CURRICULUM VITAE

Walter Stünkel

Personal data

Citizenship:	Germany
PR:	Singapore
LinkedIn-Profile:	https://sg.linkedin.com/in/walter-stunkel-21188526

Education

10/1999-04/2001	Postdoctoral fellow, National Institute of Child Health and Human Development at the National Institutes of Health, Bethesda, USA, Laboratory of Molecular Embryology (Head: Dr. Alan P. Wolffe) and Laboratory of Molecular Growth Regulation (Dr. Melvin L. DePamphilis).
04/1997-09/1999	Post-doctoral fellow, Laboratory of Papillomavirus Biology, Institute of Molecular and Cell Biology (IMCB) with Dr. Hans-Ulrich Bernard, National University of Singapore, Singapore; Lecturer (course on gene regulation) at IMCB.
10/1992 to 08/1996	Ph.D. in Molecular Biology. Program for Human Biology, Philipps University Marburg, Germany. Major subjects: Molecular Biology, Biochemistry, Pharmacology and Human Genetics. Ph.D.-Thesis: "Investigations of the chromatin structure of human RNA-Polymerase III transcribed genes" (Institute of Molecular Biology and Tumor research (IMT); laboratory of Prof. Dr. Dr. Klaus H. Seifart).
04/1988 to 09/1992	Diploma (equivalent to MSc), Nutritional Science, Justus Liebig-University, Giessen, Germany (major subject: Biochemistry).
06/1986	Abitur (confirms eligibility for university degree), Cologne, Germany.

Professional Appointments

11/2020-present Director, Preclinical Development, Rhea Pharmaceutical Sciences Pte Ltd, Singapore

Responsibilities:

- To advance Rhea's anti-infective small molecule portfolio throughout preclinical development

12/2018-11/2020 Director, Discovery Biology, Experimental Drug Development Centre (EDDC, Agency for Science, Technology and Research, A*STAR).

04/2018-12/2018 Acting Chief Scientific Officer, Experimental Biotherapeutics Centre (EBC, Agency for Science, Technology and Research, A*STAR).

04/2017-12/2018 Senior Scientific Group Leader, Experimental Biotherapeutics Centre (EBC, Agency for Science, Technology and Research, A*STAR).

Responsibilities:

- After the merger of A*STAR's previous drug discovery and development units: Management of EDDC's Discovery Biology division focusing on small molecule discovery and comprising various functional groups (such as Target Biology, In Vitro Assay Development, Cell Based Assay Biology, and High-Throughput Screening)
- Heading efforts involving project outreach, due diligence workflows and project pipeline establishment
- Scientific Lead of the Target Translation Consortium (TTC), a Singapore-wide network to advance academic discoveries into commercial drug discovery & development projects
- During the assignment at EBC: Management of biologics drug development projects (monoclonal antibodies and antibody-drug conjugates, ADCs) in collaboration with academic and industry partners
- Providing guidance in recognizing and closing existing gaps in the preclinical drug discovery process before proposed portfolio entry
- Design of project plans with timelines, milestones, decision points, budget
- Defining project teams and roles of team members
- Management of preclinical outsourcing activities at selected CROs

01/2011-03/2017 Senior Principal Investigator, Growth-Development-Metabolism Program at the Singapore Institute for Clinical Sciences (SICS, Agency for Science, Technology and Research, A*STAR); Chairman of the Institute's Safety Committee.

Responsibilities:

- Establishment of a clinical translational research laboratory with the objective to derive novel therapeutic targets and biomarker concepts for metabolic diseases such as Type II Diabetes, obesity and cardiovascular disease.
- Setting up of stem cell biology and genomic technology platforms.
- Collaborative work on early-stage biomarker discovery projects led by major nutrition companies.
- Managing early career researchers such as postdoctoral fellows and Ph.D. students.

10/2007-12/2010 Principal Research Scientist and Group Leader (Drug Discovery Research Division, Oncology), Eli Lilly & Company at the Lilly Singapore Center for Drug Discovery (LSCDD).

Responsibilities until the closure of LSCDD:

- Establishment of R&D team for functional validation of new anti-cancer small molecule drug discovery targets.
- Management of two preclinical oncology small molecule drug discovery projects.
- Management of international project teams comprising biologists and chemists across time zones and locations.
- Management of outsourcing activities following the concept of a Fully Integrated Pharmaceutical Network (FIP-Net), as well as collaborations with academic institutions within the Asia Pacific region.

