

Therapeutic and imaging potential of peptide agents in cardiocascular disease

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Abbreviations

SR-AI	Scavenger receptor type I
CsA	Cyclosporin A
ECM	Extracellular matrix
FITC	Fluorescein 5-isothiocyanate
FKBP	FK506 binding protein
G(Y)FP	Green (yellow) fluorescent protein
GPCR	G-protein coupled receptor
IL	Interleukin
NFAT	Nuclear factor of activated T-cells
ΝΓκΒ	Nuclear factor kappa B
PDGF-BB	Platelet derived growth factor-BB
vSMC	Vascular smooth muscle cell
ERK	Extracellular signal regulated kinase
CnA	Calcineurin catalytic unit A
CaN	Calcineurin
Ldlr	Low density lipoprotein receptor
ApoE	Apolipoprotein E
PE	Phycoerythrin
FACS	Fluorescence-activated cell sorting
PMA	Phorbol 12-myristate 13-acetate
AKAP79	A-kinase anchoring protein-79
Cabin-1/cain	Calcineurin binding protein-1/calcineurin inhibitory protein
DSCR-1	Down's syndrome critical region-1
CHP	Calcineurin-B homology protein
GSK3	Glycogen synthase kinase-3
ERK	Extracellular signal-regulated kinase
GST	Glutathione-S-transferase
HRP	Horseradish Peroxidase
HOBt	1-hydroxybezotriazole
TBTU	2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium
	tetrafluoroborate
Fmoc	N-(9-fluorenyl)methoxy-carbonyl
TGF-β	Transforming growth factor β
CD40L	CD154, CD40 ligand
ISR	In-stent restenosis
MMP	Matrix metalloproteinase

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Full Papers

<u>*H. Yu*</u>, J. Guo, N. Li, J. Kang, Y. Deng. Pharmacokinetics and bioavailability of ribavirin liposomes in rats. Journal of Shenyang Pharmaceutical University. 2001, 18(5), 320-323

<u>*H. Yu*</u>, K. Sliedregt, H. Overkleeft, G.A. Van der Marel, Th.J.C. Van Berkel, E.A.L. Biessen. Therapeutic potential of synthetic peptide inhibitor of nuclear factor of activated T-cells as anti-restenotic agent. Arterioscler Thromb Vasc Biol. 2006, 26: 1531-1537

<u>*H. Yu*</u>, ThJC Van Berkel, EAL. Biessen. Therapeutic Potential of VIVIT, a selective peptide inhibitor of Nuclear Factor of Activated T-cells, in cardiovascular disorders. Cardiovascular drug reviews. 2007, 25 (2), 1-13

<u>*H. Yu*</u>, F.M.E. Segers, P. Prince, Th.J.C. Van Berkel, T. Tanaka, E.A.L. Biessen. Atherosclerosis Imaging Potential of a Novel Peptide Ligand selective for SR-AI. (Submitted)

<u>*H. Yu*</u>, I. Bot, X. Xu, K. Sliedregt, H. Overkleeft, G.A. Van der Marel, Th.J.C. Van Berkel, E.A.L. Biessen. Potent Bipartite Inhibitors of Nuclear Factor of Activated T-Cells with Superior Selectivity Compared with Cyclosporin A (Submitted)

<u>*H. Yu*</u>, A.M. Woltman, C. van Kooten, P. Boross, S. Verbeek, K. Sliedregt, H. Overkleeft, G.A. Van der Marel, ThJC Van Berkel, E.A.L. Biessen. Targeting CD40 function with a selective phage display derived peptide antagonist. (Manuscript in preparation)

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Biessen EAL, <u>Yu. H</u>, K. Sliedregt, H. Overkleeft, G.A. Van der Marel, , S. Verbeek, van Kooten C, ThJC Van Berkel. Selective CD40 binding peptide (Submitted)

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<u>*H. Yu*</u>, K. Sliedregt, H. Overkleeft, van der Marel G, ThJC Van Berkel, EAL Biessen. Selective Inhibition of Nuclear Factor of Activated T-cells Signalling by Synthetic VIVIT: Promise as an Anti-restenotic Agent. (Oral presentation at the AHA Scientific Sessions 2005). Circulation. 2005, 112:II-169

A.O. Kraaijeveld, M.L. Lucerna, R. van Oort, <u>H. Yu</u>, J.W. Jukema, Th.J. Van Berkel, L.J. de Windt and E.A.L Biessen. Myocyte enhancer factor 2A is a potent regulator of angiogenesis and of erythrocyte extravasation in atherosclerotic plaques. Circulation. 2006, 114:II-103

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Curriculum Vitae

Haixiang Yu was born on Nov 26th 1976 in Baotou, Inner Mongolia, P. R. China. He went to Shenyang Pharmaceutical University in 1994 and had 4 years training in pharmaceutics. From 1998 to 2001, under the supervision of Professor Yingjie Deng, he had three years training in liposome research in the Graduate School of Shenyang Pharmaceutical University and obtained his Master's Degree in 2001. He then came to Division of Biopharmaceutics of Leiden/Amsterdam Center for Drug Research (LACDR), Leiden University, as a visiting student in Oct, 2001. He had one year training in solid phase organic synthesis and phage display under the supervision of Prof. Dr. Erik AL Biessen. He learned the basic techniques in solid phase peptide synthesis, molecular and cell biology of atherosclerosis. Starting from Oct 2002, he has been working as a Ph.D. student in the Division of Biopharmaceutics of Leiden/Amsterdam Center for Drug Research (LACDR), Leiden University, under the supervision of Prof. Dr. Erik AL Biessen and Prof. Dr. Theo J.C. Van Berkel. During his Ph.D training, his research has been mainly focused on development of peptide antagonists and their application in targeted imaging and therapeutic intervention of cardiovascular diseases. Since July 2007, he has been employed as a research associate to continue his research in cardiovascular diseases at the Division of Cardiovascular Medicine, University of Cambridge under the guidance of Professor Martin R Bennett.

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Appendix

Color figures

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Chapter 3 Fig. 3C



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Chapter 6 Fig 3C (upper), 3D (lower)

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