binning, and assembly analyses provide insight into the taxonomic or phylogenetic diversity of the community and can identify novel taxa or genomes.

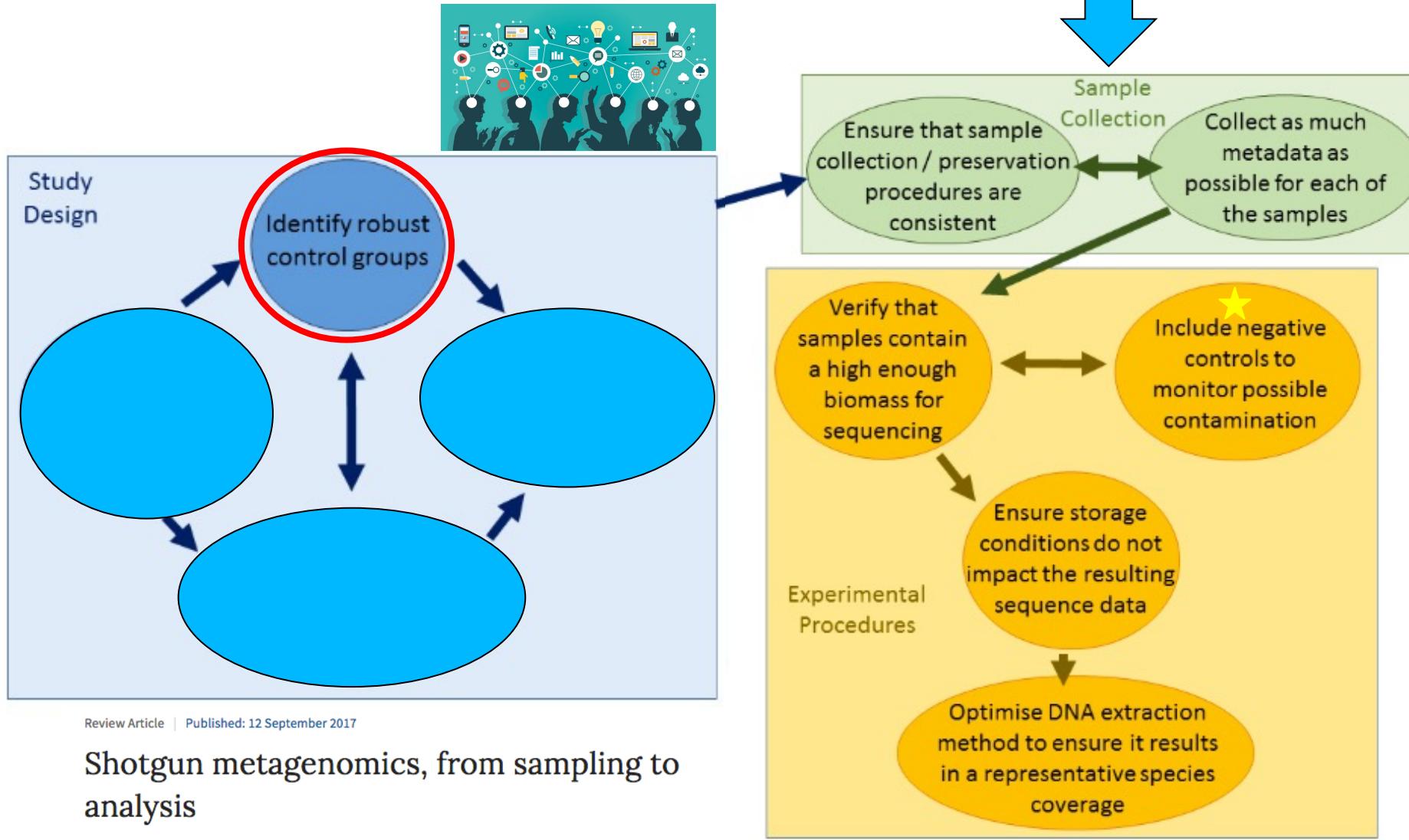
Metagenomes can also be subject to gene prediction and functional annotation, which can be used to characterize the biological functions associated with the community and identify novel genes. The results of these various analyses can be compared to those obtained through analysis of other metagenomes to quantify the similarity between communities, determine how community diversity scales with environmental covariates (i.e., community metadata), and identify taxa and functions that stratify communities of various types (i.e., biomarker detection).

Metagenomica y su “resolución biológica” [dependiente de la cobertura de secuencias]



Metagenómica (análisis e interpretación)

- Muchos estudios metagenómicos están dirigidos por el descubrimiento y “data mining” mas que por hipótesis.
- Estos estudios buscan correlaciones estadísticamente significativas entre datos metagenómicos y los metadatos asociados a un hábitat, lo cual puede llevar a significantes descubrimientos biológicos.
- La naturaleza incompleta y fragmentada de los datos metagenómicos es un reto para identificar genes.
- La medición de la diversidad es relevante para interpretar los resultados:
 - alpha – diversidad: es la biodiversidad en un hábitat definido o ecosistema.
 - beta – diversidad: compara diversidad de especies entre hábitats.
 - gamma – diversidad: es el total sobre una amplia región que contiene varios ecosistemas.



Review Article | Published: 12 September 2017

Shotgun metagenomics, from sampling to analysis

Christopher Quince, Alan W Walker, Jared T Simpson, Nicholas J Loman & Nicola Segata

Nature Biotechnology 35, 833–844 (2017) | Download Citation

- Gram (+) vs Gram(-)
- “La mano” tecnica...

Metagenómica (la importancia de los METAdatos)

- Los metadatos son tan importantes como las secuencias, son el “data about the data”:
 - Donde fueron tomadas las muestras
 - Cuando y bajo que condiciones
- En ecología microbiana las condiciones se refieren a: características físicas, químicas y otras medioambientales de la locación de las muestras.
- Por ejemplo, un metadato de una muestra de océano incluirá: fecha, hora, salinidad, intensidad de la luz, coordenadas geográficas, pH, gases solubles, etc...
- En microbiología clínica, los metadatos se refieren a la patología, historia clínica, signos vitales del paciente, localización exacta del tejido a partir del cual se tomo la muestra y las condiciones de muestreo.

Metagenómica aplicada

Meadow et al. *Microbiome* 2014, 2:7
<http://www.microbiomejournal.com/content/2/1/7>



RESEARCH

Open Access

Bacterial communities on classroom surfaces vary with human contact

James F Meadow^{1*}, Adam E Alrichter¹, Steven W Kembel^{1,2}, Maxwell Moriama^{1,3}, Timothy K O'Connor^{1,4}, Ann M Womack¹, G Z Brown^{1,3}, Jessica L Green^{1,5} and Brendan J M Bohannan¹

Data Article

Molecular investigation of bacterial communities: Data from two frequently used surfaces in the São Paulo Institute of Tropical Medicine

Tairacan Augusto Pereira da Fonseca^a, Rodrigo Pessôa^a,
Sabri Saeed Sanabani^{a,b,*}



Mapping microbial ecosystems and spoilage-gene flow in breweries highlights patterns of contamination and resistance

Nicholas A Bokulich^{1,2,3†}, Jordyn Bergsveinson⁴, Barry Ziola⁴, David A Mills^{1,2,3*}

OPEN ACCESS Freely available online



Monitoring Seasonal Changes in Winery-Resident Microbiota

Nicholas A. Bokulich^{1,2,3}, Moe Ohta^{1,2,3#}, Paul M. Richardson⁴, David A. Mills^{1,2,3*}

¹ Department of Viticulture and Enology, University of California Davis, Davis, California, United States of America, ² Department of Food Science and Technology, University of California Davis, Davis, California, United States of America, ³ Foods for Health Institute, University of California Davis, Davis, California, United States of America, ⁴ MicroTrek Inc., San Francisco, California, United States of America



Facility-Specific “House” Microbiome Drives Microbial Landscapes of Artisan Cheesemaking Plants

Nicholas A. Bokulich, David A. Mills

Department of Viticulture and Enology, Department of Food Science and Technology, and Foods for Health Institute, University of California, Davis, California, USA



Contents lists available at ScienceDirect

International Journal of Food Microbiology

journal homepage: www.elsevier.com/locate/ijfoodmicro



Bacterial biogeographical patterns in a cooking center for hospital foodservice

Giuseppina Stellato, Antonietta La Storia, Teresa Cirillo, Danilo Ercolini *

Division of Microbiology, Department of Agricultural Sciences, University of Naples Federico II, Portici, Italy



mSphere®

RESEARCH ARTICLE
Applied and Environmental Science



Microbial Community Patterns Associated with Automated Teller Machine Keypads in New York City

Holly M. Bik,^{a,*} Julia M. Maritz,^a Albert Luong,^b Hakdong Shin,^{b,*}
Maria Gloria Dominguez-Bello,^b Jane M. Carlton^a

Center for Genomics and Systems Biology, Department of Biology, New York University, New York, New York, USA; Human Microbiome Program, New York University School of Medicine, New York, New York, USA^b



REVIEW
published: 14 July 2015
doi: 10.3389/fmicb.2015.00705

Pathogens protection against the action of disinfectants in multispecies biofilms

Pilar Sanchez-Vizcute^{1,2}, Belén Orgaz³, Stéphane Aymerich^{1,2}, Dominique Le Coq^{1,2,4} and Romain Briandet^{1,2*}