05/2001-10/2007 Research Scientist, Senior Research Scientist, Group Leader (Head of the Target Identification and Biomarker Validation group) with drug discovery company S*BIO Pte Ltd (Singapore).

Responsibilities:

- Establishment of R&D team after training in the area of "Functional Validation" at Chiron Corporation (Novartis, headquarter in Emeryville, CA, USA).
- Initiation of project ideas, project prioritization and experimental assessment of new anti-cancer targets.

- Establishment of preclinical drug discovery project around histone deacetylase inhibitors (HDACi) in collaboration with chemistry team and "hit to lead" stage project management.
- Working with legal team to secure patentable discoveries such as new therapeutic targets, small molecules and novel combination therapy concepts.

Fellowships/Awards

10/1999 – 04/2001	Post-doctoral research fellowship from the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG); Supplemental Postdoctoral Visiting Fellow Award from NIH.
10/1993-10/1995	Fellowship for Ph.D.-thesis ("hessische Nachwuchsförderung"), Philipps-university Marburg.

Publications

Area: Clinical Translational Research

- D Capece, D D'Andrea, F Begalli, L Goracci, L Tornatore, J Alexander, A Di Veroli, SC Leow, J Ellis, D Verzella, J Bennett, L Savino, J McKenzie, LMF de Lima Doria, S Mason, KR Chng, H Keun, K Broniowska, **W Stunkel**, Z Takats, J Kinross, G Cruciani, and G Franzoso. Enhanced triacylglycerol catabolism by CES1/TGH promotes aggressive colorectal carcinoma. *JCI, in press*
- Kandilya D, Shyamasundar S, Singh DK, Banik A, Hande MP, **Stünkel W**, Chong YS, Dheen ST. High glucose alters the DNA methylation pattern of neurodevelopment associated genes in human neural progenitor cells in vitro. *Sci Rep.* 2020 Sep 24;10(1):15676. doi: 10.1038/s41598-020-72485-7.
- Kong CM, Arjunan S, Biswas A, **Stunkel W**, Chong YS, Bongso A, Fong CY. Changes in stemness properties, differentiation potential, oxidative stress, senescence and mitochondrial function in Wharton's jelly stem cells of umbilical cords of mothers with gestational diabetes mellitus. *Stem Cell Rev.* 2019 Jun;15(3):415-426
- Caldez MJ, Van Hul N, Koh HWL, Teo XQ, Fan JJ, Tan PY, Dewhurst MR, Too PG, Talib SZA, Chiang BE, **Stünkel W**, Yu H, Lee P, Fuhrer T, Choi H, Björklund M, Kaldis P. Metabolic Remodeling during Liver Regeneration. *Dev Cell.* 2018 Oct 15. pii: S1534-5807(18)30780-9. doi

- Min ATL, Langley SR, Tan CF, Fang CJ, Khoo CM, Leow MK, Khoo EYH, Moreno Moral A, Pravenec M, Rotival M, Sadananthan SA, Velan SS, Venkataraman K, Chong YS, Lee YS, Xueling S, **Stunkel W**, Liu MH, Tai ES, Petretto E. Ethnicity-specific skeletal muscle transcriptional signatures and their relevance to insulin resistance in Singapore. *J Clin Endocrinol Metab*. 2018 Aug 21. doi: 10.1210/jc.2018-00309
- Banik A, Kandilya D, Ramya S, **Stünkel W**, Chong YS, Dheen ST. Maternal Factors that Induce Epigenetic Changes Contribute to Neurological Disorders in Offspring. *Genes (Basel).* 2017 May 24;8(6). pii: E150. doi: 10.3390/genes8060150
- Ng R, Hussain NA, Zhang Q, Chang C, Li H, Fu Y, Cao L, Han W, **Stunkel W**, Xu F. miRNA-32 Drives Brown Fat Thermogenesis and Trans-activates Subcutaneous White Fat Browning in Mice. *Cell Rep.* 2017 May 9;19(6):1229-1246. doi: 10.1016/j.celrep.2017.04.035
- Amrithraj AI, Kodali A, Nguyen L, Teo AKK, Chang CW, Karnani N, Ng KL, Gluckman PD, Chong YS, **Stünkel W.** Gestational Diabetes Alters Functions in Offspring's Umbilical Cord Cells With Implications for Cardiovascular Health. *Endocrinology.* 2017 Jul 1;158(7):2102-2112. doi: 10.1210/en.2016-1889
- Xiaojia Ge, Shi Chi Leow, Durgalakshmi Sathiakumar, **Walter Stünkel**, Asim Shabbir, Jimmy Bok Yan So, Davide Lomanto and Craig McFarlane. Isolation and Culture of Human Adipose-derived Stem Cells from Subcutaneous and Visceral White Adipose Tissue Compartments. *Bio-protocol,* Vol 6, (22), 2016. https://doi.org/10.21769/BioProtoc.2027
- Tan PY, Chang CW, Duan K, Poidinger M, Ng KL, Chong YS, Gluckman PD & **Stünkel W.** E2F1 orchestrates transcriptomics and oxidative metabolism in Wharton's jelly derived mesenchymal stem cells from growth-restricted neonates. *PLoS One*. 2016 Sep 15;11(9):e0163035. doi: 10.1371/journal.pone.0163035
- Leow SC, Poschmann J, Too PG, Yin J, Joseph R, McFarlane C, Dogra S, Shabbir A, Ingham PW, Prabhakar S, Leow MK, Lee YS, Ng KL, Chong YS, Gluckman PD, **Stünkel W.** The transcription factor SOX6 contributes to the developmental origins of obesity by promoting adipogenesis. *Development.* 2016 Mar 15; 143(6):950-61. doi: 10.1242/dev.131573
- Joseph R, Poschmann J, Sukarieh R, Too PG, Julien SG, Xu F, Teh AL, Holbrook JD, Ng KL, Chong YS, Gluckman PD, Prabhakar S, **Stünkel W.** ACSL1 Is Associated With Fetal Programming of Insulin Sensitivity and Cellular Lipid Content. *Mol Endocrinol*. 2015 Jun; 29(6):909-20. doi: 10.1210/me.2015-1020

