

CURRICULUM VITAE

HANNU K KOISTINEN

DATE OF BIRTH: 1969

CITIZENSHIP: Finnish

In my D.Sc. project we found that glycodelin, a reproduction related lipocalin protein, has different tissue specific glycoforms that have different biological activities. I have since continued this study as an international collaborative effort, in which we have found a cascade of glycodelin mediated activities regulating the activity of spermatozoa. Glycodelin is currently considered a remarkable example how glycosylation dictates the function of a glycoprotein. After finishing my D.Sc. degree, I worked in GlaxoSmithKline (UK) as a Post Doctoral Research Fellow for 2.5 years. In addition to scientific work, which resulted in a discovery of a potential novel mechanism for amyotrophic lateral sclerosis, this period gave important experience for drug discovery and development. Currently, I am a senior scientist and PI in Department of Clinical Chemistry, Haartman Institute, University of Helsinki. My group consists of one senior scientist, 2 PhD students, and 2 laboratory technicians. I lead international collaborative project studying prostatic proteases and aiming to develop activity modulators for those.

EDUCATION

- 1996 **M.Sc. in Technology** (Biochemistry), Helsinki Univ. of Technology, Finland
- 2000 **Doctor of Science**, Laboratory of Biochemistry and Microbiology, Department of Chemical Technology, Helsinki University of Technology, Finland (Thesis: "Glycodelin isoforms: Physicochemical and functional characterization")
- 2007 **Adjunct professor (Docent)** (Biochemistry, University of Helsinki)

CAREER TO DATE

- 2010-15 **Academy Research Fellow**
- 2009- **Principal investigator**, Faculty of Medicine, University of Helsinki, 2009
- 2004- **Senior Scientist**, Department of Clinical Chemistry, Institute of Clinical Medicine/Haartman Institute, University of Helsinki, Finland
- 2001-4 **Post Doctoral Research Fellow** (2001-3 Marie Curie Industrial Host Fellowship), Neurology & GI CEDD, GlaxoSmithKline, Harlow, UK
- 1994-2001 **Research Fellow**, Research Laboratory, Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Finland
- 1992-1994 **Part time research assistant**, Helsinki University Central Hospital, Finland

INTERNATIONAL MOBILITY

Neurology & GI CEDD, GlaxoSmithKline, Harlow, UK, 2001-4

MEMBERSHIPS IN SCIENTIFIC SOCIETIES

Societas biochemica, biophysica et microbiologica Fenniae, member
International Proteolysis Society, member 2007-
Finnish Peptide Society, member of a board of directors, 2008-, **chair** 2011-
European Peptide Society, member 2008-
American Association for Cancer Research, Active Member 2008-
The American Society for Cell Biology, Regular member 2010-

EDITORIAL BOARD MEMBERSHIPS, REVIEWS FOR INTERNATIONAL SCIENTIFIC JOURNALS AND OTHER REVIEWS

The Open Prostate Cancer Journal 2008- (Member of the Editorial Advisory Board)
Reviews for several journals including Clin Cancer Res, PLOS One, Int J Cancer, Cancer Immunology Immunotherapy and BMC Cancer

The Academy of Finland's science competition for senior secondary students, review of applications 2010, 2011 and 2012

REVIEWS FOR DOCTORAL THESIS

Sini Nurmenniemi, "Analysis of cancer cell invasion with novel in vitro methods based on human tissues" University of Oulu, 2011.

Mari Peltola, "Free Prostate-specific Antigen Forms and Kallikrein-related Peptidase 2: Tools for Prostate Cancer Diagnostics" University of Turku, 2012.

SUPERVISED DOCTORAL DISSERTATIONS AND MASTERS THESES

Lei Zhu, Thesis: "Development of novel assays for measuring different molecular forms of prostate specific antigen", 2009

Can Hekim, Thesis: "hK2 and PSA: Functions and targets for treatment of prostate cancer", 2012

Elina Lehtinen, Master's thesis, 2012

Currently supervising two PhD students.

AWARDS

Poul Astrup prize (3rd prize), 2008

PRESENTATIONS IN INTERNATIONAL CONFERENCES OR CONGRESSES

1st International Symposium on Kallikreins & Kallikresin-Related Peptidases, Lausanne, Switzerland 1-3.9.2005. Presentation.

2nd International Symposium on Kallikreins & Kallikrein-Related Peptidases, Santorini, Greece 16-10.2007. Invited lecture.

LabMed 2008, XXXI Nordic Congress in Clinical Chemistry, Helsinki, Finland, 14-18.6.2008, Astrup prize competition presentation.

