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ΙΚΥ

Abstract #70

Comorbidities Risk Assessment: a predictive approach

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INTRODUCTION

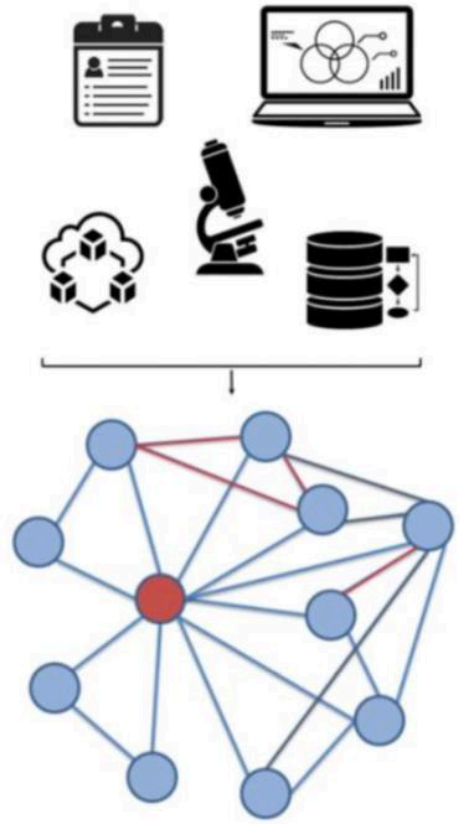
- Complex disease traits and clinical phenotypes stem from genetic and environmental influences (e.g. diet, viral biomolecules/stimuli)
- Problematic self-regulation of the inflammasome may serve as a paradigm
- Inflammatory responses shift a defense mechanism into a perpetuating inflammatory response leading to disease comorbidities

AIM OF THE STUDY

- Herein, we developed a predictive approach for comorbidities risk assessment that highlight inflammasome-centered molecular signatures (criterion: disease severity)

METHODS

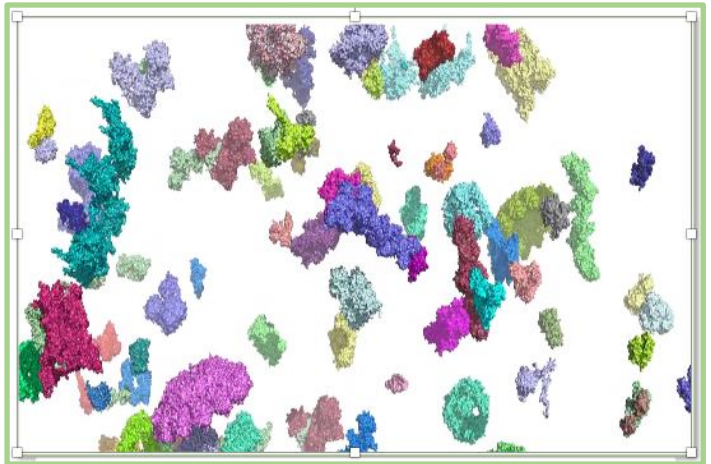
- An in-depth *in silico* analysis of disease traits and clinical phenotypes as well as tissue-specific datasets were integrated with functional data from publicly available data repositories and databases
- R and Python programming languages were employed
- Two strategies were implemented: agnostic and targeted analysis
- Extensive data and text mining for extra filtering of outcomes was followed
- Protein networks revealed missense variants of interest
- Data and text mining were performed to account for biases
- Knowledge graphs were empowered via data integration

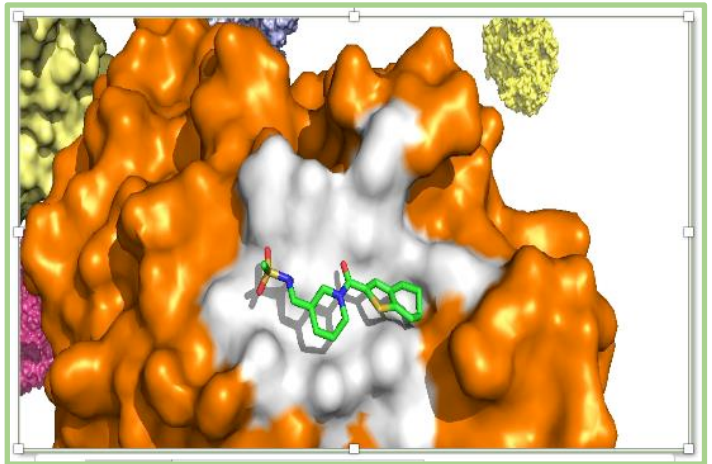


RESULTS

- Our approach detected patterns of comorbidities as the net result of genetic and environmental influences (e.g. diet, viral biomolecules/stimuli)