- Sukarieh R, Joseph R, Leow SC, Li Y, Löffler M, Aris IM, Tan JH, Teh AL, Chen L, Holbrook JD, Ng KL, Lee YS, Chong YS, Summers SA, Gluckman PD, **Stünkel W**. Molecular pathways reflecting poor intrauterine growth are found in Wharton's jelly-derived mesenchymal stem cells. *Hum Reprod*. 2014 Aug 16. pii: deu209.
- Cheong CY, Chng K, Lim MK, Amrithraj AI, Joseph R, Sukarieh R, Tan YC, Chan L, Tan JH, Chen L, Pan H, Holbrook JD, Meaney MJ, Chong YS, Gluckman PD, **Stünkel W**. Alterations to DNA methylation and expression of CXCL14 are associated with suboptimal birth outcomes. *J Hum Genet.* 2014 Aug 7. doi: 10.1038/jhg.2014.
- Ong ML, Tan PY, MacIsaac JL, Mah SM, Buschdorf JP, Cheong CY, **Stunkel W**, Chan L, Gluckman PD, Chng K, Kobor MS, Meaney MJ, Holbrook JD. Infinium Monkeys: Infinium 450K Array for the Cynomolgus macaque (Macaca fascicularis). *G3* (Bethesda). 2014 May 8;4(7):1227-34. doi: 10.1534/g3.114.010967.
- Teh AL, Pan H, Chen L, Ong ML, Dogra S, Wong J, MacIsaac JL, Mah SM, McEwen LM, Saw SM, Godfrey KM, Chong YS, Kwek K, Kwoh CK, Soh SE, Chong MF, Barton S, Karnani N, Cheong CY, Buschdorf JP, **Stünkel W**, Kobor MS, Meaney MJ, Gluckman PD, Holbrook JD. The effect of genotype and in utero environment on interindividual variation in neonate DNA methylomes. *Genome Res.* 2014 Jul; 24(7):1064-74. doi: 10.1101/gr.171439.
- Shu-E Soh, Mya Thway Tint, Peter D Gluckman, Keith M Godfrey, Michael J Meaney, Anne Rifkin-Graboi, Yiong Huak Chan, **Walter Stunkel**, Joanna D Holbrook, Kenneth Kwek, Yap-Seng Chong, Seang Mei Saw and the GUSTO Study group (2013). Cohort Profile: Growing Up in Singapore Towards healthy Outcomes (GUSTO) Birth Cohort Study. *Int J Epidemiol.* 2013 Sep 25.
- Pan H, Chen L, Dogra S, Teh AL, Tan JH, Lim YI, Lim YC, Jin S, Lee YK, Ng PY, Ong ML, Barton S, Chong YS, Meaney MJ, Gluckman PD, **Stünkel W**, Ding C, Holbrook JD (2012). Measuring the methylome in clinical samples: improved processing of the Infinium Human Methylation 450 Bead Chip Array. *Epigenetics*. Oct;7(10):1173-87
- **Stünkel W**, Pan H, Chew SB, Tng E, Tan JH, Chen L, Joseph R, Cheong CY, Ong ML, Lee YS, Chong YS, Saw SM, Meaney MJ, Kwek K, Sheppard AM, Gluckman PD, GUSTO Study Group, Holbrook JD (2012). Transcriptome changes affecting Hedgehog and cytokine signaling in the umbilical cord: Implications for disease risk. *PLoS One*. 2012;7(7):e39744