¹ INRA, UMR1319 MICALIS, Jouy-en-Josas, France, ² AgroParisTech, UMR MICALIS, Jouy-en-Josas, France, ³ Department of Nutrition, Food Science and Technology, Faculty of Veterinary, Complutense University of Madrid, Madrid, Spain, ⁴ CNRS, Jouy-en-Josas, France

Metagenómica aplicada

Trends in Biotechnology

CellPress

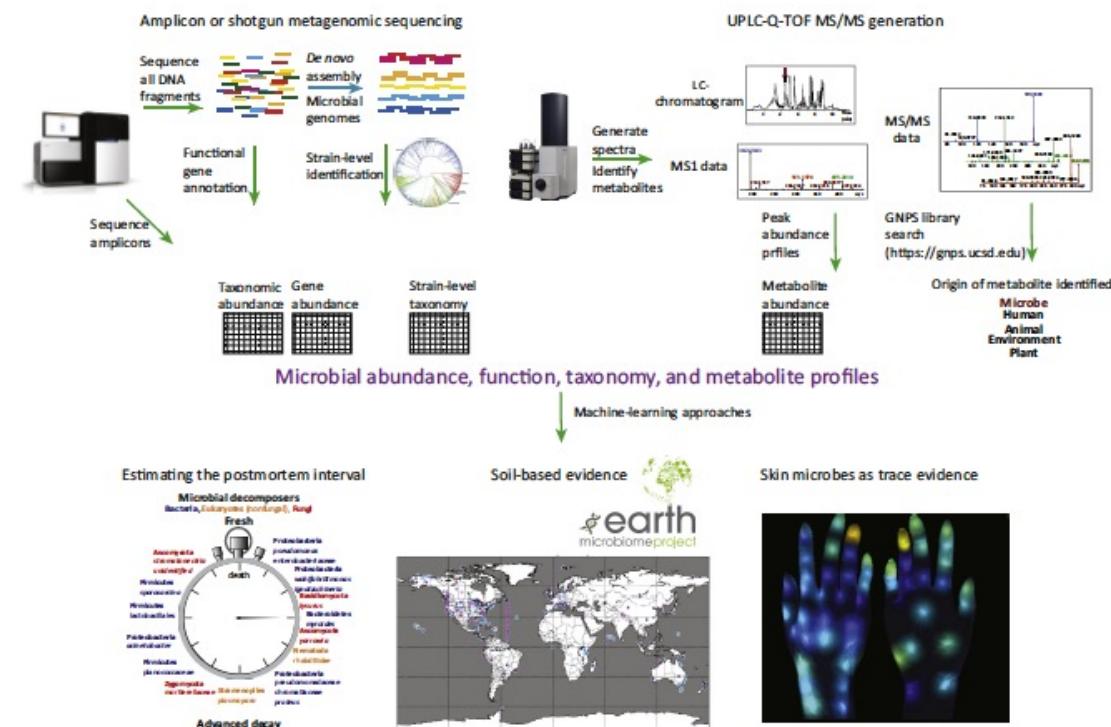
Opinion

Microbiome Tools for Forensic Science

Jessica L. Metcalf,^{1,*,@} Zhenjiang Z. Xu,² Amina Bouslimani,³
Pieter Dorrestein,^{2,3,4,5} David O. Carter,⁶ and Rob Knight^{2,5,7,@}

Key Figure

Microbiome Tools Hold Great Promise for Forensic Science



Metatranscriptómica

Introducción a la transcriptómica

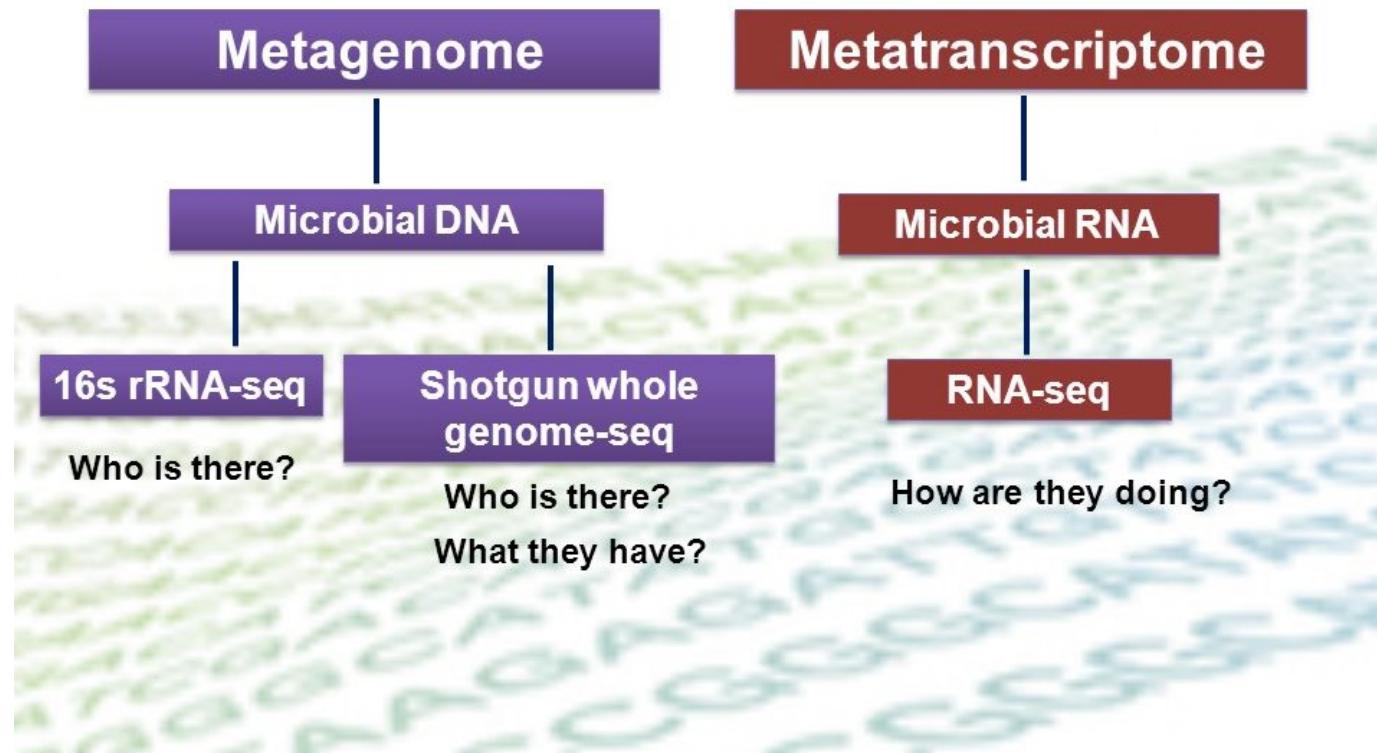
Un genoma dos transcriptomas



¿Qué información nos proporciona el transcriptoma?

- Qué genes están activos e inferir fenotipo (genómica funcional)
- El transcriptoma puede representar < 2% del genoma.
- Perfiles de co-expresión: genes expresados simultáneamente
- Permite la identificación de potenciales elementos regulatorios
- Conocimiento aplicable a estudios del desarrollo y de la respuesta al ambiente por parte de un organismo.

Metagenome/Metatranscriptome



Meta-transcriptómica

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Feb. 2011, p. 1153–1161
0099-2240/11/\$12.00 doi:10.1128/AEM.02345-10
Copyright © 2011, American Society for Microbiology. All Rights Reserved.

Vol. 77, No. 4

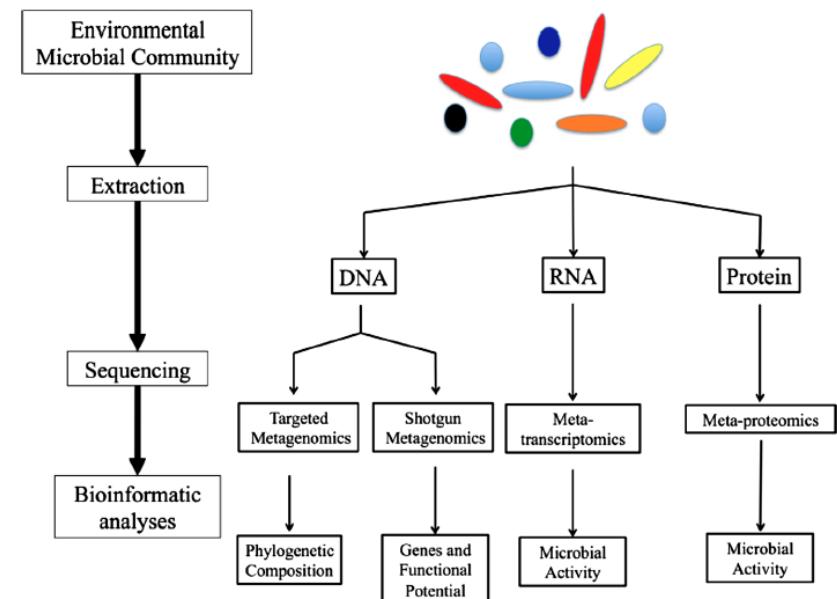
MINIREVIEW

Metagenomic Analyses: Past and Future Trends[▽]

Carola Simon¹ and Rolf Daniel^{1,2*}

Abteilung Genomische und Angewandte Mikrobiologie¹ und Göttingen Genomics Laboratory,² Institut für Mikrobiologie und Genetik,
Georg-August-Universität, Grisebachstr. 8, 37077 Göttingen, Germany

- Metagenomic DNA-based analyses cannot differentiate between expressed and nonexpressed genes, it fails to reflect the actual metabolic activity.
- In metatranscriptomics, RNA is extracted from an environmental sample. The RNA is converted into cDNA and sequenced in a similar fashion to metagenomics.
- Metatranscriptomics is the study of transcribed genes from a microbial community.





