Expanded View Figures

Figure EV1. Quantitative description of the PPI network by resource.

- A Number of nodes and interactions. The light dots represent the shared nodes and edges (in more than one resource), while the dark ones show their total numbers.
- B Causality: number of connections by direction and effect sign.
- C Coverage of the networks on various groups of proteins. Dots show the percentage of proteins covered by network resources for the following groups: cancer driver genes from COSMIC and IntoGen, kinases from kinase.com, phosphatases from Phosphatome.net, receptors from the Human Plasma Membrane Receptome (HPMR) and transcription factors from the TF census. Gray bars show the number of proteins in the networks.



Figure EV1.



Figure EV2. Quantitative description of the transcriptional network by resource.

A-C Panels and notations are the same as on Fig EV1.

Annotations in OmniPath												
miuk	IS	lines with the same `record_id`										
http://omni	pathdb.org/a	notations?proteins=MTOR / belong to the same piece of data										
uniprot gonos	(mbol course											
P42345 MTOR P42345 MTOR P42345 MTOR	kinase.com kinase.com	group Atypical 94an atypical PIKK family										
P42345 MTOR	kinase.com	subfamily FRAP 94 FRAP Subfamily kinase										
P42345 MTOR	HPA organ	kidney 1204876										
P42345 MTOR	HPA tissue	cells in tubules 1204876 according to kinase.com										
P42345 MTOR	HPA Level	Medium 12048/6										
P42345 MTOR	HPA progra	expressed at a medium level in										
P42345 MTOR	HPA favour	hele False 1204876										
P42345 MTOR	HPA pathol	bay False 1204876 Kidney Lubule cells according to										
P42345 MTOR	DGIdb catego	SERINE THREONINE KINASE 4549 Human Protein Atlas										
P42345 MTOR	DGIdb catego	TY TRANSCRIPTION FACTOR BINDING HUMANIAN TOLENT ALLAS										
P42345 MTOR	DGIdb catego	ry PHOSPHATIDYLINOSITOL 3 KINASE 4551										
P42345 MTOR	DGIdb catego	ry TUMOR SUPPRESSOR 4552 clinically actionable										
P42345 MTOR	DGIdb catego	ry KINASE 4553										
P42345 MTOR	DGIdb catego	blue seale genome 4554 according to DGldb										
P42345 MTOR	DGIdb catego	TY UNA REPAIR 4555										
P42345 MTOR	Cignor pathys	AMI DCDADI 212										
P42345 MTOR	Signor pathwa	(MILEDURADE 515)										
P42345 MTOR	Signor pathwa	AMILETET 315part of the Insulin Receptor pathway										
P42345 MTOR	Signor pathwa	Insulin Recentor 316 according to SICNOD										
P42345 MTOR	Signor pathwa	ATOR Signaling 317										
P42345 MTOR	Signor pathwa	/ AML miRNA 318										
parame	eters: bit.ly/2r	n2U4Lt ● examples: bit.ly/2ku19nN ● in pypath: bit.ly/2k4lA9F										

Figure EV3. Example of the annotations query in the OmniPath web service.

For the protein mTOR a large variety of information is available from different databases. The "record_id" binds together the fields of the record from the original resource. Each field has a "label" and a "value".

Inter-cellular signaling roles in OmniPath

Interleukin-6 and Cadherin-1

http://omnipathdb.org/intercell?proteins=IL6.CDH1														
gene:	category	parent	database	scope	aspect	source	transm	ireceive	rsecret	edom tra	nsmom peri			
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CDH1	basolateral cell me	nlasma membrane		Innonic	Incotional	TESOUCCE SI	uer False	nom	LUI			UVV L	παι συι	11
CDH1	plasma membrane tra	plasma membrane	tMenbranone	Seneric	locational	resource si	Dec.Fatse	• False	filse	True	False F			
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CDH1	adhesion	adhesion	HGNC	generic	functional	resource_s	pec:True	while	ъ НС	NC a	eave it i	ie a t	vno1 co	adhorin
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IL6	ligand	ligand	iTALK	generi	ICNIC	CallD	annal		a ble	thor	dotabo	000		
IL6	cytokine	ligand	iTALK	specifi	IGING.	Cellel	Ioner	JD al	10.0	uiei	ualava	ses		
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Figure EV4. Example of the intercell query in the OmniPath web service.

Each category has a parent category and a database of origin. The scope of a category is either "generic" (e.g., ligand) or "specific" (e.g., interleukin). The aspect is either "locational" or "functional". Further attributes show whether the protein is a signal transmitter or a receiver, and whether it is secreted, or a transmembrane or peripheral protein of the plasma membrane.



Figure EV5. OmniPath-based NicheNet analysis to predict over-expressed ligands in SARS-CoV-2 infection potentially affecting the expression of inflammatory response related genes in Calu3 cells.

- A Most significantly enriched gene sets after SARS-CoV-2 infection on the Calu3 cell line. Inflammatory response is highlighted in red.
- B Results of NicheNet's ligand activity analysis: Number of over-expressed ligands after SARS-CoV-2 infection and their potential to predict the inflammatory response gene set based on the Pearson correlation coefficient. The top 12 ranked ligands, out of a total of 117 over-expressed ligands, were selected.
- C Regulatory potential of the top ranked ligands and target genes from the inflammatory response program based on NicheNet's prior knowledge model.
- D Ligand–receptor interaction potential based on NicheNet's prior knowledge model between the top ranked ligands and the receptors expressed in the Calu3 cell line.