Biographical information

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Summary:

Studied Chemistry and Biochemistry. Worked in Poland, Germany, Denmark and Canada. Has academic and industrial experience. Conducted research teams with up to 30 scientists and technicians. Has substantial experience in insect endocrinology, protein chemistry and proteomics. Developed methods for large scale quantitative proteomic analysis of animal tissue and clinical material.

Key scientific achievements:

- Developed the filter aided sample preparation FASP and related methods allowing in-depth protein identification and mapping posttranslational modifications in complex proteomes.
- Invented label and standard free computational approaches for determination of protein concentrations (the Total Protein Approach) and protein copy numbers (the Proteomic Ruler) in complex biological samples
- Discovered human proteins originating from translation of unpredicted ORFs (NARR protein)
- Discovered two families of high-mobility proteins in dipteran insects

Publication metrics:

- 124 publications
- 7514 citations*
- 1139 citations in 2017*
- Hirsh factor: 38*

*ISI, webofknowledge.com (Jan 2018)

Current position: Group leader

Academic degrees:

- Adjunct Professor at Uppsala University, Dept. of Pharmacology, 2017
- Professor (apl.) at University of Göttingen, Germany, 2000
- Habilitation (im Fach Entwicklungsbiologie), University of Göttingen, Germany, 1995
- Ph.D. (chemistry), Technical University of Wrocław, Poland, 1986
- M.Sc. (pure and applied chemistry), University of Wrocław, Poland, 1979

Teaching:

- At Technical University of Wrocław
  - 1979-1986 Laboratory courses in biochemistry, organic chemistry and biotechnology
- At University of Göttingen
  - 1989-2001 Laboratory courses in developmental biology
  - 1995-2001 Lecture series: 'Proteins and nucleic acids'
  - 1989-2001 Supervisor to diploma and PhD students
  - 2003-2005 Proteomic courses in Göttingen

Corporate experience:

- 2004-2005 Director of Biochemistry; Protana Inc., Toronto, Canada
- 2001-2004 Director of Protein Analysis / Biochemistry; MDS Proteomics Inc., Odense, Denmark

Previous professional and educational positions:

- 1996-2000: *Oberassistent*, University of Göttingen,
- 1989-1996: Research Associate (*wissenschaftlicher Assistent*), University of Göttingen
- 1987-1988: Fellow of the *Alexander von Humboldt Stiftung*
- 1982-1986: Scientist, Technical University of Wrocław

Editorial activities:

- Editor-in-Chief 'Proteomes', http://www.mdpi.com/journal/proteomes
- Editorial Board Member 'Amino Acids', https://link.springer.com/journal/726
- Advisory board member 'Zoologia Poloniae', http://www.degruyter.com/view/j/zoop
- Frequent reviewer for Nature Methods, Nature Communications, Analytical Chemistry, Journal of Proteome Research, Journal of Proteomics, Proteomics

Professional carrier

A. Academic

1981-1990. Analysis of metabolism, transport and receptors of the juvenile hormones. (15 publications)

- Analyzed the activities of juvenile hormone (JH) binding proteins in the insect haemolymph and peripheral tissues of *Galleria mellonella* and *Chironomus thummi*. Described for the first time high affinity JH binding proteins from epidermal tissue.
- Studied synthesis and metabolism of the juvenile hormones during larval development and metamorphosis of *G. mellonella*. Demonstrated reactivation of juvenile hormone by the imaginal wing disc. Showed importance of epoxide hydrolases for the regulation of JH titer.
- Developed a technique for visualization of juvenile hormone binding proteins on blots using H^3-labeled hormone. Discovered different classes of JH binding proteins on 2D page blots

Methodology: protein binding and hormone metabolism assays using tritiated hormones, protein purification techniques including gel filtration, isoelectric focusing, gradient ultracentrifugation, in vitro hormone synthesis assays, thin-layer chromatography, non-denaturing condition-2D-PAGE

Key publications

1. Tissue specific juvenile hormone degradation in Galleria mellonella. **Wiśniewski JR**, Rudnicka M, Kochman M. Insect Biochem. 1986, 16:843-849.
2. Identification of juvenile-hormone-binding proteins on blotted electropherograms using tritiated juvenile hormones. **Wiśniewski JR**. Experientia 1989, 45:1124-1128.

1990-2001. Structure and function of high mobility group (HMG) proteins (21 publications)

- Identified and sequenced HMG proteins from dipteran insects. For the first time demonstrated the occurrence of HMG proteins in invertebrates providing evidence on DNA and proteins level.
- Expressed in bacteria the novel HMG proteins and studied their interaction with DNA. Demonstrated strong DNA bending upon protein binding with essential consequences in chromatin organization.
- Mapped posttranslational modifications of the HMG proteins and analyzed their role in modulation of DNA binding showing that phosphorylation reduces the tightness of the protein binging to DNA.
- Studied organization of the human HMG proteins complex with DNA. Identified protein region involved in contact to DNA
- Raised antibodies against various HMG proteins and studied their subcellular localization. Demonstrated a HMG protein variant-specific distribution of the HMG protein in polytene chromosomes.