Meta-transcriptómica

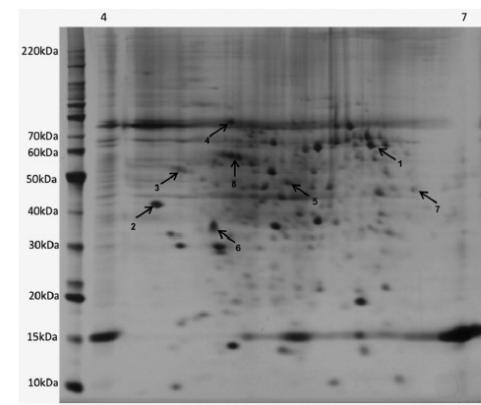
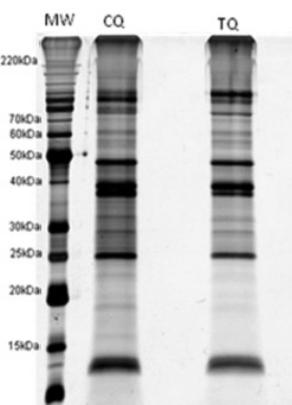
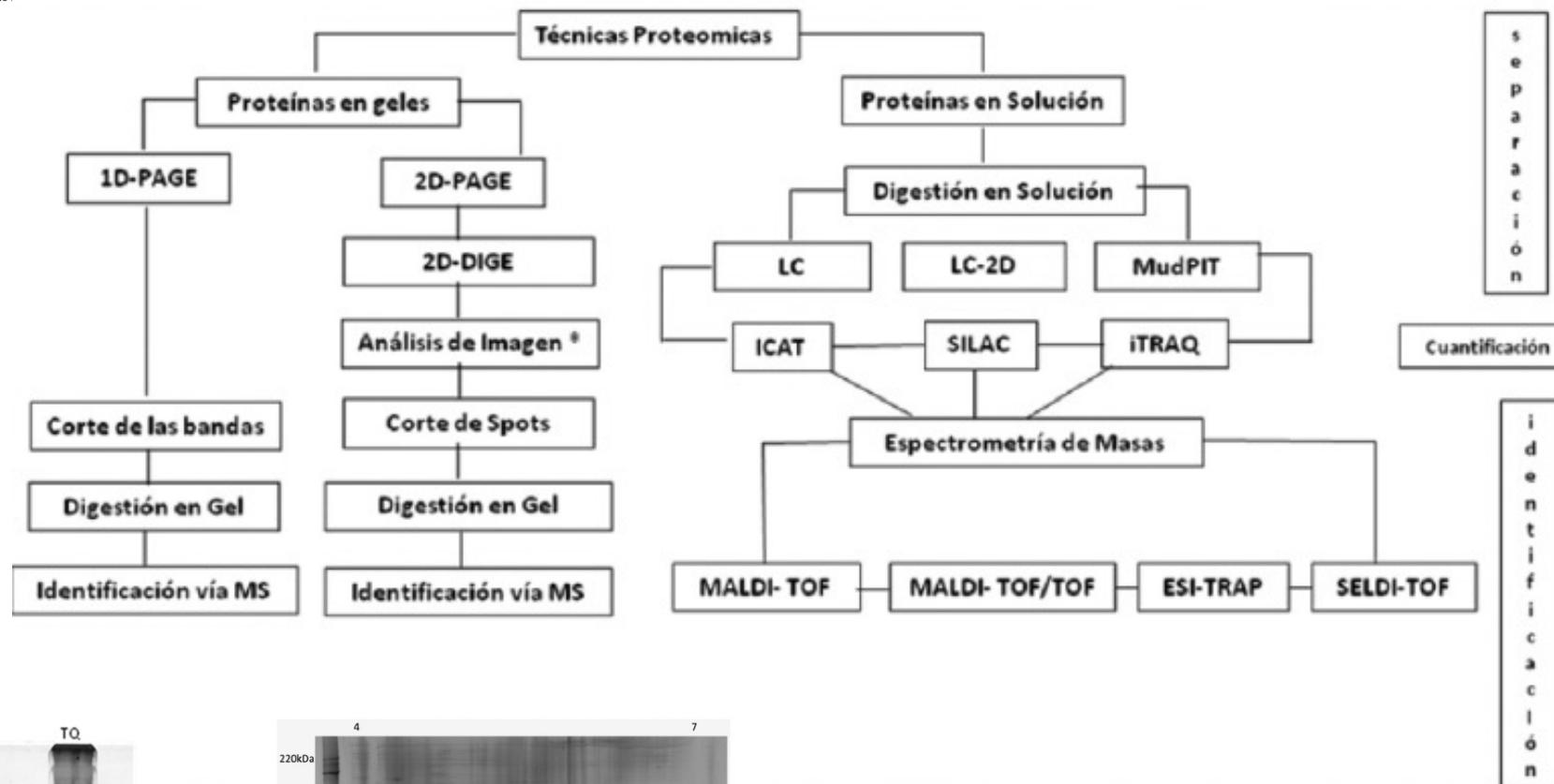
Application of meta-omics techniques to understand greenhouse gas emissions originating from ruminal metabolism

Robert J. Wallace^{1*}, Timothy J. Snelling¹, Christine A. McCartney¹, Ilma Tapio² and Francesco Strozzi³

- Hungate 1000 project (www.hungate1000.org.nz): The aim of the project is to produce a reference set of 1000 rumen microbial genome sequences from cultivated rumen bacteria and methanogenic archaea, together with representative cultures of rumen anaerobic fungi and ciliate protozoa.
- Shi et al investigated methane production in a cohort of New Zealand sheep using metagenomics and metatranscriptomic techniques that aimed at understanding microbiological differences between animals that produced low and high amounts of methane
- Three of the ten most increased transcripts in the high producers coded for enzymes in the methanogenesis pathway. The idea that the transcriptome is more responsive as a measurement of methane emissions has gained currency.

Metaproteómica

Proteómica (métodos)



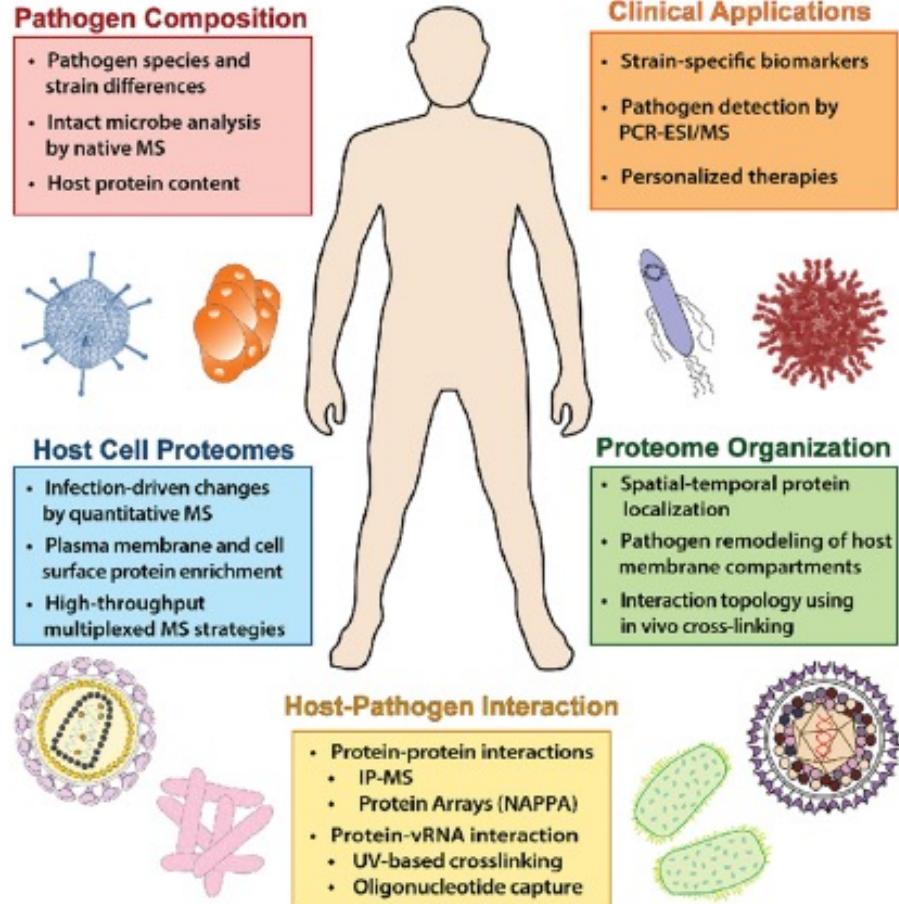
Spot	Proteína	Taxonomía	PlasmoDB/NCBIGH	n.º Péptidos ²	Puntaje Mascot ³
1	HSP60	<i>Plasmodium falciparum</i>	PF10_0153	11	77/54
2	Proteína de unión a calcio	<i>Plasmodium falciparum</i>	PF11_0098	5	143/54
3	Disulfuro isomerasa	<i>Plasmodium falciparum</i>	MAL8P1.17	11	140/54
4	HSP70	<i>Plasmodium falciparum</i>	PF10875w	23	1040/54
5	Disulfuro isomerasa	<i>Plasmodium falciparum</i>	MAL8P1.17	29	759/54
6	Peroxiredoxina	<i>Plasmodium falciparum</i>	PF10_0268	8	68/54
7	Enolasa	<i>Plasmodium falciparum</i>	PF10_0155	22	874/54
8	Espectrina cadena alfa	<i>Homo sapiens</i>	gi 115298659	43	470/83

