Insulin and cellular stress induced glucose uptake in 3T3-L1 adipocytes

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Curriculum Vitae

Merlijn Bazuine was born in Linschoten, the Netherlands, 29th of September 1973.

After graduating *cum laude* from Athenaeum "F. de Munnik" (Utrecht) in 1992 a study of Biology was started at Leiden University (Leiden). In 1993 the propaedeutics were passed *cum laude*, followed by a specialization in Molecular Biology, Biochemistry and Molecular Oncology.
Aside from courses followed during the specialization studies, a cordial invitation of prof. J. Reedijk to attend a seminar in Bio-Inorganic Chemistry lectured by prof. S.J. Lippard from the Massachusetts Institute of Technology (USA) was accepted. (20 Aug. 1995-24 Aug. 1995, Müllheim an der Ruhr, Germany).

After graduating at Leiden University, a Ph.D.-study on the "Identification of the catalytic domain of the *Escherichia coli* UvrABC Nucleotide Excision Repair complex" under supervision of Dr. N. Goosen was taken up at the Molecular Genetics department (Leiden University) in Nov. 1996.
From Feb. 1998-March 1999 work was performed as a European Union Marie Curie fellow on a project entitled, "Dissection of the human ATM-dependent signal transduction pathway activated in response to DNA-damage inflicted by ionising radiation." at the laboratories of prof. D.P Lane, department of Biochemistry (University of Dundee, UK).
In April 1999 a Ph.D.-study entitled, "Dissection of signalling intermediates involved in insulin-stimulated glucose transport and their deregulation in insulin resistance" on a grant of the Dutch Diabetes Foundation was taken up at the department of Molecular Cell Biology at the laboratories of prof. J.A. Maassen (Leiden University).
In 2001 the author was involved in the committee organising the annual MGC-ICRF PhD-student meeting in Bruges (Belgium).
In February 2004, a brief stay in the group of prof. S.W Cushman (NIH, Bethesda, USA) on a collaborative research effort investigating the effects of SB203580 on GLUT4 mediated glucose uptake was also supported by a grant from the Dutch Diabetes Foundation.

After completion of these studies the author will continue with his exploits into 3T3-L1 adipocytes and insulin-signalling as a post-doctoral fellow at the Life Sciences Institute, University of Michigan in the USA at the laboratories of prof. A.R. Saltiel (Ann Arbor, USA).

Publications

Bazuine M, Carlotti F, Rabelink MJWE, Vellinga J, Hoeben RC, and Maassen JA (2004) Inhibition of p38 MAPK blocks the insulin-induced enhancement of glucose turnover by the GLUT4 transporter in 3T3-L1 adipocytes. *Submitted*

Bazuine M, Van den Broek PJA, and Maassen JA (2004) Genistein inhibits GLUT4-mediated glucose uptake in 3T3-L1 adipocytes independent of effects on tyrosine kinase activity. *Submitted.*

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Abbreviations

14-3-3	A protein-family named after a combination of its chromatographic fraction number and its migration position in the subsequent starch-gel electrophoresis.
3T3-L1	adipogenic cLone 1 of NIH Swiss mouse cells
a	atypical
A	alanine (ala)
α-chain	extracellular part of the insulin receptor
adipocyte	fat-cell
AFX	ALL1 Fused gene from chromosome X
AGC-family	protein kinase superfamily archetyped by Protein Kinase A, Protein Kinase C and cGMP-dependent protein kinase.
α-helix	right handed helix
AMPK	AMP activated protein Kinase
AP	Adaptor Protein
APC	Adenomatous Polyposis of the Colon mutated
APS	Adapter protein with Pleckstrin homology and Src homology 2 domains
ARP	Actin-Related Protein
as	alternative splicing
ASIP	Atypical pkc Specific Interacting Protein (PAR3)
ATM	Ataxia Telangiectasia Mutated
ATP	Adenosine-Tri-Phosphate, the cellular fuel
ATR	ATm and Rad3 related
β-catenin	cadherin-associated inhibitory protein beta
β-cell	cell-type in the islets of Langerhans responsible for insulin-secretion
β-chain	intracellular part of the insulin receptor
BCR	Breakpoint Cluster Region
c	conventional
C3G	Crk sh3 domain-binding Guanine nucleotide-releasing factor
cAMP	cyclic AMP, a cellular second messenger
CAP	Cbl Associating Protein
CAV	CAVeolin
Cav-actin	Caveolin associated actin
CBL	Cas ns-1 murine B-cell Lymphoma
CDC42	Cell Division Cycle protein 42
CEACAM-1	CarcinoEmbryonic Antigen-related Cell Adhesion Molecule 1
C/EBP	CCAAT/Enhancer Binding Protein
CHOP	C/EBP HOmologues Protein (GADD153)
CIP4	Cdc42 Interacting Protein 4 (TRIP10)
CLIP-170	Cytoplasmic LInker Protein of 170kDa
cortical-actin	actin cytoskeleton running parrallel under the plasma-membrane
COS	simian CV-1 containing Origin-defective SV40
CRB3	CRumBs related 3
CREB	cAMP Responsive Element Binding protein
CRK	avian sarcoma virus CT10 Related Kinase
CSK	Cytoplasmic Src tyrosine Kinase
C-terminal	by convention, the end of a protein : -COOH
cytoskeleton	the actin and microtubular network within a cell
D	Aspartic acid (asp)
DAF	Dauer Arrest Phenotype
DAG	DiAcylGlycerol
DAXX	Death-domain associated protein
db/db	genetically diabetic mouse C57BL/6J-strain (leptin receptor mutant)
DMEM	Dulbecco's Modified Eagle Medium
E	Glutamic acid (glu)
E2F	E1A-dependent activator of the adenovirus E2-promoter transcription Factor
EGF	Epidermal Growth Factor
ELK	Ets-Like target of extracellular (stimulus) regulated Kinase
ER	Endoplasmic Reticulum
ERK	Extracellular (stimulus) Regulated Kinase (MAPK)
ES-cells	pluripotent Embryonic Stem cell

