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Research interests

Liesbeth Marian Veenhoff
Born 23-11-1972, NL
Partner of Jan Jacob Schuringa, mother of two born 2003 and 2005
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Training

Master: University of Groningen; August 1996; Biology (Biochemistry/Molecular Biology)
PhD: University of Groningen; 7 September 2001, supervisor Prof. Dr. Poolman; Cum Laude

Work experience since completing PhD

2002-2003 post doctoral HFSP fellow, Rockefeller University (New York, USA), 1fte
2004-2010 post doctoral veni & vidi fellow, University of Groningen (NL), 0.8fte
2010-2012 Assistant Prof, University Medical Center Groningen (NL), 1fte
2012-present Group leader European Research Institute for the Biology of Ageing (ERIBA), University Medical Center Groningen (NL)
(UHD/Associate Prof since 2015, ius promovendi since 2018),

Brief summary of research over the last five years

My group has made important contributions in the nuclear transport field studying the mechanism of transport of membrane proteins. Specifically, we discovered that, while the majority of membrane proteins simply reach the inner membrane by diffusion, a selective and energy-dependent transport mechanism exists for two yeast proteins, and likely for a third human protein. Intriguingly, these three proteins all act in nuclear pore complex (NPC) assembly and quality control, which led me to question whether this special transport mechanism may be important for NPC quality control. In collaboration with others, my team developed new methods and generated a first system-wide inventory of the molecular changes in mitotic ageing yeast. We found that a major signature of ageing cells is an altered stoichiometry in protein complexes, which was particularly strong for the NPC. To then answer the many unresolved questions with regard to the function of the NPCs in ageing cells, we follow nuclear transport in ageing yeast cells. Using microfluidic devices, we monitor cells over their entire life span under perfectly controlled environmental conditions. My team found that NPC quality control is compromised in ageing cells, and associated with reduced transport across the nuclear envelope. Altogether, my research lines—related to the function of the NPC, on the one hand, and to understanding what cellular ageing is on a molecular level, on the other—have now converged and jointly point to the importance of NPC quality control.

Grants, scholarships and prizes

PI
2020 'Quality control of nuclear pores', NWO-Vici Science Domain
2020 'Guardians of protein disorder', NWO-XL Science Domain (previously ENW-GROOT) consortium grant, I act as project leader.
2017 'Unravelling the molecular mechanism of impaired nuclear transport in ALS' Netherlands Organization for Scientific Research (BBoL-NWO)
2016 Aspasia, Netherlands Organization for Scientific Research (NWO)
2015 'A mother's sacrifice: asymmetric inheritance of ageing factors' Netherlands Organization for Scientific Research (NWO-ALW)
2013 'Ageing of the Nuclear Pore Complex: relating structure and function' Netherlands Organization for Scientific Research (ECHO-NWO).
2008 'Composition, function, and dynamics of the yeast nuclear envelope' financed by the Netherlands Organization for Scientific Research (Vidi-NWO)

2004 Veni-NWO

2002 Human Frontiers Fellowship long term fellowship

2001 My thesis 'Mechanistic aspects and structural organization of a secondary sugar transporter' was awarded with the honour 'Cum laude' representing the top 5 % of PhD theses.

1996 The Unilever Research Award 1996 for the best master student research project 'Purification and reconstitution of transport proteins'.

Co-PI

2010 Co-author on the proposal for the Systems Biology Centre for Energy Metabolism and Ageing. Funding for 1 PhD student, project leader. (NWO)

2008 Co-author on collaborative project "transport through a polymer network". Funding for 1 PhD student. (Zernike institute for Advanced Material)

2008 The Netherlands Proteomics Centre funds proteome research on the yeast nucleus. Funding for 1 PhD student.

Research output

De Novo Computational Design of Disordered Fg-Nucleoporins

De Vries, H., Fragasso, A., Otto, T., Klughammer, N., Andersson, J., Sluis, E. V. D., Steen, A., Dahlin, A., Veenhoff, L., Dekker, C., Giessen, E. V. D. & Onck, P., 12-Feb-2021, In: *Biophysical Journal*. 120, 3, p. 29a-30a

A physicochemical perspective of aging from single-cell analysis of pH, macromolecular and organellar crowding in yeast

Mouton, S. N., Thaller, D. J., Crane, M. M., Rempel, I. L., Terpstra, O. T., Steen, A., Kaeberlein, M., Lusk, C. P., Boersma, A. J. & Veenhoff, L. M., 29-Sep-2020, (E-pub ahead of print) In: *eLife*. 9, 23 p., 54707.