Proteomics Tracing the Footsteps of Infectious Disease*

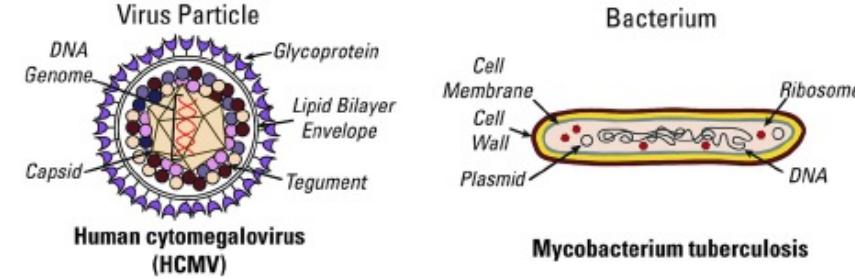
Todd M. Greco‡ and Ileana M. Cristea‡§

Proteómica (aplicaciones)

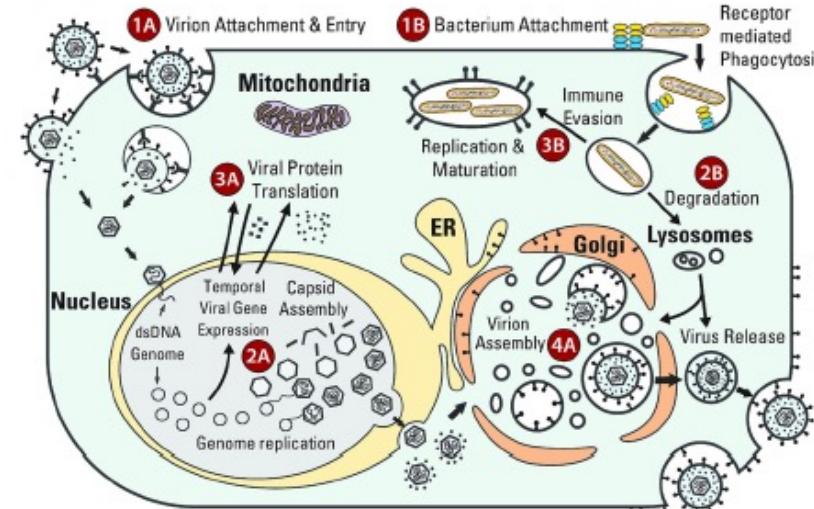
PROTEOMICS & INFECTIOUS DISEASES



A Structural Features of Representative Pathogens



B Pathogen Infection of a Host Cell





Paul Wilmes¹, Anna Heintz-Buschart¹ and Philip L. Bond^{2*}

¹ Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg

² Advanced Water Management Centre, University of Queensland, Brisbane, Australia

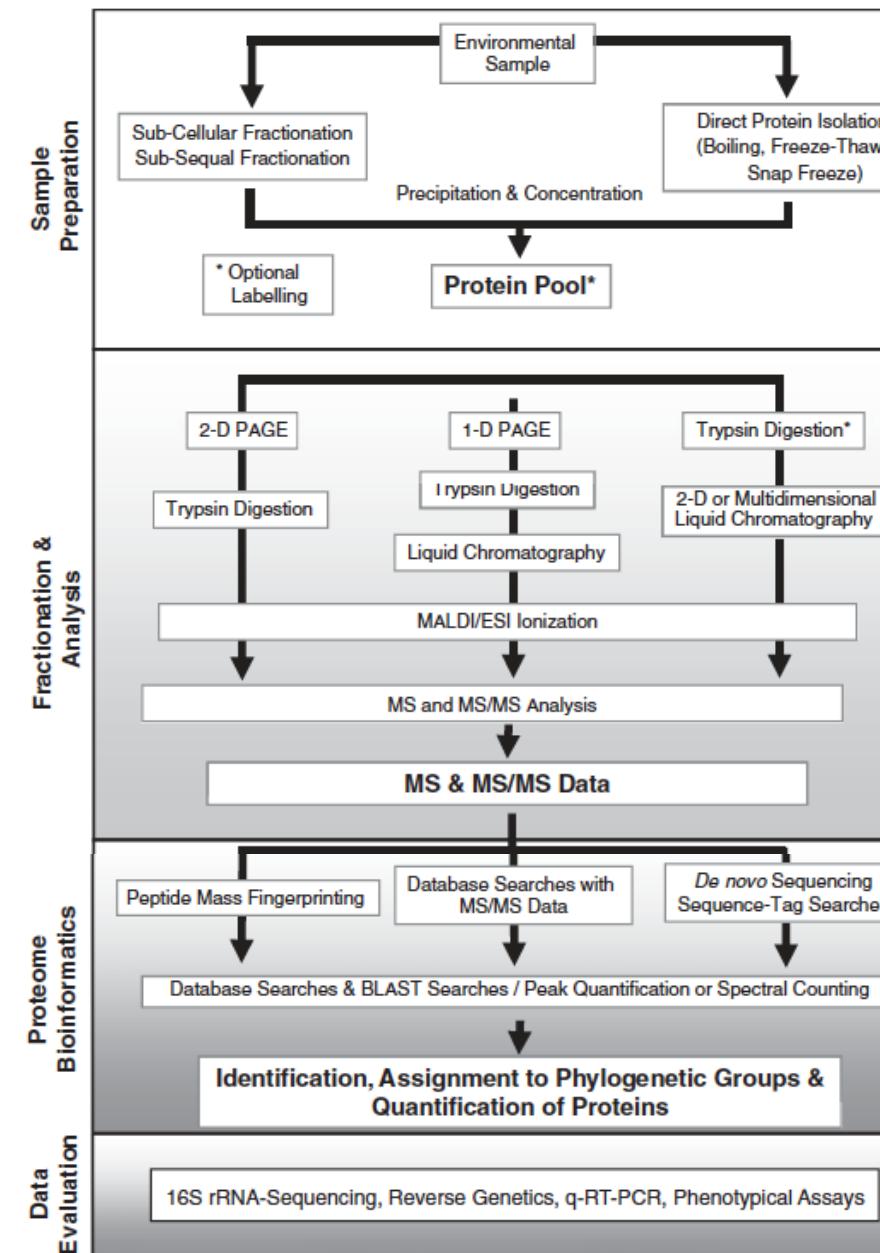
Objetivos general de la metaproteómica

- We originally defined metaproteomics as “the large-scale characterization of the entire protein complement of environmental microbiota at a given point in time”.
- Metaproteomics offers the ability to resolve the major catalytic units of microbial populations and thereby allows the establishment of genotype-phenotype linkages from *in situ* samples.
- Metagenomics and metatranscriptomics, to allow metaproteomics to fulfil its keystone role in microbial systems ecology in the future.

Environmental proteomics: Analysis of structure and function of microbial communities

Thomas Schneider and Kathrin Riedel

Metaproteómica (flujo de trabajo)



Metaproteómica (aplicaciones)

Table 1. Estimated microbial species and protein richness as well as numbers and examples of proteins identified

Ecosystem	Estimated number of taxa ^{a)}	Estimated number of unique proteins ^{b)}	Number of identified proteins ^{c)}	Examples of signature proteins and potential biomarkers
Acid mine drainage biofilm	159 [25]	477 000	4259 [22]	Specific cytochromes involved in iron oxidation [2, 15].
Activated sludge	1000 [73]	3 000 000	5000 [69]	Proteins constituting exopolymeric substances [12–14]
Ocean water	160 [74]	480 000	5600 [28]	Proteorhodopsins [30, 31], transport proteins [30, 31]
Surface freshwater	20 000 [75]	60 000 000	1800 [37]	N and P cycling [41], anthropogenic contaminant degradation [45]
Soil	50 000 [76]–8 000 000 [50]	150 000 000–24 000 000 000	7000 [56]	Saprophytic enzymes [53, 54], Nif proteins [55], methane monooxygenase [55]
<i>Human-associated</i>				
Saliva	>5400 [77]	16 200 000	>2000 [78]	Glycoproteinolytic enzymes [78]
Feces	>21 000 [77]	>63 000 000	>2900 [62]	Carbohydrate active enzymes [62]

a) As defined by author(s) of referenced work.

b) Estimated number of unique proteins based on average environmental microbial genome size of 3 Mbp and 1 kbp of sequence coding for one gene. Uniqueness does not include strain-level variation. Numbers do not reflect intra- and intertaxon protein abundance differences.

c) As defined by author(s) of referenced work.