Etk	Ephrin-like Tyrosine Kinase
Exo70	Exocyst complex 70
FCS	Foetal Calf Serum
FFA	Free Fatty Acid
FIRKO	Fat-specific Insulin Receptor Knock-Out mouse
FKHR	ForKhead transcription factor mutated in Human alveolar Rhabdomyosarcoma
FLAIR	FLuorescence Activation Indicator for Rho proteins
flot	Flotillin
Foxo	Alternative names for FKHR
FRET	Fluorescence Resonance Energy Transfer
Fyn	Fgr, src and Yes related Novel kinase (Syn)
G_0	Gap-phase-0 (terminally differentiated)
$G_{1/2}$	Gap-phase-1/-2
G	glycine (gly)
Gab-1	Grb-2 Associated Binder-1
GC	GlucoCorticoid
GEF	Guanosine-nucleotide Exchange Factor
GFP	Green Fluorescent Protein
GLUT4	GLUcose Transporter 4
GPCR	G-Protein Coupled Receptor
G-protein	GTP-binding protein
GRB10	Growth-factor Receptor Binding protein 10
GS	Glycogen Synthetase
GSK	Glycogen Synthetase Kinase
GSV	GLUT4 Storage vesicle
GTP	Guanosine Tri Phosphate
HeLa	Henrietta Lacks cervical adenocarcinoma cell-line
HSL	Hormone Sensitive Lipase
HM	Hydrophobic Motif
HMIT1	Human Myo-Inositol transporter
HSP27	Heat Shock Protein of 27 kDa
HSP90	Heat Shock Protein of 90 kDa
hVH	human homologue of Vaccinia Virus H1 phosphatase (MKP8)
IBMX	Iso-Buthyl-Methyl-Xanthine
i	inhibitory
I	Isoleucine (ile)
IC_{50}	50% Inhibitory Concentration
ICE	Interleukin 1b Converting Enzyme
IGF-I	Insulin-like Growth Factor I
IκB	Inhibitor of nuclear factor kappa B
IKK-β	I-kappa B Kinase beta
IL-4	InterLeukin 4
ILK	Integrin Linked Kinase
INPPL1	INositol Polyphosphate Phosphatase Like 1
ins	insulin
Itk	Interleukin-2-inducible T-cell Kinase
ip_3	Inositol-Tri-Phosphate
IQGAP	IQ-motif containing GTPase Activating Protein
IR	Insulin Receptor
IRR	Insulin-Related Receptor
IRS	Insulin Receptor Substrate
JNK	Jun N-terminal Kinase
Juxtamembrane	the area directly below the plasma-membrane
L	Leucine (leu)
LAR	Leukocyte Antigen Related
LDM	Low Density Microsomes
LIMK	LIM-domain protein Kinase
Lnk	rat Lymph Node TCR-signal linKer
M	Methionine (met)
M	Mitosis