Area: Small Molecule Drug Discovery

- **Walter Stünkel** and Robert M. Campbell (2011) Sirtuin 1 (SIRT1): The Misunderstood HDAC. *J Biomol Screen*. Dec; 16(10):1153-69
- Wang H, Yu N, Song H, Chen D, Zou Y, Deng W, Lye PL, Chang J, Ng M, Sun ET, Sangthongpitag K, Wang X, Wu X, Khng HH, Fang L, Goh SK, Ong WC, Bonday Z, **Stünkel W**, Poulsen A, Entzeroth M. (2009) N-Hydroxy-1,2-disubstituted-1H-benzimidazol-5-yl acrylamides as novel histone deacetylase inhibitors: Design, synthesis, SAR studies, and in vivo antitumor activity. *Bioorg Med Chem Lett*. Mar 1;19(5):1403-8. Epub 2009 Jan 19
- **Walter Stünkel** , Bee Keow Peh, Yong Cheng Tan, Vasantha M. Nayagam, Xukun Wang, Manuel Salto-Tellez, BinHui Ni, Michael Entzeroth and Jeanette Wood (2007) Functions of the SIRT1 protein deacetylase in cancer. *Biotechnol J*. Nov;2(11):1360-8.
- Vasantha M. Najagam, Xukun Wang, Yong Cheng Tan, Kee Chuan Goh , Tony Ng, Haishan Wang, Hong Yan Song, BinHui Ni, Michael Entzeroth, and **Walter Stünkel**. (2006) SIRT1 modulating compounds from high throughput screening as anti-inflammatory and insulin sensitizing agents. *J Biomol Screen*. Dec;11(8):959-67
- Kee Chuan Goh, Haishan Wang, Niefang Yu, Yifa Zhou, Yin Zheng, ZeYi Lim, Kanda Sangthongpitag, Lijuan Fang, Mark Du, Xukun Wang, A. B. Jefferson, Janet Rose, Blanche Shamoon, Christoph Reinhard, Brad Carte, Michael Entzeroth, BinHui Ni, Marcia L. Taylor, and **Walter Stünkel**. (2004) PLK1 as a potential drug target in cancer therapy. *Drug Dev. Res.* Vol. 62 (4): 349-362

Area: Academic Ph.D. and Postdoctoral Research

- Tan, S.-H, Baker, C.C. **Stünkel, W**. and Bernard, H.-U. (2003) A Transcriptional Initiator Overlaps with a Conserved YY1 Binding Site in the Long Control Region of Human Papillomavirus Type 16. *Virology*. 305 (2): 486-501
- **Stünkel, W**., Ait-Si-Ali,S., Jones, P.L. and Wolffe, A.P. (2001) Programming the transcriptional state of replicating methylated DNA. *J. Biol. Chem*. 276 (23): 20743-9
- **Stünkel, W**., Tan, S.-H., Huang, Z., and Bernard, H.-U. (2000) A nuclear matrix attachment region within the E6 oncogene of human papillomavirus-16 silences or activates gene expression depending on the physical state of the DNA. *J. Virol*. 74:2489-2501.