Enhancing metaproteomics—The value of models and defined environmental microbial systems

Florian-Alexander Herbst¹, Vanessa Lünsmann^{2,3}, Henrik Kjeldal¹, Nico Jehmlich², Andreas Tholey⁴, Martin von Bergen^{1,2}, Jeppe Lund Nielsen¹, Robert L. Hettich⁵, Jana Seifert⁶ and Per Halkjær Nielsen¹

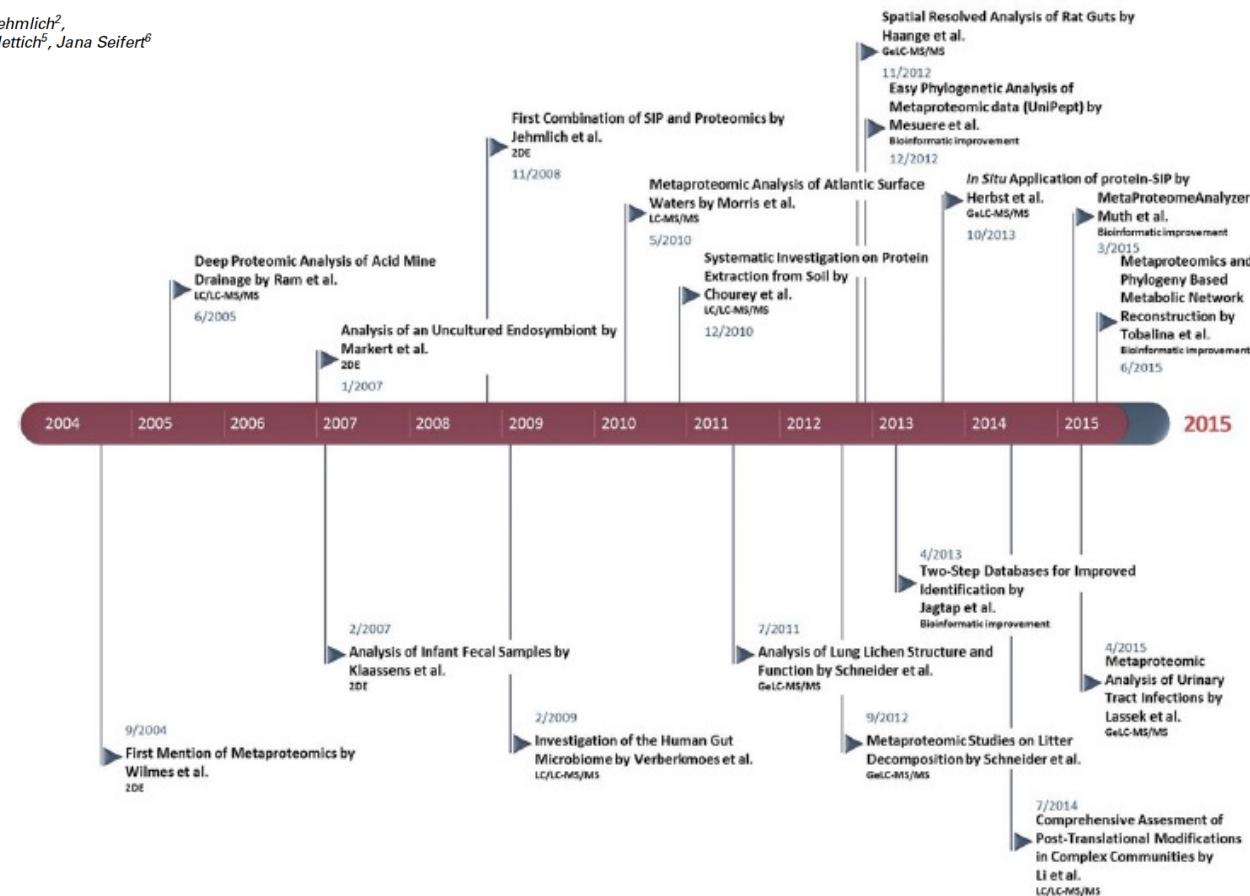


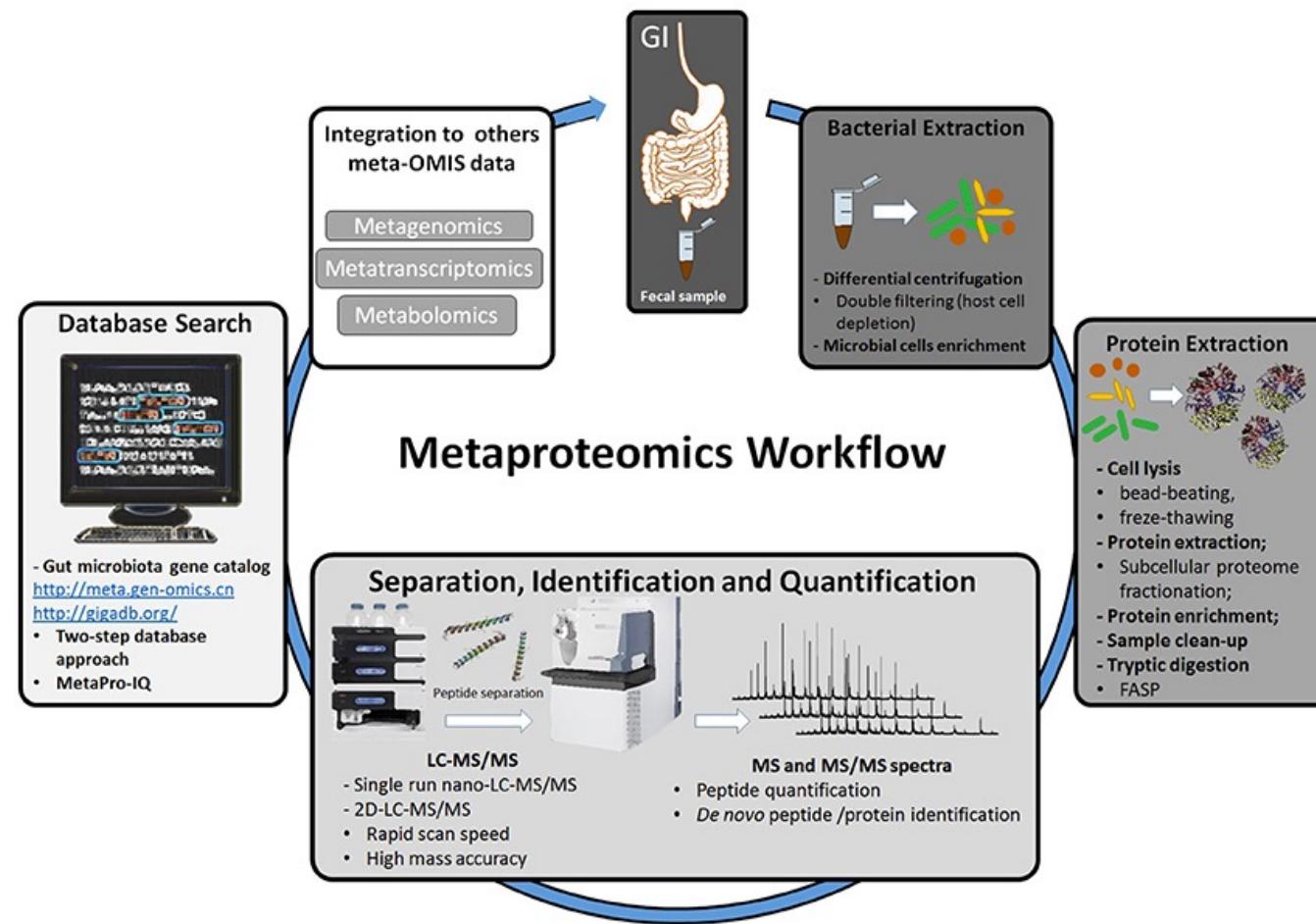
Figure 1. Limited selection of exemplary articles in Metaproteomics: Wilmes et al. [1], Ram et al. [15], Markert et al. [16], Klaassens et al. [17], Jehmlich et al. [24], Verberkmoes et al. [12], Morris et al. [8], Chourey et al. [25], Schneider et al. [26], Schneider et al. [19], Haange et al. [18], Mesuere et al. [22], Jagtap et al. [27], Herbst et al. [28], Li et al. [29], Muth et al. [21], Lassek et al. [20], Tobalina et al. [23].

First metaproteomic studies were conducted using primarily 2DE strategies and commonly identified very few (<50) proteins. The advantage of comprehensive (LC)/LC-MS/MS techniques for metaproteomics soon became apparent and enabled the identification of up to 2000 or even 4000 proteins.

