Supplementary Tables

NLRP1- A CINDERELLA STORY: a perspective of recent advances in NLRP1 and the questions they raise.

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Mutation	Region	GoF/LoF	Disease	Phenotype	Ref.
A54T	PYD	GoF	Multiple self-healing palmoplantar carcinoma (MSPC), familial keratosis lichenoides chronica (FKLC).		20
A66V	PYD	GoF	MSPC, FKLC.		20
M77T	PYD	GoF	MSPC, FKLC, Corneal intraepithelial dyskeratosis.	Corneal lesions and thickening	20, 58
L155H	Linker (PYD-NACHT)	GoF	Vitiligo, autoinflammatory disease, COVID-19 severity*	Increased IL-1β processing.	21, 59, 60
G578S	NACHT	GoF	Multiple sclerosis and malignant Melanoma.	Vertigo, weakness of limbs, sight issues, melanoma. Increase gene expression in IL-1β, NFKB1, JUN and P38 pathways.	29
p.R726W	Linker (NACHT-LRR)	GoF	NAIAD – NLRP1-associated autoinflammation with arthritis and dyskeratosis.	Recurrent fever, dyskeratosis, increased Neutrophils. IL-18 and cleaved caspase-1	24
T755N	Linker (NACHT-LRR)	GoF	Juvenile onset recurrent respiratory papillomatosis.	Laryngeal lesions, papilloma growth, warts, mild keratosis pilaris.	61
L813P	LRR	GoF	Differed between siblings, one with Multiple keratoacanthomas, one with familial keratosis lichenoides chronica.	Erythema, anaemia, blistering, eye inflammation, hyperkeratotic plugs, papillomatosis, failure to thrive.	22
p.F787_R843del	LRR	GoF	MSPC, FKLC.		20
M1184V	FIIND	GoF	Asthma*, Vitiligo.	Increased IL-1β processing.	27, 60
P1214R	FIIND	GoF	NAIAD – NLRP1-associated autoinflammation with arthritis and dyskeratosis.	Recurrent fever, dyskeratosis, increased Neutrophils. IL-18 and cleaved caspase-1	24
G167S	DPP9	LoF (in DPP9)	Hatipoğlu syndrome.	Recurrent HSV infection, airway inflammation, skin pigmentation anomalies.	34
R252P	DPP9	LoF (in DPP9)	Hemophagocytic lymphohistiocytosis–like hyperinflammation	Pancytopenia, skin manifestations, increased susceptibility to infections	35
R147C, Asn864ThrfsTer4 (frameshift), T246S, T878M, T995I, M1119V, V1241L.		N/A	Multiple Sclerosis*		29
rs12150220	N/A	N/A	Type 1 diabetes*		62
rs8079034C and rs878329C	N/A	N/A	Psoriasis*		23
rs2137722/G-rs12150220/T-rs2670660/G	N/A	N/A	Leprosy*	Genetic association with SNPs, if missing rs2137722 then only associated with one form of leprosy.	63
rs2670660, rs12150220-rs2670660	N/A	N/A	Systemic Lupus*	Increased rash, nephritis and arthritis	64
* Genetic association disease studies					

Supplementary Table 1. Summary of NLRP1 gain of function variants and their disease associations.

Activator	Human / Mouse	Mechanism	Ref.
Val-BoroPro / Talabostat	Mouse and Human	Inhibits DPP9 inhibitory complex	3, 33, 65
Anthrax Lethal Factor	Mouse	Functional degradation	7, 8
Toxoplasma Gondii infection	Mouse	N/A	66, 67
UVB Radiation	Human	Ribotoxic Stress	32, 36, 37
Anisomycin	Human	Ribotoxic Stress	32
Hygromycin	Human	Ribotoxic Stress	32
Doxyvinenol	Human	Ribotoxic Stress	32
Diptheria toxin	Human	Ribotoxic Stress	42, 43
Exotoxin A (pseudomonas)	Human	Ribotoxic Stress	42, 43
Sidl (Legionella)	Human	Ribotoxic Stress	42
Cholix toxin	Human	Ribotoxic Stress	43
Nigericin	Human	Ribotoxic Stress	52
dsRNA (Poly(I:C))	Human	Direct Sensing	30
dsDNA (Poly(dA:dT))	Human	Direct Sensing	48
Viral 3C Proteases	Human	Protease activity - Tripwire	49
Alphavirus	Human	Ribotoxic Stress	38

Supplementary Table 2. Summary of NLRP1 agonists and species specificity