- O'Connor, M.J., **Stünkel, W**., Koh, C.-H., Zimmermann, H., and Bernard, H.-U. (2000). The differentiation specific factor CDP/hCut represses transcription and replication of human papillomaviruses through a conserved silencing element. *J. Virol*. 74:401-410
- **Stünkel, W.** and Bernard, H.-U. (1999). The chromatin structure of the Long Control Region of human papillomavirus type 16 represses viral oncoprotein expression. *J. Virol*. 73:1918-1930
- O'Connor, M.J., **Stünkel, W.**, Zimmermann, H., Koh, C.-H., and Bernard, H.-U. (1998). A novel YY1-independent silencer represses the activity of the human papillomavirus type 16 enhancer. *J. Virol*. 72:10083-10092
- Spangenberg, C., Eisfeld, K., **Stünkel, W**., Luger, K., Flaus, A., Richmond, T.J., Truss, M. and Beato, M. (1998). The mouse mammary tumour virus promoter positioned on a tetramer of histones H3 and H4 binds nuclear factor 1 and OTF1. *J. Mol. Biol*. 278:725-739.
- **Stünkel W**., Kober, I. and Seifart, K.H. (1997). A nucleosome positioned in the distal promoter region activates transcription of the human U6 gene. *Mol. Cell. Biol*. 17:4397-4405.
- **Stünkel W.** (1996) "Untersuchungen zur Chromatinstruktur humaner RNA-Polymerase III transkribierter Gene: Transkription des chromatinassoziierten 5S rRNA-und U6 snRNA-Genes und strukturelle Analyse der regulativ wirksamen Chromatinelemente" (Inaugural-Dissertation zur Erlangung des Doktorgrades der Humanbiologie, Dr.rer.physiol., Fachbereich Humanmedizin der Phillips Universitaet Marburg, Germany)
- **Stünkel W**., Kober, I., Kauer, M., Taimor, G. and Seifart, K.H. (1995) Human TFIIIA alone is sufficient to prevent nucleosomal repression of a homologous 5S gene. *Nucleic. Acids. Res*. 23: 109-116.
- Ziegler K. and **Stünkel, W**. (1992) Tissue-selective action of pravastatin due to hepatocellular uptake via a sodium-independent bile acid transporter. *Biochim. Biophys. Acta*. 1139: 203-209.

Patent-Publications

- Goh, Kay Lin, Khng, HH., Sabanayagam, V.M., Sangthongpitag, K., **Stünkel, W**., Tan, Y.C., Wood, J.M. (2008) Combination of Benzimidazole anti-cancer agent and a second anti-cancer agent. PCT, WO/2008/108741
- **Stünkel, W**., Sabanayagam, Vasantha, Malar. (2007) Method of predicting a response to HDAC inhibitors. PCT, WO/2007/053114
- **Stünkel, W.,** Wang H., Yin, Z. (2005) Biaryl linked hydroxamates: Preparation and pharmaceutical applications. PCT, WO 2005/040161 A1

Selected Poster-Presentations

- Roy Joseph, **Walter Stunkel**, Mark Phong, Siew Chinn Fong, Lei Li, Robert M. Campbell. (2010) The histone lysine-methyltransferase NSD1 and its functional role in non-small cell lung cancer (NSCLC). *AACR 101 Annual Meeting*

- **Walter Stunkel**, Kian Peng Koh, Vasantha Nayagam, Yong Cheng Tan, Xiaofeng Wu, ChangYong Hu, Zahid Bonday, Xukun Wang, Alice Lo, Kelly Ying, Eng Boon, Robert Hewitt, Kanda Sangthongpitag, Michael Entzeroth, and Jeanette Wood. (2007) Dot1L mediated histone H3-(Lys 79) methylation activates the p21Waf1 gene and functions as a biomarker for apoptotic sensitivity towards HDAC inhibitors. *Clin Cancer Res* 13:A33

- Kee C. Goh, Wai C. Ong, Changyong Hu, Hannes Hentze, Ai L. Liang, **Walter Stunkel**, Yong C. Tan, Kanda Sangthongpitag, Siok K. Goh, Shirly Sieh, Zahid Q. Bonday, Anthony D. William, Angeline Lee, Stephanie Blanchard, Te C. Liu, Martin Sattler, James D. Griffin, Brian W. Dymock, Ethirajulu Kantharaj, and Jeanette M. Wood (2007) SB1518: A Potent and Orally Active JAK2 Inhibitor for the Treatment of Myeloproliferative Disorders. *Blood* (ASH Annual Meeting Abstracts) 110: Abstract 538

- Kanda Sangthongpitag, Haishan Wang, **Walter Stunkel**, Zahid Bonday, Khee Chuan Goh, Xukun Wang, Xiaofeng Wu, Changyong Hu, Eric Sun, Michael Entzeroth, Venkatesh Reddy, Evelyn Goh, Pauline Yeo, Chen Chien-Shing, Gedas Greicius, Sven Pettersson, Kantharaj Ethirajulu and Jeanette Wood. (2007) SB939: a potent, orally-active HDAC inhibitor for the treatment of haematologic malignancies and solid tumors. AACR *Centennial Conference on Translational Cancer Medicine*-- Nov 4-8, 2007; Singapore