Methodology: Edman sequencing, amino acid analysis, cloning and expression in bacteria, mobility shift assay, protein footprinting, DNA footprinting, LC-MS/MS analysis, immunofluorescence, microinjection into *Xenopus* oocyte, fluorescence resonance energy transfer (FRET)measurements, antibody production

Key publications

1. Insect proteins homologous to mammalian high mobility group protein 1. Characterization and DNA-binding properties. **Wiśniewski JR**, Schulze E. J Biol Chem. 1992, 267:17170-7.
2. High affinity interaction of dipteran high mobility group (HMG) proteins 1 with DNA is modulated by COOH-terminal regions flanking the HMG box domain. **Wiśniewski JR**, Schulze E. J Biol Chem. 1994, 269:10713-9.
3. Protein footprinting reveals specific binding modes of a high mobility group protein I to DNAs of different conformation. Frank O, Schwanbeck R, **Wiśniewski JR**. J Biol Chem. 1998, 273:20015-20.
4. Constitutive phosphorylation of the acidic tails of the high mobility group 1 proteins by casein kinase II alters their conformation, stability, and DNA binding specificity. **Wiśniewski JR**, Szewczuk Z, Petry I, Schwanbeck R, Renner U. J Biol Chem. 199, 274:20116-22.

2006-2018 Development of methods for large scale proteomic analysis (>70 publications)

- Developed filter aided sample preparation (FASP) methods for sample preparation. These methods facilitate protein digestion and sample purification. A variation of the method using multiple protein digestion steps significantly increases the number of peptide and proteins identifications and offer and peptide fractionation strategy. Analysis of the on-filter retained DNA enables calculation of cell number equivalents.
- Established workflows for identification of proteins from formalin fixed and paraffin embedded (FFFPE) tissue. Combination of heat induced antigen retrieval with the FASP protocol enable analysis of minute amounts of microdissected FFPE material with a proteome coverage of 10,000 proteins per sample.
- Introduced and validated the 'Total Protein Approach' for absolute quantification of proteins in complex protein mixtures without standards and biochemical assays. This computational approach allows calculation of concentrations on a sole basis of mass spectrometric data. Thus, often critical for analytical accuracy labelled standards, calibration curves, and biochemical determination of total protein are no more required.
- Proposed the "Histone ruler" concept for calculation of protein copy number without standards and cell counting. This concept bases on the experimental evidence that in eukaryotic cells the mass of DNA roughly equals the mass of total histones. Since the mass of DNA per cell is usually known the protein content per cell can be calculated using the 'Total Protein Approach' data and the protein copy numbers can be assessed.
- Developed a fast and sensitive assays for determination of total protein and total peptide. This methods basses on fluorescence of the 'solvent accessible' indole of tryptophan. The method allows determination of total protein and peptides in the

presence on a variety of reagents, which are not compatible with classical colorimetric assays such as BCA and Bradford. Because the assay directly exploits spectral properties of proteins the measurements can be very fast.

- Discovered proteins originating from translation of alternative and unpredicted DNA sequences. The 'nine amino acid repeat' (NARR) proteins and the proteins with N-terminal ET-extensions have been discovered by manual analysis of non-assigned mass spectra.

Methodology: LC-MS/MS, ultrafiltration, fluorescence, antibody production, western blotting

Key publications

1. Universal sample preparation method for proteome analysis. **Wiśniewski JR**, Zougman A, Nagaraj N, Mann M. Nat Methods. 2009, 6:359-62.
2. Combination of FASP and StageTip-based fractionation allows in-depth analysis of the hippocampal membrane proteome. **Wiśniewski JR**, Zougman A, Mann M. J Proteome Res. 2009, 8:5674-8.
3. Proteome, phosphoproteome, and N-glycoproteome are quantitatively preserved in formalin-fixed paraffin-embedded tissue and analyzable by high-resolution mass spectrometry. Ostasiewicz P, Zielinska DF, Mann M, **Wiśniewski JR**. J Proteome Res. 2010, 9:3688-700.
4. Extensive quantitative remodeling of the proteome between normal colon tissue and adenocarcinoma. **Wiśniewski JR**, Ostasiewicz P, Duś K, Zielińska DF, Gnad F, Mann M. Mol Syst Biol. 2012, 8:611.
5. A "proteomic ruler" for protein copy number and concentration estimation without spike-in standards. **Wiśniewski JR**, Hein MY, Cox J, Mann M. Mol Cell Proteomics. 2014, 13:3497-506.
6. The impact of high-fat diet on metabolism and immune defense in small intestine mucosa.**Wiśniewski JR**, Friedrich A, Keller T, Mann M, Koepsell H.J Proteome Res. 2015, 14:353-65.

B. Corporate (2001-2005)

- Worked on developing of proteomic platforms for drug target discovery.
- Developed methods for proteomics analysis of membrane proteins. Methods for enrichment of plasma membrane form frozen tissue and 'on membrane' protein digestion allowed the first large scale identification of brain channels and neurotransmitter receptors and their comparative analysis between distinct parts of mouse brain.
- Created approaches for identification of N-glycosylated peptides in plasma

Key publications

1. Integrated analysis of protein composition, tissue diversity, and gene regulation in mouse mitochondria. Mootha VK, Bunkenborg J, Olsen JV, Hjerrild M, **Wiśniewski JR**, Stahl E, Bolouri MS, Ray HN, Sihag S, Kamal M, Patterson N, Lander ES, Mann M. Cell. 2003, 115:629-40.
2. Proteomic mapping of brain plasma membrane proteins. Nielsen PA, Olsen JV, Podtelejnikov AV, Andersen JR, Mann M, **Wiśniewski JR**. Mol Cell Proteomics. 2005, 4:402-8.