Metaproteomics as a Complementary Approach to Gut Microbiota in Health and Disease

Bernardo A. Petriz^{1*} and Octávio L. Franco²

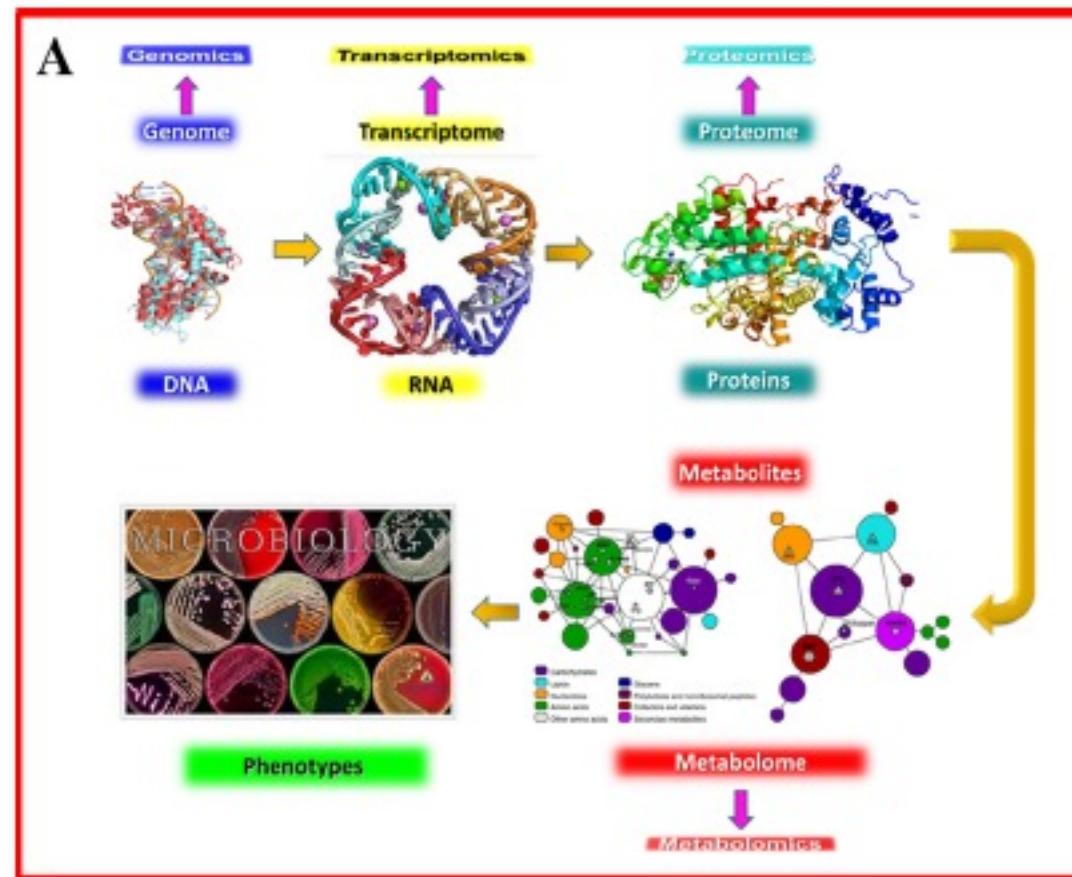
Metaproteómica (intestino humano)



Metaproteómica (retos – identificación de proteínas)

- Several challenges hold back protein identification, which greatly depends on the database design, capacity and quality influencing the resulting peptide sequence matches.
- The confidence of protein assignments to taxa is limited by the species present in the database, and functional assignments are often therefore more robust than taxonomic assignments of proteins.
- Another approach is to combine metagenomic with metaproteomic analysis, thus providing an enhanced means to reconstruct the microbial processes of a community.

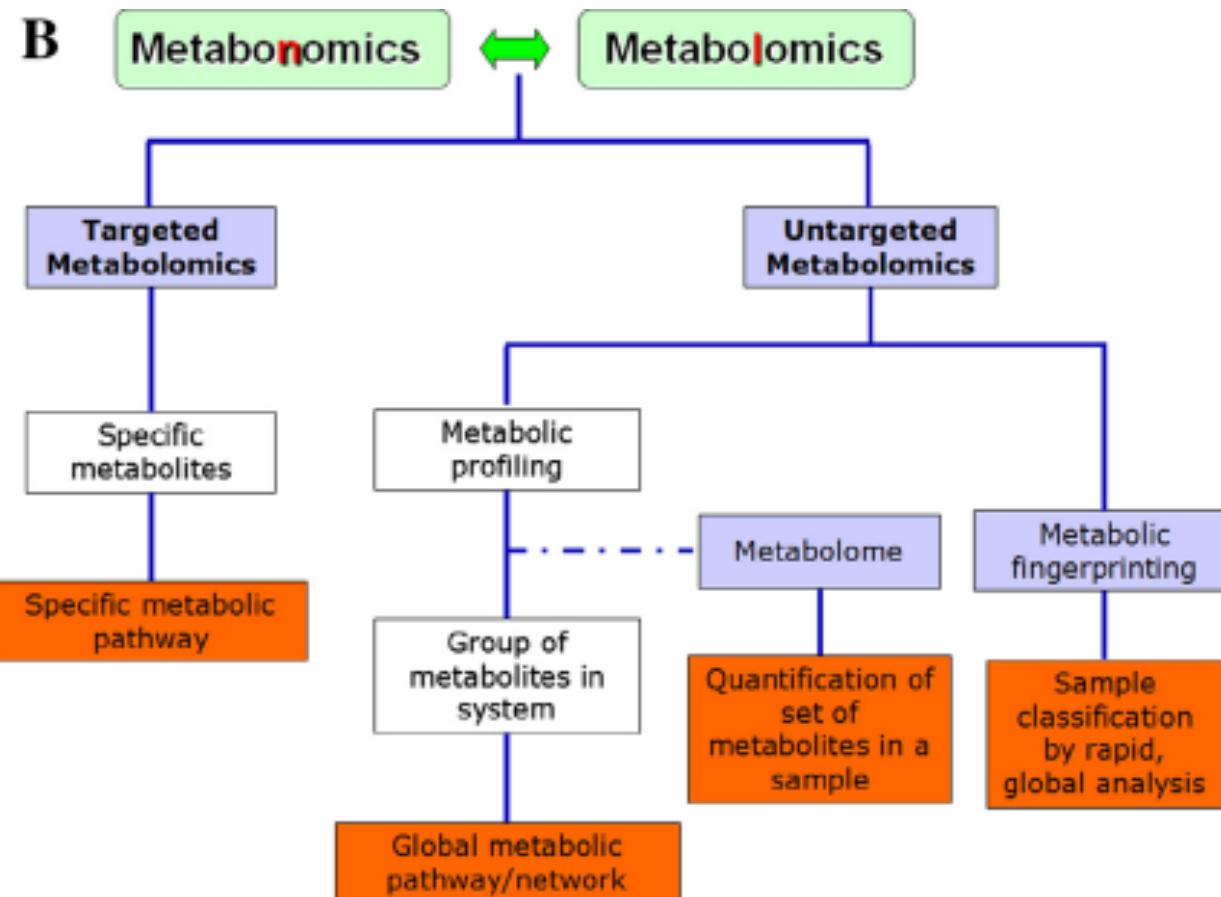
Metabolómica



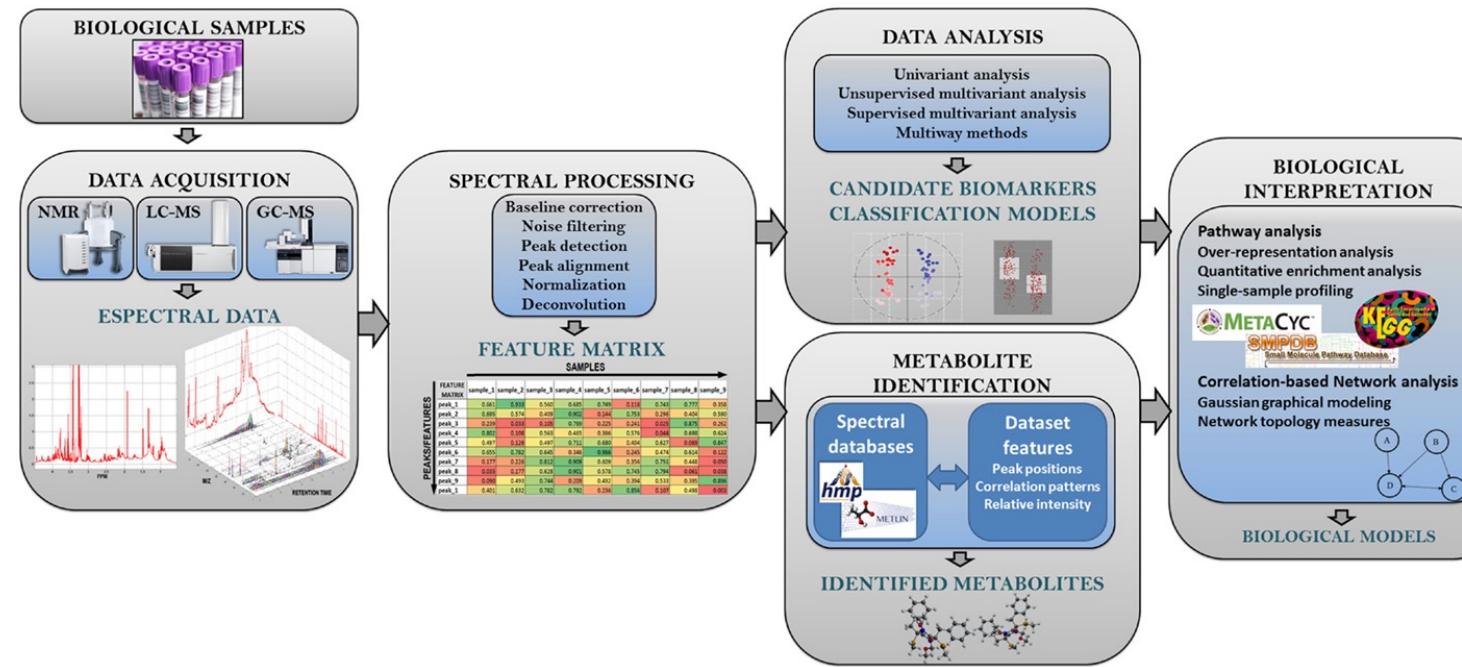
Metabolómica (definición)

- La metabolómica es el “estudio sistemático de las huellas únicas que dejan los procesos celulares específicos en su paso”, es decir, el estudio del perfil de los metabolitos (intermediarios, secundarios, hormonas y otras moléculas de señalización).
- Los metabolitos pueden revelar una patología o un estadio celular específico. Complementando con la medición simultánea y cuantitativa de transcriptos y proteínas.
- En la medicina tradicional china (1500 – 2000 ADC) los médicos usaban hormigas para la evaluación de la orina de pacientes para detectar si contenía altos niveles de glucosa como indicador para la diabetes.