- *In silico* analyses resulted in 1,156 missense variants of key interest either at the orthosteric or allosteric site of key proteins





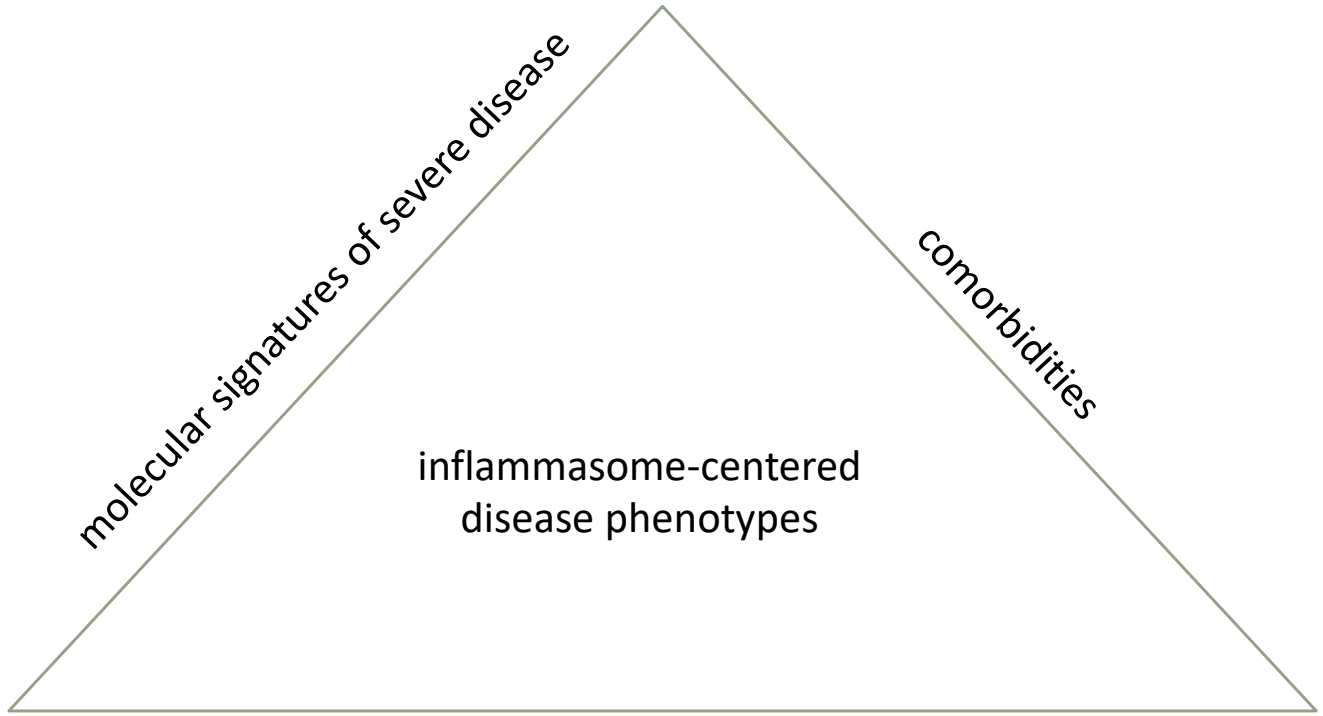
RESULTS

Toward an inflammasome-centered molecular signature

#Uploaded_variation	Location	Allele	IMPACT	SYMBOL	mino_acid	genet_gene	variant_zigosity_mean	MAF	MAF(EUR	MAF(TSI)
rs1146593	1:75769201-75769201	C	MODERATE	ACADM	T/P	ACAD8	1,684210526	0.12 (A)	0.06 (A)	0.05 (A)
rs1144566	1:182600491-182600491	A	MODERATE	RGS16	H/L	RGS1	1,973684211	**0.01** (T)	**0.02** (T)	**0.00** (T)
rs1443549	11:20601610-20601610	A	MODERATE	SLC6A5	A/D	SLC6A4	1,842105263	0.01 (C)	0.00 (C)	0.00 (C)
rs4268467	11:46681370-46681370	A	MODERATE	ARHGAP1	K/N	ARHGAP31	1,894736842	< 0.01 (T)	0.00 (T)	0.00 (T)
rs1017594	11:47309565-47309565	A	MODERATE	MADD	L/M	MADD	2	**0.01** (T)	0.00 (T)	0.00 (T)
rs2253849	12:10451071-10451071	A	MODERATE	KLRC1	N/I	KLRK1	1,815789474	**0.01** (T)	0.00(T)	0.00(T)
rs582954	12:70534944-70534944	T	MODERATE	PTPRB	D/E	PTPRK	2	**0.02** (A)	**0.06** (A)	**0.09** (A)
rs4482094	12:80460849-80460849	A	MODERATE	PTPRQ	A/D	PTPRK	2	**0.17** (C)	**0.12** (C)	**0.08** (C)
rs1169305	12:120999579-120999579	C	MODERATE	HNF1A	S/R	HIF1A	1,815789474	0.01 (A)	0.00(A)	0.00(A)
rs4238526	15:81308654-81308654	T	MODERATE	IL16	L/F	IL15	1,894736842	0,01(A)	0.00(A)	0.00(A)
rs2471844	16:4890808-4890808	C	MODERATE	PPL	C/W	PML	2	**0.07** (A)	0.00(A)	0.00(A)
rs4344749	16:28830990-28830990	T	MODERATE	ATXN2L	Q/H	ATXN2	1,973684211	< 0.01 (A)	0.00(A)	0.00(A)
rs584542	2:21009931-21009931	A	MODERATE	APOB	I/F	APOB	2	**0.01** (T)	0.00(T)	0.00(T)