Erratum

Liu, B., Mavrova, S. N., van den Berg, J., Kristensen, S. K., Mantovanelli, L., Veenhoff, L. M., Poolman, B. & Boersma, A. J., 22-May-2020, In: *ACS Sensors*. 5, 5, p. 1500-1500 1 p.

Flexible and Extended Linker Domains Support Efficient Targeting of Heh2 to the Inner Nuclear Membrane

Rempel, I. L., Popken, P., Ghavami, A., Mishra, A., Hapsari, R. A., Wolters, A. H. G., Veldsink, A. C., Klaassens, M., Meinema, A. C., Poolman, B., Giepmans, B. N. G., Onck, P. R., Steen, A. & Veenhoff, L. M., 4-Feb-2020, In: *Structure*. 28, 2, p. 185-195.e5 17 p.

A genome-wide screen identifies genes that suppress the accumulation of spontaneous mutations in young and aged yeast cells

Novarina, D., Janssens, G. E., Bokern, K., Schut, T., van Oerle, N. C., Kazemier, H. G., Veenhoff, L. M. & Chang, M., 1-Feb-2020, In: *Aging Cell*. 19, 2, 13 p., e13084.

Poor old pores-The challenge of making and maintaining nuclear pore complexes in aging

Rempel, I. L., Steen, A. & Veenhoff, L. M., 23-Jan-2020, In: *The FEBS Journal*. 287, 6, p. 1058-1075 18 p.

Macromolecular Crowding Measurements with Genetically Encoded Probes Based on Förster Resonance Energy Transfer in Living Cells

Mouton, S., Veenhoff, L. M. & Boersma, A. J., 2020, In: *Methods in Molecular Biology*. 2175, p. 169-180 11 p.

A physicochemical roadmap of yeast replicative aging

Mouton, S. N., Thaller, D. J., Crane, M. M., Rempel, I. L., Steen, A., Kaeberlein, M., Lusk, C. P., Boersma, A. J. & Veenhoff, L. M., Nov-2019, In: *bioRxiv*.

Age-dependent deterioration of nuclear pore assembly in mitotic cells decreases transport dynamics

Rempel, I. L., Crane, M. M., Thaller, D. J., Mishra, A., Jansen, D. P. M., Janssens, G., Popken, P., Akşit, A., Kaeberlein, M., van der Giessen, E., Steen, A., Onck, P. R., Lusk, C. P. & Veenhoff, L. M., 3-Jun-2019, In: *eLife*. 8, 26 p., e48186.

The Effect of FG-Nup Phosphorylation on NPC Selectivity: A One-Bead-Per-Amino-Acid Molecular Dynamics Study

Mishra, A., Sipma, W., Veenhoff, L. M., Van der Giessen, E. & Onck, P. R., 1-Feb-2019, In: *International Journal of Molecular Sciences*. 20, 3, 18 p., 596.

The influence of fluorescent protein maturation on FRET measurements in living cells

Liu, B., Mavrova, S. N., van den Berg, J., Kristensen, S. K., Mantovanelli, L., Veenhoff, L. M., Poolman, B. & Boersma, A. J., 28-Sep-2018, In: ACS Sensors. 3, 9, p. 1735-1742

Increased genome instability is not accompanied by sensitivity to DNA damaging agents in aged yeast cells

Novarina, D., Mavrova, S. N., Janssens, G. E., Rempel, I. L., Veenhoff, L. M. & Chang, M., Jun-2017, In: Dna repair. 54, p. 1-7 7 p.