30th European Peptide Symposium, Helsinki, Finland 31.8-5.9.2008. Presentation.

4th International Symposium on Kallikreins & Kallikresin-Related Peptidases, Rhodes, Greece 2-4.9.2011. Presentation.

ComBio2011, Cairns, Australia, 25-29.10.2011. Presentation.

ORGANIZING ACTIVITY

9th Biannual peptide symposium of the Finnish peptide society, Scientific committee, 2009, Helsinki, Finland

10th Biannual peptide symposium of the Finnish peptide society, Scientific committee, 2011, Tahko, Finland

Forthcoming 11th Biannual peptide symposium of the Finnish peptide society, Chairman, August, 2013, Helsinki, Finland

Publications

Author in 71 original articles in refereed international scientific journals, 16 review articles in refereed international scientific journals, 6 articles in refereed international edited volumes and in international scientific conference proceedings, and 3 articles in Finnish scientific journals. These publications have been cited ca. 1500 times (without self-citations). The journals include *Endocrine Reviews*, *Journal of Clinical Investigation*, *Blood*, *Human Reproduction Update*, *Journal of Cell Science*, *Journal of Biological Chemistry* (9 articles), *Trends in Endocrinology and Metabolism*, *Cancer Research*, *International Journal of Cancer*, *Diabetes*, *Clinical Chemistry* (3 articles) and leading journals of Reproductive biology and Urology.

Major collaborators in publications are Professor Markku Seppälä (University of Helsinki, Finland), Professor Ulf-Håkan Stenman (University of Helsinki), Professor William SB Yeung (University of Hong Kong), Dr. Philip CN Chiu (University of Hong Kong), Adjunct Professor Ale Närvänen (University of Eastern Finland), and Professors Anne Dell and Howard R Morris (Imperial College, London, UK). I have authored with all of them >10 publications.

Representative publications

- Seppälä M, Taylor RN, **Koistinen H**, Koistinen R, Milgrom E. Glycodelin: A Major Lipocalin Protein of the Reproductive Axis with Diverse Actions in Cell Recognition and Differentiation. *Endocr Rev* (2002) 23, 401-430.
- Hekim C, Leinonen J, Närvänen A, **Koistinen H**, Zhu L, Koivunen E, Väisänen V, Stenman U-H. Novel peptide inhibitors of human kallikrein 2 (hK2). *J Biol Chem* (2006) 281, 12555-60. *Development of first hK2-inhibiting peptides.*
- Zhu L, **Koistinen H**, Wu P, Närvänen A, Schallmeiner E, Fredriksson, Landegren U, Stenman U-H. Ultrasensitive proximity ligation assay for active PSA. *Biol Chem* (2006) 34, 444-450. *Development of novel sensitive proximity-ligation based assay for active PSA. The assay utilizes PSA-binding peptide and antibodies.*
- Chiu PC, Chung MK, Koistinen R, **Koistinen H**, Seppälä M, Ho PC, Ng EH, Lee KF, Yeung WS. Glycodelin-A interacts with fucosyltransferase on human sperm plasma membrane to inhibit spermatozoa-zona pellucida binding. *J Cell Sci* (2007) 120, 33-44.
- Pakkala M, Hekim C, Soininen P, Leinonen J, **Koistinen H**, Weisell J, Stenman UH, Vepsäläinen J, Närvänen A. Activity and stability of human kallikrein-2-specific linear and cyclic peptide inhibitors. *J Pept Sci* (2007) 13, 348-53. *Stabilization of hK2-inhibitory peptides against preteolytic digestion.*
- Mattsson JM, Valmu L, Laakkonen P, Stenman U-H, **Koistinen H**. Structural characterization and anti-angiogenic properties of prostate-specific antigen isoforms in seminal fluid. *The Prostate* (2008) 68, 945-954. *This paper shows that antiangiogenic activity of PSA is related to its proteolytic activity.*
- Koistinen H**, Wohlfahrt G, Mattsson JM, Wu P, Lahdenperä J, Stenman U-H. Novel small molecule inhibitors for prostate specific antigen. *The Prostate* (2008) 68, 1143-1151. *Development of novel small molecule inhibitors for PSA by high-throughput screening.*
- Hautala LC, Koistinen R, Seppälä M, Bützow R, Stenman U-H, Laakkonen P, **Koistinen H**. Glycodelin reduces breast cancer xenograft growth in vivo. *Int J Cancer* (2008) 123, 2279-2284. *This paper describes cell differentiation and tumor growth suppressive effects of glycodelin in three-dimensional cell culture model and in xenograft-tumor model.*
- Koistinen H**, Koistinen R, Zhang W-M, Valmu L, Stenman U-H. Nexin-1 inhibits the activity of human brain trypsin. *Neuroscience* (2009) 160, 97-102. *Identification of first brain-derived endogenous inhibitor for human trypsin-3.*
- Zhu L, **Koistinen H**, Landegren U, Stenman U-H. Proximity Ligation Measurement of the Complex between Prostate Specific Antigen and α 1-Protease Inhibitor. *Clin Chem* (2009) 55, 1665-71.
- Jäämaa S, af Hällström TM, Sankila A, Rantanen V, **Koistinen H**, Stenman U-H, Zhang Z, Yang Z, De Marzo AM, Taari K, Ruutu M, Andersson LC, Laiho M. DNA Damage Recognition via Activated ATM and p53 Pathway in Nonproliferating Human Prostate Tissue. *Cancer Res* (2010) 70, 8630-8641. *Characterization of DNA damage recognition and PSA expression in prostate tissue culture model.*
- Oiva J, Itkonen OM, Koistinen R, Hotakainen K, Zhang W-M, Kempainen E, Puolakkainen P, Kylänpää L, Stenman U-H, **Koistinen H**. Specific immunoassay for trypsinogen-3: Increased levels of trypsinogen-3 in acute pancreatitis. *Clin Chem* (2011) 57, 1506-1513. *Establishment of the first specific immunoassay for trypsinogen-3. Trypsinogen-3 levels were found to be increased in serum of pancreatitis patients.*
- Härkönen HH, Mattsson JM, Määttä JAE, Stenman U-H, **Koistinen H**, Matero S, Windshügel B, Poso A, Lahtela-Kakkonen M. The Discovery of Compounds Stimulating the Activity of the Kallikrein-Related Peptidase 3 (KLK3). *ChemMedChem* (2011) 6, 2170-2178.