rs1878529	2:102932971-102932971	G	MODERATE	TMEM182	R/G	TMEM187	2	0.03 (A)	0.08 (A)	0.07 (A)
rs2271767	2:191414601-191414601	A	MODERATE	MYO1B	L/M	MYO9B	2	0.25 (T)	0.04 (T)	0.02 (T)
rs2257495	20:46367543-46367543	T	MODERATE	ELMO2	D/E	ELMO1	2	0.01 (A)	0.00 (A)	0.00 (A)
rs2427240	20:61910571-61910571	G	MODERATE	CDH4	D/E	CD14	1,842105263	0.30 (C)	0.21 (C)	0.07 (C)
rs1352882	3:62243879-62243879	G	MODERATE	PTPRG	I/M	PTPRK	1,973684211	0.02 (C)	0.00 (C)	0.00 (C)
rs2692696	3:133766289-133766289	C	MODERATE	TF	I/L	TNF	1,973684211	0.01 (A)	0.00 (A)	0.00 (A)
rs958415	4:125408634-125408634	G	MODERATE	FAT4	D/E	FUT4	1,842105263	0.01 (T)	0.00 (T)	0.01 (T)
rs2431663	5:172769708-172769708	C	MODERATE	DUSP1	I/M	DUSP10	2	0.15 (G)	0.06 (G)	0.07 (G)
rs1065076	6:31509904-31509904	G	MODERATE	MICB	T/A	MICA	2	0.20 (A)	0.27 (A)	0.21 (A)
rs1049086	6:32662127-32662127	T	MODERATE	HLA-DQB1	D/E	HLA-DQA1	1,842105263	0.37 (A)	0.40 (A)	0.37 (A)
rs3181009	7:103103446-103103446	G	MODERATE	NAPEPLD	D/H	NAPEPLD	2	0.14 (C)	0.00 (C)	0.00 (C)
rs1757095	9:115086115-115086115	A	MODERATE	TNC	Q/L	TNF	2	< 0.01 (T)	0.06 (T)	0.07 (T)
rs2488602	9:123371268-123371268	A	MODERATE	CRB2	V/E	CRB1	1,973684211	< 0.01 (T)	0.00(T)	0.00(T)
rs1065711	CHR_HSCHR6_MHC_COX	G	MODERATE	HLA-C	V/A	HLA-C	1,921052632	0.11 (G)	0.12 (G)	0.09 (G)

SUMMARY

A predictive evaluation of comorbidity development risk may identify those patients at high risk and thus, empower optimum patient stratification via inflammasome-centered molecular signatures.



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