MAPK	Microtubuli Associated Protein Kinase (ERK)
MAPKAP-K2	MAPK Activated Protein Kinase 2
MCSF	Macrocyte Colony Stimulating Factor
MDM-2	Mouse Double Minute 2
MEK	MAPK/ERK Kinase
metabolic	stimulation of food consumption and storage
mitogenic	stimulation of cell-division
MKK	MAP Kinase Kinase
MKP	MAP Kinase Phosphatase
mLGL	mammalian Lethal Giant Larvae
mSOS	mammalian Son-Of-Sevenless
MT	MicroTubuli
mTOR	mammalian Target Of Rapamycin
Munc-18c	Mouse homologue of UNC-18 (*UNCoordinated C.elegans*) C
n	novel
N	Asparagine (asn)
Nck	NotI-linking clone from Chromosome 3 associating with tyrosine Kinases
NE	NorEpinephrine
NGF	Neuroblast Growth Factor
NIH/3T3	contact-inhibited NIH Swiss cell-line : similar (but not identical) to 3T3 and BALB/c3T3 seeded in a $3*10^5$ cell/plate concentration, confluence is reached in 3 generations (~3 days)
N-terminal	by convention the start of a protein : $-NH_2$
N-WASP	Neural Wiskott-Aldrich Syndrome Protein
ob/ob	genetically obese mouse C57BL/6J-strain (leptin mutant)
P	Proline (pro)
p38 MAPK	38 kDa (stress-induced) MAPK family member
p85	85 kDa (regulatory) subunit of PI-3'kinase
p110	110 kDa (catalytic) subunit of PI-3'kinase
PAK	p21 (Ras) Activated Kinase
PALS1	PApillon Lefevre Syndrome mutated (not so)
PAR	PARtition defective (*C. elegans*)
PC12	rat PheoChromocytoma cell-line 12
PC-PLD	Phosphatidyl-Choline PhosphoLipase D
PDK1	Phosphatidyl-Inositol Dependent protein Kinase
PH	Pleckstrin Homology
PHAS	Properties of Heat and Acid Stability (4EBP1)
PM	Plasma Membrane
PI-3'kinase	Phosphatidyl Insoitol 3'kinase
PIF-pocket	Pdk1 Interacting hydroPhobic pocket
PIK	Phosphatidyl-Inositol Kinase
pip_3	Phosphatidyl Inositol (3',4',5') tri-Phosphate, a cellular second messenger
PKA	Protein Kinase A
PKB	Protein Kinase B
PKC	Protein Kinase C
PLC	PhosphoLipase C
PMA	Phorbol 12-Myristate-13-Acetate
PP1	Protein Phosphatase 1
$PP2A_c$	Protein Phosphatase 2A Catalytic subunit
PPAR	Peroxisome Proliferator-Activated Receptor
PR65	65 kDa PP2A Regulatory subunit
PRAK	P38 MAPK Regulated/Activated protein Kinase
PRb	Retinoblastoma protein
Pref-1	Preadipocyte Factor 1
PRK	PKC Related Kinase
PTB	Phospho-Tyrosine Binding
PTEN	Phosphatase and TENsin homologue on chromosome 10
PTG	Protein Targeting to Glycogen
PTP	Phospho-Tyrosine Phosphatase
pY	phospho-Tyrosine

Q	Glutamine (gln)
R	Restriction point
Rab4	Ras associated GTP-Binding protein 4
Rac	RAs related C3 botulinum toxin substrate
RACK	Receptor for Activated C Kinases
Raf	Replication defective Acute transForming retroviral gene
RAICHU	Ras And Interacting CHimaeric Unit
RAS	Receptor Activated Substrate
Rho	Ras HOmologue
RING	Really Interesting New Gene
s	stimulatory
S	Serine (ser)
S	Synthesis-phase
SAP	Serum response factor Accessory Protein
Sec3	Homologues of *S. cerevisiae* SECretion defective
SH2	Src-Homology 2
SH2-B	SH2-containing Binding protein
SH3	Src Homology 3
Shc	SH2 Containing sequence
SHIP	SH2 containing Inositol Posphatase
SHP-2	Src Homology 2-containing protein tyrosine Phosphatase
SIP	SIAH-1 Interacting Protein
siRNA	short interfering RNA
SK-N-SH	SK-Neuroblastic Sympathoblast of Human
SMURF	SMAD Ubiquitination Regulatory Factor-1
SNAP-23	Soluble NSF Attachment Protein/Synaptosomal Associated Protein 23
SNARE	Soluble N-ethylmaleimide sensitive-factor Attachment protein REceptor
SoHo	SOrbin HOmology
Src	Schmidt-Ruppin A2 Rous sarComa virus
SREBP	Sterol Regulatory Element Binding Protein
STAT5A	Signal Transducer and Activator of Transcription 5A
Ste	STErility in mating pheromone mutants of *S.cerevisiae*
Synip	Syntaxin Inhibitory Protein
Syntaxin4	Synaptic vesicle translocation inhibited when mutated
T	target-membrane
T	Threonine (thr)
TAPP-1	TAndem PH-containing Protein-1
TC10	TeratoCarcinoma clone 10
TEC	Transient Erythroblastopenia of Childhood mutated
TGF-β	Transforming Growth Factor beta
TGN	Trans Golgi Network
TKB	Tyrosine Kinase Binding
TNF-α	Tumor Necrosis Factor alpha
Tomosyn	TOMO[“friend” in Japanese] of SYNtaxin-1
TVS	Tubulo-Vesicular Structure
TX-100	Triton X-100
V	vesicle
VAMP	Vesicle Associated Membrane Protein
Vps34p	*S. cerevisiae* Vascuolar Protein Sorting mutant 34
W	Tryptophan (trp)
WD	named after conserved tryptophan- and aspartic acid residues
Wnt10b	*D.melanogaster Wingless* and *M.musculus INT* genes
WW	named after two conserved tryptophan-residues
X	any amino-acid
Y	Tyrosine (tyr)