Development of kinase inhibitors and activity-based probes

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Development of Kinase Inhibitors and Activity-based Probes

PROEFSCHRIFT

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List of Abbreviations

Å	Ångström
ab	antibody
ABP	activity-based probe
ABPP	activity-based protein profiling
abs	absorption
Ac	acetyl
ACN	acetonitrile
ADP	adenosine diphosphate
AfBP	affinity-based probe
AGC	PKA, PKG and PKC
AKT	V-AKT murine thymoma viral oncogene homolog 1
ALL	acute lymphoblastic leukemia
AML	acute myeloid leukemia
AMP	adenosine monophosphate
aq.	aqueous
ARG	arginine
arom , ar	aromatic
ATM	ataxia telangiectasia mutated
ATP	adenosine triphosphate
ATR	ataxia telangiectasia and Rad3-related
βARK	β-andrenergic receptor kinase
BMSC	bone marrow stromal cell
BCR	B-cell receptor
BCR-Abl	breakpoint cluster region Abelson
BODIPY	4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene
Boc	*tert*-butyloxycarbonyl
Boc_2O	*tert*-butyloxycarbonic anhydride
bs	broad singlet
BTK	bruton's tyrosine kinase
CaMK	Ca^{2+}/Calmodulin dependent kinase
cAMP	cyclic adenosine monophosphate'
CBB	Coomassie brilliant blue
Cbz-Cl	carbobenzoxy chloride
CCMS	capture compound mass spectrometry
CDK	cyclin-dependent kinase
cGMP	cyclic guanosine monophosphate
CLL	chronic lymphocytic leukemia
CLK	Cdc-like kinase
CK1	casein kinase 1
c/m	chloroform/methanol
CMGC	CDK, MAPK, GSK3 and CLK
CML	chronic myeloid leukemia
CSK	C-terminal Scr kinase
CSNK1D	casein kinase 1 delta
CuAAC	copper(I)-catalyzed alkyne-azide [2+3] cycloaddition
Cy	cyanine dye
Cys	cysteine
Δ	heating (reflux)
δ	chemical shift
d	doublet
Da	Dalton
Das.	dasatinib

DC	dual color molecular weight marker SDS-PAGE
DCE	dichloroethane
DCM	dichloromethane
dd	doublet of doublets
DDR	discoidin domain receptor
DIAD	diisopropyl azadicarboxylate
DiBAl-H	diisobutylaluminium hydride
DiPEA	*N, N*-diisopropyl-*N*-ethylamine
DLBCL	diffuse large B-cell lymphoma
DMEM	Dulbecco's modified eagle medium
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
dt	double triplet
DTT	dithiothreitol
DUS2	dihydrouridine synthase 2
EGFR	epidermal growth factor receptor
em	emission
EPHA	ephrin receptor kinase
eq.	equivalents
ERK	extracellular signal-regulated kinase
ESI	electronspray ionization
Et	ethyl
Et_2O	diethyl ether
EtOAc	ethylacetate
EtOH	ethanol
FACS	fluorescence activated cell sorting
FAK	focal adhesion kinase
FDA	Food and Drug Administration
FGFR	fibroblast growth factor receptor
FL	FLT3 ligand
FLT3	FMS-like tyrosine kinase 3
FMS	Feline McDonough Sarcoma
FOXO3	forkhead box O3
FSBA	5'-fluorosulfonylbenzoyl 5'-adenosine
FYN	Fgr/Yes related novel protein
GABA	γ-aminobutyric acid
GSK3	glycogen synthase kinase
GTP	guanosine triphosphate
H	hour(s)
HATU	1-[Bis(dimethylamino)-methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate
HEK	human embryonic kidney cell line
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid
HPLC	high performance liquid chromatography
HRMS	high-resolution mass spectrometry
HWE	Horner-Wadsworth-Emmons
Hz	hertz
Ibr.	ibrutinib
IC_{50}	half maximal inhibitory concentration
ICAP	isotope-coded ATP ABPP probe
IEDDA	inverse-electron demand Diels-Alder

Im.	imatinib
IMAP	immobilized metal ion affinity-based fluorescence polarization
Ig	immunoglobulin
IR	infrared-spectrometry
ITAM	immunoreceptor tyrosine-based activation motif
ITD	internal tandem duplication
J	coupling constant
JAK	Janus kinase
K_i	inhibitor constant
KR	kinase reaction
Lck	lymphocyte-specific protein tyrosine kinase
LCMS	liquid chromatography mass spectrometry
LIMK	LIM domain kinase
LY N	Lck/Yes novel
Lys	lysine
M	molar
m	multiplet
MAPK	mitogen-activated protein kinase
MCL	mantle cell lymphoma
MDS	myelodysplasia
MEK	MAPK/ERK kinase
MeOH	methanol
min	minutes
mTor	mechanistic target of rapamycin
m/z	mass-to-charge ratio
NFAT	nuclear factor of activated T cells
NFκB	nuclear factor κ B
NHS	*N*-hydroxysuccinimide
NMR	nuclear magnetic resonance
NQO2	NAD(P)H quinone dehydrogenase 2
PBS	phosphate buffered saline
PDB	protein data bank
PDGFRB	platelet derived growth factor receptor beta
PDK1	phosphoinositide-dependent protein kinase 1
PE	petroleum ether
PET	positron emission tomography
PH	pleckstrin homology
Ph	phenyl
PI	phophoinositide
PI3K	phophatidylinositol-3-kinase
PIKK	PI3K-related kinase
PIM	proviral integration site MuLV (murine leukemia virus)
PIP3	phosphatidylinositol 3,4,5 triphosphate
PKA	protein kinase A
PKB	protein kinase B
PKC	protein kinase C
PKG	protein kinase G
PLCγ2	phospholipase C gamma 2
PNP	para-nitrophenyl
ppm	parts per million
PTK	protein tyrosine kinase
q	quartet
quant.	quantitative
Ras	Rat sarcoma
Raf	rapidly accelerated fibrosarcoma

R_f	retention factor
RGC	receptor guanylate cyclase
ROCK	Rho-associated, coiled-coil containing protein kinase
RP	reversed phase
RT	room temperature
Rt	retention time
RTK	receptor tyrosine kinase
S	substrate
s	singlet
S6K	p70 S6 kinase
SAR	structure-activity relationships
sat.	saturated
SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel
Ser	serine
SH	Src homology
Src	sarcoma
STAT-5	signal transducer and activator of transcription 5
STE	homologues of yeast sterile kinase
STK	serine/threonine kinase 25
Su	succinimide
Syk	spleen tyrosine kinase
t	triplet
*t*Bu	*tert*-butyl
*t*BuOH	*tert*-butanol
td	triplet of doublets
TEA	triethylamine
TFA	trifluoroacetic acid
TH	Tec homology
THF	tetrahydrofuran
THPTA	Tris (3-hydroxypropyl triazolylmethyl amine
Thr	threonine
TLC	thin layer chromatography
TK	tyrosine kinase
TKD	tyrosine kinase domain
TKL	TK-like
TR-FRET	time resolved fluorescence resonance energy transfer
Tris	2-amino-2-(hydroxymethyl)-1,3-propanediol
Ts	tosyl
Tyr	tyrosine
UV	ultra violet
v	volume
Val	valine
YES	Yamaguchi (Y73 virus), Esh avian sarcoma oncogene
WM	Waldenström's macroglobulinemia
ZAK	α motif leucine zipper containing kinase