A simple microfluidic platform to study age-dependent protein abundance and localization changes in *Saccharomyces cerevisiae*

Cabrera, M., Novarina, D., Rempel, I. L., Veenhoff, L. M. & Chang, M., 13-Apr-2017, In: Microbial Cell. 4, 5, p. 169-174 6 p.

The Natural Variation in Lifespans of Single Yeast Cells Is Related to Variation in Cell Size, Ribosomal Protein, and Division Time

Janssens, G. E. & Veenhoff, L. M., 1-Dec-2016, In: PLoS ONE. 11, 12, 18 p., e0167394.

Evidence for the hallmarks of human aging in replicatively aging yeast

Janssens, G. E. & Veenhoff, L. M., Jul-2016, In: Microbial Cell. 3, 7, p. 263-274 12 p.

Intrinsically Disordered Proteins: Gatekeepers of the Nuclear Pore Complex

Ghavami, A., Veenhoff, L. M., Van der Giessen, E. & Onck, P. R., 16-Feb-2016, In: Biophysical Journal. 110, 3, suppl. 1, p. 358A-358A 1 p.

Protein biogenesis machinery is a driver of replicative aging in yeast

Janssens, G. E., Meinema, A. C., Gonzalez, J., Wolters, J. C., Schmidt, A., Guryev, V., Bischoff, R., Wit, E. C., Veenhoff, L. M. & Heinemann, M., 1-Dec-2015, In: eLife. 4, 24 p., e08527.

Active Nuclear Import of Membrane Proteins Revisited

Laba, J. K., Steen, A., Popken, P., Chernova, A., Poolman, B. & Veenhoff, L. M., 13-Oct-2015, In: Cells. 4, 4, p. 653-673 21 p.

Conservation of inner nuclear membrane targeting sequences in mammalian Pom121 and yeast Heh2 membrane proteins

Kralt, A., Jagalur, N. B., van den Boom, V., Lokareddy, R. K., Steen, A., Cingolani, G., Fornerod, M. & Veenhoff, L. M., 15-Sep-2015, In: Molecular Biology of the Cell. 26, 18, p. 3301-3312 12 p.

Distinctive Properties of the Nuclear Localization Signals of Inner Nuclear Membrane Proteins Heh1 and Heh2

Lokareddy, R. K., Hapsari, R. A., van Rheenen, M., Pumroy, R. A., Bhardwaj, A., Steen, A., Veenhoff, L. M. & Cingolani, G., 7-Jul-2015, In: Structure. 23, 7, p. 1305-1316 12 p.

Size-dependent leak of soluble and membrane proteins through the yeast nuclear pore complex

Popken, P., Ghavami, A., Onck, P. R., Poolman, B. & Veenhoff, L. M., 1-Apr-2015, In: Molecular Biology of the Cell. 26, 7, p. 1386-1394 9 p.

Intrinsically disordered linker and plasma membrane-binding motif sort *ist2* and *ssy1* to junctions

Kralt, A., Carretta, M., Mari, M., Reggiori, F., Steen, A., Poolman, B. & Veenhoff, L. M., Feb-2015, In: Traffic. 16, 2, p. 135-147 13 p.

Probing the Disordered Domain of the Nuclear Pore Complex through Coarse-Grained Molecular Dynamics Simulations

Ghavami, A., Veenhoff, L. M., van der Giessen, E. & Onck, P. R., 16-Sep-2014, In: Biophysical Journal. 107, 6, p. 1393-1402 10 p.

Traffic to the inner membrane of the nuclear envelope

Laba, J. K., Steen, A. & Veenhoff, L. M., Jun-2014, In: Current Opinion in Cell Biology. 28, p. 36-45 10 p.

Quantitative Analysis of Membrane Protein Transport Across the Nuclear Pore Complex

Meinema, A. C., Poolman, B. & Veenhoff, L. M., May-2013, In: *Traffic*. 14, 5, p. 487-501 15 p.