Metabolómica (terminología)



Metabolómica (técnicas)



- **Métodos de separación:** cromatografía de gases (GC), cromatografía líquida (LC), electroforesis capilar (EC).
- **Métodos de detección:** espectrometría de masas (MS), espectroscopía de resonancia magnética nuclear (NMR).

Metabolómica (aplicaciones)

- Los metabolitos producidos por las bacterias intestinales son accesibles por las células del hospedero y de esta manera influencia procesos fisiológicos tanto en el intestino como sistémicos.
- Analizar la actividad de la microbiota mas que su composición y estructura.
- Metabolitos como marcadores de la salud mejorada o reducida del intestino.

Metabolómica (aplicaciones)

Table 1. List of bacterial metabolites that may be found in the intestine

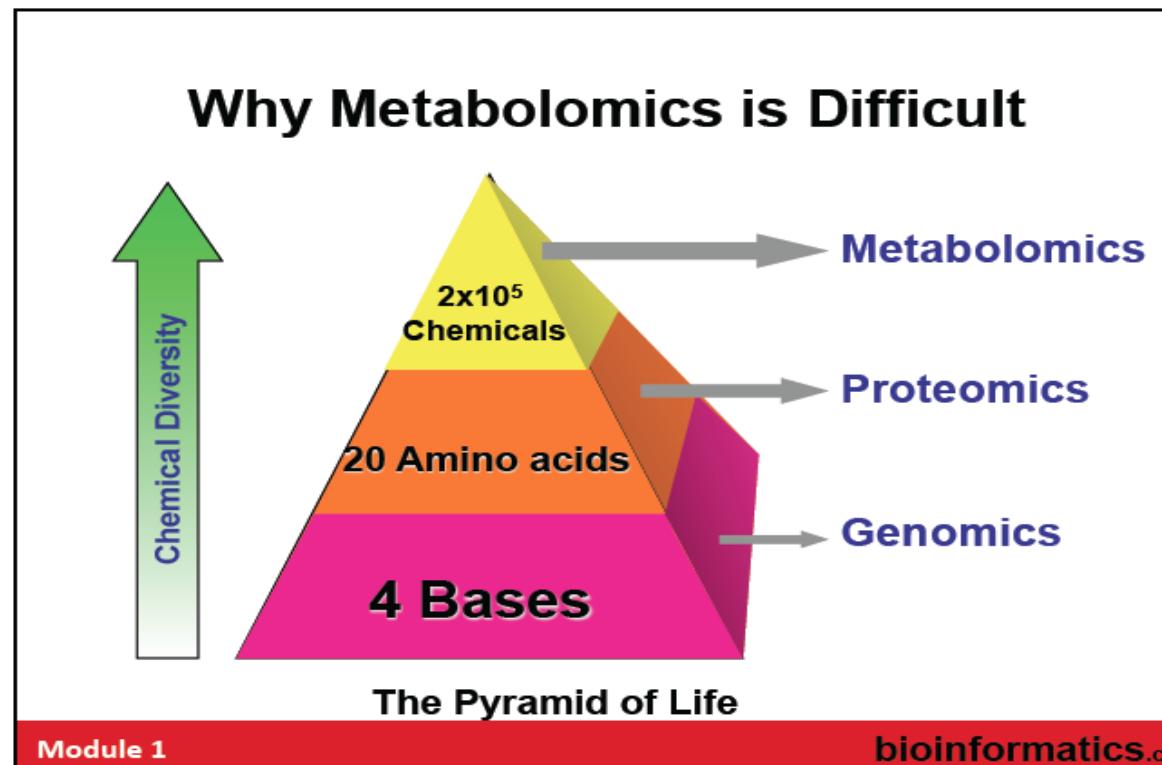
Type of metabolite	Metabolites
Metabolites derived from bacterial energy metabolism	'Terminal' metabolites from carbohydrate fermentation SCFA: formate, acetate, propionate, butyrate, longer-chain fatty acids Branched-chain fatty acids 'Intermediate' metabolites from carbohydrate fermentation Partially degraded oligomeric carbohydrates (disaccharides, oligosaccharides, complex proteoglycans from mucins, etc.) Alcohols: methanol, ethanol, etc. Gaseous metabolites Fermentation gases: hydrogen, methane, carbon dioxide Highly volatile compounds: hydrogen sulfide
Metabolites derived from bioconversion of plant secondary compounds	Metabolites of fatty acid and lipid bioconversion Long-chain aldehydes Fatty acids Metabolites from protein fermentation Branched-chain fatty acids Ammonia and amines Aromatic derivatives of amino acids: phenols, cresols, indoles, etc.
Metabolites from bacterial cytosolic compartment or secondary metabolism (spilled over by excess production, efflux or upon cell lysis)	Products of lignin/polyphenols bioconversion: equol, enterolactone, etc. Vitamins and cofactors (often in very small concentrations) Peptides (quorum-sensing signals of Gram-positive bacteria) Homoserine lactone (quorum-sensing signals of Gram-negative bacteria) Nucleic acids (free DNA, microRNA, etc.) Bacteriocins
Metabolites of the enterohepatic circulation	Bile acids Cholesterol, coprostanol Hormones and derivatives Glucuronide conjugates
Enzymes	Reductases Glucuronidases Glycohydrolases
Bacterial cell wall components I (of which several are immunoactive)	Lipopolysaccharide Polysaccharide A Peptidoglycan-derived structures Capsular polysaccharides (glycocalix)

Environmental metabolomics: a critical review and future perspectives

Jacob G. Bundy · Matthew P. Davey ·
Mark R. Viant

Metabolómica ambiental

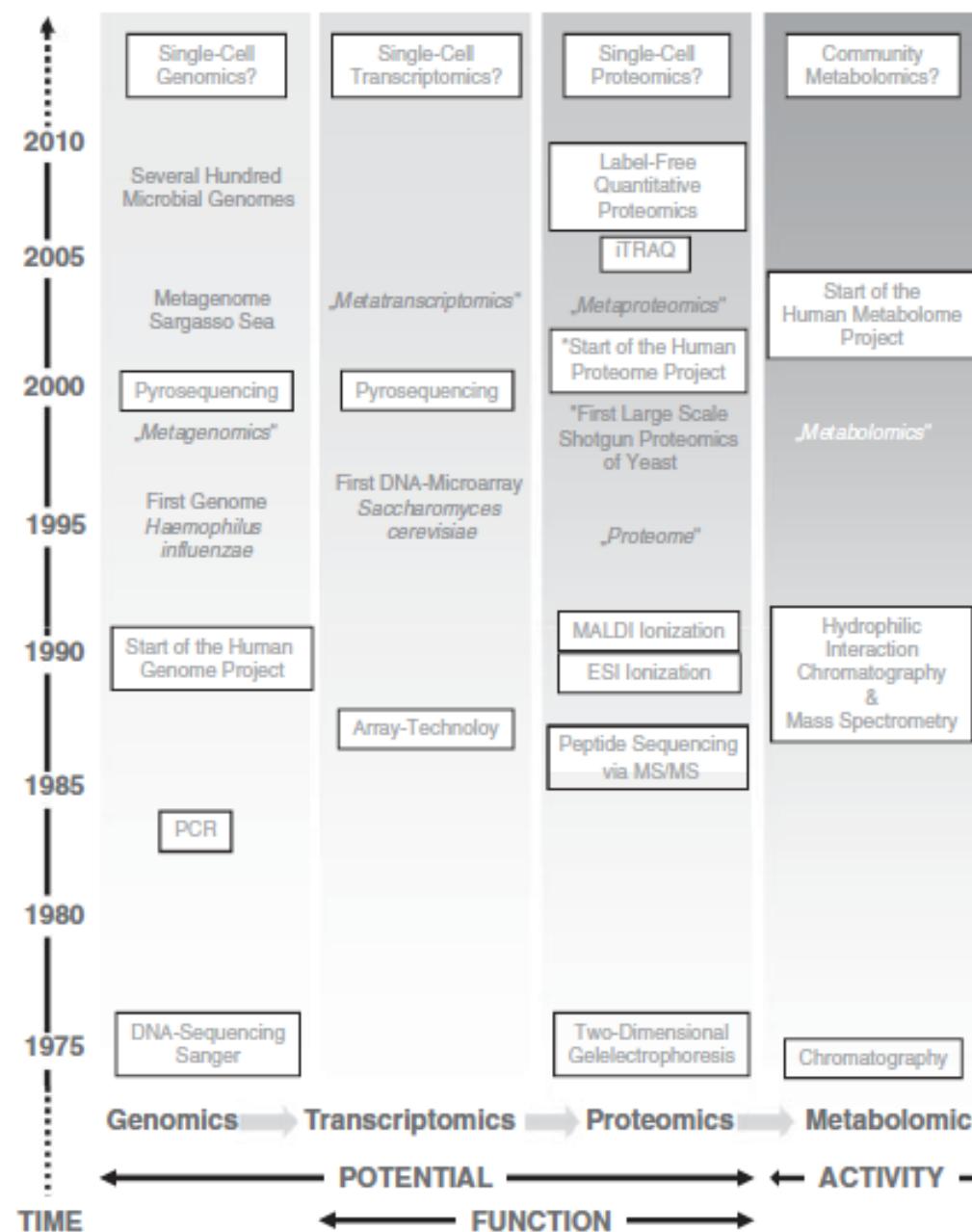
- Es la aplicación de la metabolómica para caracterizar las interacciones de los organismos con su ambiente. Tiene ventajas para estudiar las interacciones organismo-medio, para evaluar salud y función del organismo a nivel molecular.