Discovery of the first small drug-like molecules that stimulate PSA-activity by molecular modeling and virtual screening.

- Hautala LC, Greco D, Koistinen R, Heikkinen T, Heikkilä P, Aittomäki K, Blomqvist C, **Koistinen H**, Nevanlinna H. Glycodelin expression associates with differential tumour phenotype and outcome in sporadic and familial non-BRCA1/2 breast cancer patients. *Breast Cancer Res Treat* (2011) 128, 85-95.
- Lee C-L, Chiu PCN, Pang P-C, Chu IK, Lee K-F, Koistinen R, **Koistinen H**, Seppälä M, Morris HR, Tissot B, Panico M, Dell A, Yeung WSB. Glycosylation Failure Extends to Glycoproteins in Gestational Diabetes Mellitus: Evidence From Reduced α 2-6 Sialylation and Impaired Immunomodulatory Activities of Pregnancy-Related Glycodelin-A. *Diabetes* (2011) 60, 909-917.
- Lee C-L, Lam EYF, Lam KKW, **Koistinen H**, Seppälä M, Ng EHY, Yeung WSB, Chiu PCN. Glycodelin-A stimulates interleukin-6 secretion from human monocytes and macrophages through L-selectin and extracellular signal-regulated kinases pathway. *J Biol Chem* (2012) 287, 36999-37009.
- Mattsson JM, Närvänen A, Stenman U-H, **Koistinen H**. Peptides Binding to Prostate-Specific Antigen Enhance Its Antiangiogenic Activity. *The Prostate* (2012) 72, 1588-1594.
Peptides that stimulate the enzymatic activity of PSA also stimulate the antiangiogenic activity of PSA.
- Zhu L, Jäämaa S, af Hällström TM, Laiho M, Sankila A, Nordling S, Stenman U-H, **Koistinen H**. PSA Forms Complexes With α_1 -Antichymotrypsin in Prostate. *The Prostate* (2013) 73, 219-226.
- Meinander K, Weisell J, Pakkala M, Tadd AC, Hekim C, Kallionpää R, Widell K, Stenman U-H, **Koistinen H**, Närvänen A, Vepsäläinen J, Luthman K, Wallén EAA. Pseudopeptides with a Centrally Positioned Alkene-Based Disulphide Bridge Mimetic Stimulate Kallikrein-Related Peptidase 3 Activity. *Med Chem Commun* (2013), 4, 549 - 553.
- Lee CL, Chiu PCN, Hautala L, Salo T, Yeung WSB, Stenman UH, **Koistinen H**. Human chorionic gonadotropin and its free β -subunit stimulate trophoblast invasion independent of LH/hCG receptor. *Mol Cell Endocrinol* (2013) 375, 43-52.
First report showing LHCGR independent effect of hCG- β -subunit on trophoblast invasion. Methods include primary cells and organotypic invasion model.