Nuclear transport factor directs localization of protein synthesis during mitosis (Corrigendum; vol 11, pg 350, 2009)

van den Bogaart, G., Meinema, A. C., Krasnikov, V., Veenhoff, L. M. & Poolman, B., Apr-2013, In: *Nature Cell Biology*. 15, 4, p. 441 1 p.

The transport of integral membrane proteins across the nuclear pore complex

Meinema, A. C., Poolman, B. & Veenhoff, L. M., 2012, In: *Nucleus-Austin*. 3, 4, p. 322-329 8 p.

Long Unfolded Linkers Facilitate Membrane Protein Import Through the Nuclear Pore Complex

Meinema, A. C., Laba, J. K., Hapsari, R. A., Otten, R., Mulder, F. A. A., Kralt, A., van den Bogaart, G., Lusk, C. P., Poolman, B. & Veenhoff, L. M., 1-Jul-2011, In: *Science*. 333, 6038, p. 90-93 4 p.

Undifferentiated Embryonic Cell Transcription Factor 1 Regulates ESC Chromatin Organization and Gene Expression

Kooistra, S. M., van den Boom, V., Thummer, R. P., Johannes, F., Wardenaar, R., Tesson, B. M., Veenhoff, L. M., Fusetti, F., O'Neill, L. P., Turner, B. M., de Haan, G., Eggen, B. J. L. & O'Neill, L. P., Oct-2010, In: *STEM CELLS*. 28, 10, p. 1703-1714 12 p.

Molecular sieving properties of the cytoplasm of Escherichia coli and consequences of osmotic stress

Mika, J. T., van den Bogaart, G., Veenhoff, L., Krasnikov, V. & Poolman, B., Jul-2010, In: *Molecular Microbiology*. 77, 1, p. 200-207 8 p.

A karyopherin acts in localized protein synthesis

Veenhoff, L. M., Meinema, A. C. & Poolman, B., 1-Apr-2010, In: *Cell Cycle*. 9, 7, p. 1281-1285 5 p.

Proteomics of Saccharomyces cerevisiae Organelles

Wiederhold, E., Veenhoff, L. M., Poolman, B. & Slotboom, D. J., Mar-2010, In: *Molecular & Cellular Proteomics*. 9, 3, p. 431-445 15 p.

Correction to: Transport and Sorting of the Solanum tuberosum Sucrose Transporter SUT1 Is Affected by Posttranslational Modification (vol 20, pg 2497, 2008)

Kruegel, U., Veenhoff, L. M., Langbein, J., Wiederhold, E., Liesche, J., Friedrich, T., Grimm, B., Martinoia, E., Poolman, B. & Kuehn, C., Dec-2009, In: *Plant Cell*. 21, 12, p. 4059-4060 2 p.

Orthogonal Separation Techniques for the Characterization of the Yeast Nuclear Proteome

Gauci, S., Veenhoff, L. M., Heck, A. J. R. & Krijgsveld, J., Jul-2009, In: *Journal of Proteome Research*. 8, 7, p. 3451-3463 13 p.

Nuclear transport factor directs localization of protein synthesis during mitosis

Bogaart, G. V. D., Meinema, A. C., Krasnikov, V., Veenhoff, L. M. & Poolman, B., Mar-2009, In: *Nature Cell Biology*. 11, 3, p. 350-U269 14 p.

Transport and Sorting of the Solanum tuberosum Sucrose Transporter SUT1 Is Affected by Posttranslational Modification

Kruegel, U., Veenhoff, L. M., Langbein, J., Wiederhold, E., Liesche, J., Friedrich, T., Grimm, B., Martinoia, E., Poolman, B., Kuehn, C., Krügel, U. & Kühn, C., Sep-2008, In: *Plant Cell*. 20, 9, p. 2497-2513 17 p.

Determining the architectures of macromolecular assemblies

Alber, F., Dokudovskaya, S., Veenhoff, L. M., Zhang, W., Kipper, J., Devos, D., Suprpto, A., Karni-Schmidt, O., Williams, R., Chait, B. T., Rout, M. P. & Sali, A., 29-Nov-2007, In: *Nature*. 450, 7170, p. 683-694 12 p.