Environmental proteomics: Analysis of structure and function of microbial communities

Thomas Schneider and Kathrin Riedel

Omicas y meta-omicas (resumen)



“Network medicine” y microbioma

Network medicine



The NEW ENGLAND JOURNAL of MEDICINE

HOME | ARTICLES & MULTIMEDIA | ISSUES | SPECIALTIES & TOPICS | FOR AUTHORS

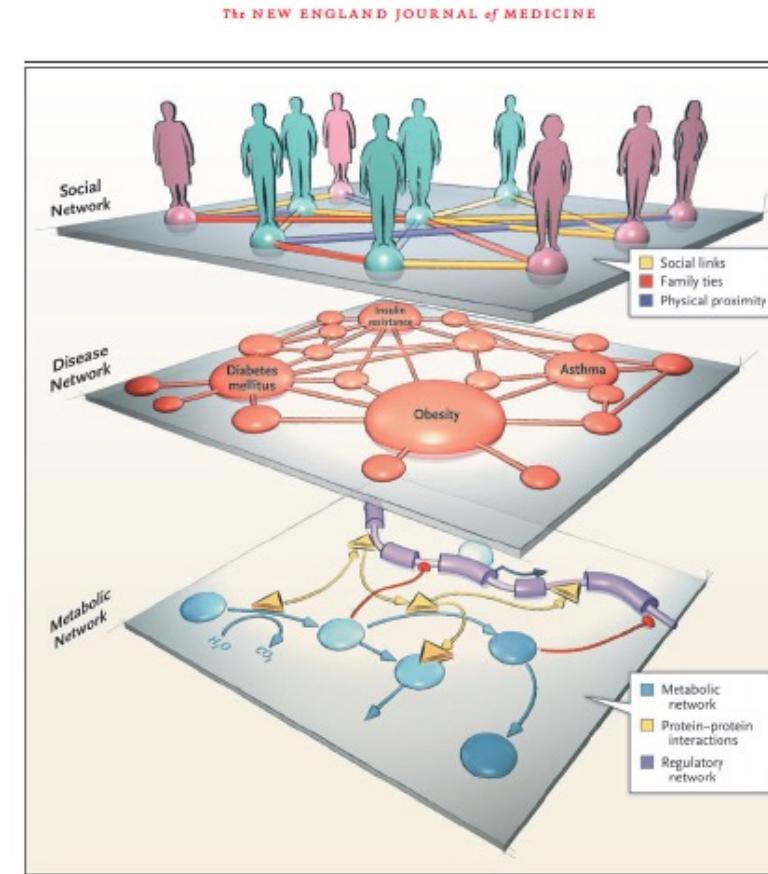
EDITORIAL

Network Medicine — From Obesity to the “Diseasome”

Albert-László Barabási, Ph.D.

N Engl J Med 2007; 357:404-407 | July 26, 2007 | DOI: 10.1056/NEJMMe078114

“To understand various disease mechanisms, it is not sufficient to know the precise list of “disease genes”; instead, we should try to map out the detailed wiring diagram of the various cellular components that are influenced by these genes and gene products”.



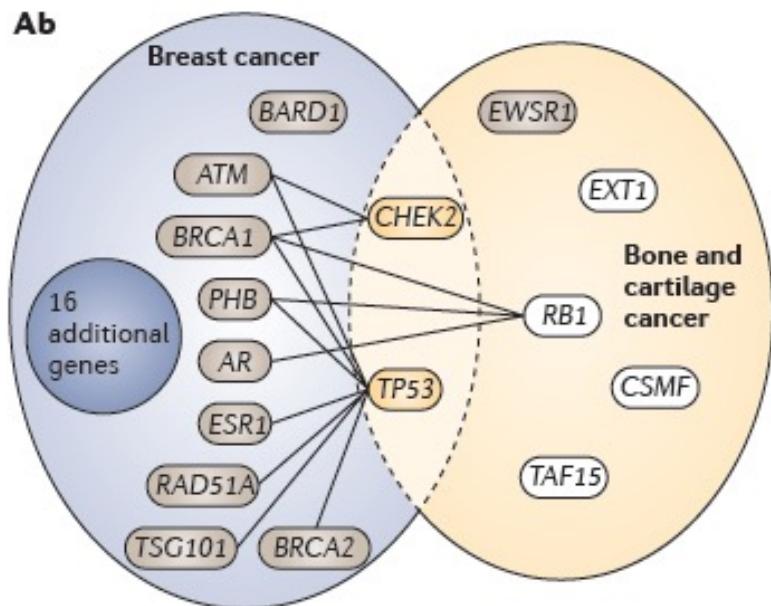
Network medicine

REVIEWS

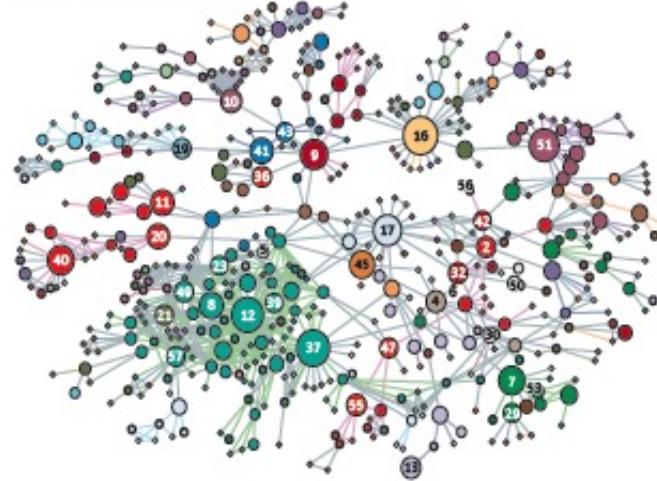
Network medicine: a network-based approach to human disease

Albert-László Barabási^{*+§}, Natali Gulbahce^{*+||} and Joseph Loscalzo[§]

56 | JANUARY 2011 | VOLUME 12



Aa Human disease network



- | | | |
|---------------------------|--------------------------|---------------------------------------|
| ① Aldosteronism | ② Epilepsy | ⑪ Myocardial infarction |
| ② Alzheimer's disease | ③ Fanconi's anaemia | ⑫ Myopathy |
| ③ Anaemia, congenital | ④ Fatty liver | ⑬ Nucleoside phosphorylase deficiency |
| dyserythropoietic | ⑤ Gastric cancer | ⑭ Obesity |
| ④ Asthma | ⑥ Gilbert's syndrome | ⑮ Paraganglioma |
| ⑤ Ataxia-telangiectasia | ⑦ Glaucoma 1A | ⑯ Parkinson's disease |
| ⑥ Atherosclerosis | ⑧ Goltire congenital | ⑰ Pheochromocytoma |
| ⑦ Blood group | ⑨ HARP syndrome | ⑱ Prostate cancer |
| ⑧ Breast cancer | ⑩ HELLP syndrome | ⑲ Pseudohypoaldosteronism |
| ⑨ Cardiomyopathy | ⑪ Haemolytic anaemia | ⑳ Retinitis pigmentosa |
| ⑩ Cataract | ⑫ Hirschsprung disease | ㉑ Schizoaffective disorder |
| ⑪ Charcot-Marie-Tooth | ⑬ Hyperbilirubinaemia | ㉒ Spherocytosis |
| disease | ⑭ Hypertension | ㉓ Spina bifida |
| ⑫ Colon cancer | ⑮ Hypertension diastolic | ㉔ Spinocerebellar atrophy |
| ⑬ Complement component | ⑯ Hyperthyroidism | ㉕ Stroke |
| deficiency | ⑰ Hypoadrenalinism | ㉖ Thyroid carcinoma |
| ⑭ Coronary artery disease | ⑱ Leigh syndrome | ㉗ Total lipoide organization |
| ⑮ Coronary spasm | ⑲ Leukaemia | ㉘ defect |
| ⑯ Deafness | ⑳ Low renin hypertension | ㉙ Trifunctional protein deficiency |
| ⑰ Diabetes mellitus | ㉁ Lymphoma | ㉚ Unipolar depression |
| ⑱ Endopeptidase | ㉂ Mental retardation | |
| ⑲ Epidermolysis bullosa | ㉃ Muscular dystrophy | |

COMMENT

Open Access



The microbiome in precision medicine: the way forward

Joseph F. Petrosino

Editorial summary

Novel associations between the human microbiome and health and disease are routinely emerging, and important host-microbiome interactions are targets for new diagnostics and therapeutics. Understanding how broadly host-microbe associations are maintained across populations is revealing individualized host-microbiome phenotypes that can be integrated with other 'omics' data sets to enhance precision medicine.

