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Design and synthesis of NLR and TLR based ligand-antigen conjugates

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Design & Synthesis of NLR and TLR based ligand-antigen conjugates

A focus on NOD2, NOD1 and TLR2 ligand modifications

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In the middle of difficulties lie opportunities – Albert Einstein

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List of Abbreviations

Ac	acetyl	Fmoc	9H-fluorenylmethyloxy-carbonyl
AcOH	acetic acid	GlcNAc	<i>N</i> -acetyl glucosamine
All	allyl	h	hour
APC	antigen presenting cell	HATU	2-(1H-7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyl-uronium hexafluorophosphate methanaminium
aq	aqueous	HEK	human embryonic kidney
ar	aryl	HCTU	2-(6-chloro-1H-benzotriazole-1-yl)-1,1,3,3-tetramethylaminium hexafluorophosphate
BMDC cell	bone marrow dendritic cell	HOBt	1-hydroxybenzotriazole
BOP	benzotriazole-1-yl-oxy-tris-dimethylamino-phosphonium hexafluorophosphate	HPLC	high performance liquid chromatography
Boc	<i>tert</i> -butyloxycarbonyl	HRMS	high resolution mass spectrometry
Boc ₂ O	di- <i>tert</i> -butyl dicarbonate	Hz	hertz
Bu	butyl	<i>i</i>	iso
^t Bu	<i>tert</i> -butyl	IR	infrared
Bu ₃ SnH	tributyltin hydride	IL	interleukin
Calc.	calculated	<i>J</i>	coupling constant
C _q	quaternary carbon atom	Lev	levulinoyl
CSA	camphor sulfonic acid	LC/Ms	liquid chromatography mass spectrometry
d	doublet	LPS	lipopolysaccharide
δ	chemical shift	m	multiplet
DAP	diaminopimelic acid	M	molar/mass
DBU	1,8-diazabicycloundec-7-ene	MDP	<i>N</i> -acetylmuramyl-L-alanine-D-isoglutamine
DC	dendritic cell	Me	methyl
DCE	dichloroethane	MeCN	acetonitrile
DCM	dichloromethane	MeOH	methanol
dd	double doublet	MHC I	major histocompatibility complex class I
DIC	<i>N,N</i> -diisopropylcarbodiimide	min	minutes
DMAP	<i>N,N</i> -dimethylaminopyridine	mg	milligram
DEVA ₅ K	DEVSGLEQLSIIINFEKLAATAAK	MS	mass spectrometry
DiPEA	<i>N,N</i> -diisopropylethylamine	Mtt	methyl trityl
DMF	<i>N,N</i> -dimethylformamide	MurNAc	<i>N</i> -acetylmuramic acid
DMSO	dimethyl sulfoxide	<i>m/z</i>	mass to charge ratio
EDC	1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide	NaH	sodium hydride
eq	equivalent	NaOMe	sodium methoxide
Et	ethyl	NH ₄ HCO ₃	ammonium bicarbonate
EtOAc	ethylacetate	nM	nanomolar
Et ₃ N	triethylamine		
Et ₂ O	diethyl ether		

NMP	<i>N</i> -methyl-2-pyrrolidone	rt	room temperature
NMR	nuclear magnetic resonance	Rt	retention time
NLR	NOD-like receptor	s	singulet
NOD	Nucleotide-binding Oligomerization Domain	SAR	structure- activity relationship
NOD1-L	NOD1 ligand	SPPS	solid phase peptide synthesis
NOD2-L	NOD2 ligand	t	triplet
PAMPS	pathogen associated molecular patterns	TFA	trifluoro acetic acid
PE	petroleum ether	THF	tetrahydrofuran
PG	peptidoglycan	TIS	triisopropyl silane
Ph	phenyl	TLC	tin layer chromatography
ppm	parts per million	TMSOTf	trimethylsilyl trifluoromethanesulfonate
PyBOP	benzotriazol-1-yl-oxy-tris-pyrrolidinophosphonium hexafluorophosphate	TLR	Toll-like receptor
PRR	pattern recognition receptors	TLR2-L	TLR2 ligand
PRR-L	PRR ligand	μM	micromolar
Pd(PPh ₃) ₄	palladium tetrakis	UV	ultraviolet
q	quartet		
RP-HPLC	reversed phase high performance liquid chromatography		

Three-letter codes for amino acids are used following the rules as proposed by the IUPAC-IUB commission on Biochemical Nomenclature. *J.Biol.Chem.*, **1966**, *241*, 2491-2495.