The molecular architecture of the nuclear pore complex

Alber, F., Dokudovskaya, S., Veenhoff, L. M., Zhang, W., Kipper, J., Devos, D., Suprpto, A., Karni-Schmidt, O., Williams, R., Chait, B. T., Sali, A. & Rout, M. P., 29-Nov-2007, In: *Nature*. 450, 7170, p. 695-701 7 p.

Oligomeric state of membrane transport proteins analyzed with blue native electrophoresis and analytical ultracentrifugation

Heuberger, E. H. M. L., Veenhoff, L. M., Duurkens, R. H. T., Friesen, R. H. E. & Poolman, B., 5-Apr-2002, In: Journal of Molecular Biology. 317, 4, p. 591-600 10 p.

Cleave to Leave: Structural Insights into the Dynamic Organization of the Nuclear Pore Complex

Dokudovskaya, S., Veenhoff, L. M. & Rout, M. P., 2002, In: Molecular Cell. 10, 2, 3 p.

Combined in-gel tryptic digestion and CNBr cleavage for the generation of peptide maps of an integral membrane protein with MALDI-TOF mass spectrometry

Montfort, B. A. V., Doeven, M. K., Canas, B., Veenhoff, L. M., Poolman, B. & Robillard, G. T., 2002, In: Biochimica et Biophysica Acta-Bioenergetics. 1555, 1-3, p. 111 - 115 5 p.

Quaternary structure and function of transport proteins

Veenhoff, L. M., Heuberger, E. H. M. L. & Poolman, B., 2002, In: Trends in Biochemical Sciences. 27, 5, p. 242 - 249 8 p.

Hierarchical control versus autoregulation of carbohydrate utilization in bacteria

Gunnawijk, M. G. W., van den Bogaard, P. T. C., Veenhoff, L. M., Heuberger, E. H. M. L., de Vos, W. M., Kleerebezem, M., Kuipers, O. P. & Poolman, B., 2001, In: Journal of Molecular Microbiology and Biotechnology. 3, 3, p. 401 - 413 13 p.

Mechanistic aspects and structural organization of a secondary sugar transporter

Veenhoff, L. M., 2001, Groningen: s.n..

The lactose transport protein is a cooperative dimer with two sugar translocation pathways

Veenhoff, L. M., Heuberger, E. H. M. L. & Poolman, B., 2001, In: EMBO Journal. 20, 12, p. 3056 - 3062 7 p.

Close Approximation of Putative α -Helices II, IV, VII, X, and XI in the Translocation Pathway of the Lactose Transport Protein of *Streptococcus thermophilus*

Veenhoff, L. M., Geertsma, E. R., Poolman, B. & Knol, J., 2000, In: The Journal of Biological Chemistry. 275, 31, p. 23834 - 23840 7 p.

Structural information on a membrane transport protein from nuclear magnetic resonance spectroscopy using sequence-selective nitroxide labeling

Spooner, P. J. R., Veenhoff, L. M., Watts, A. & Poolman, B., 1999, In: Biochemistry. 38, 30, p. 9634 - 9639 6 p.

Substrate recognition at the cytoplasmic and extracellular binding site of the lactose transport protein of *Streptococcus thermophilus*

Veenhoff, L. M. & Poolman, B., 1999, In: The Journal of Biological Chemistry. 274, 47, p. 33244 - 33250 7 p.

Structure-function relationships in the lactose transport protein of *Streptococcus thermophilus*

Poolman, B., Gunnawijk, M. G. W., Postma, P. W. & Veenhoff, L. M., 1997, In: The FASEB Journal. 11, 9, p. 1321 1 p.

Unidirectional reconstitution of a secondary transport protein

Veenhoff, L. M. & Poolman, B., 1997, In: The FASEB Journal. 11, 9, p. 1322 1 p.

Unidirectional reconstitution into detergent-destabilized liposomes of the purified lactose transport system of *Streptococcus thermophilus*

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