BIOGRAPHICAL SKETCH

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NAME: Grisshammer, Reinhard

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Staff Scientist, CCR NCI NIH

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date	FIELD OF STUDY
Ludwig-Maximilians-Universität, Munich, Germany	Diploma	1985	Biology and Chemistry
Johann-Wolfgang Goethe Universität, Frankfurt, Germany	Ph.D.	1990	Biology
Medical Research Council, Centre for Protein Engineering, Cambridge, UK	Postdoctoral	1991-1996	Membrane protein structure

A. Personal Statement

I have been working on the structure and function of integral membrane proteins, in particular of G protein-coupled receptors, since more than 25 years. During my postdoctoral time, I have established a recombinant production and purification system for the neurotensin receptor, accompanied by biochemical and pharmacological characterization. Combining the concept of conformational thermostabilization (in collaboration with Chris Tate, Cambridge, UK) with the T4 lysozyme approach and lipidic cubic phase techniques, we have determined several structures of the neurotensin receptor in an active-like state, bound to its peptide agonist. In addition, our experimental repertoire includes the nanodisc technology used to study detailed aspects of the signaling properties of the neurotensin receptor. More recently, I have focused on the structure determination of NTSR1 signaling complexes by cryo-EM.

B. Positions and Honors

Positions and Employment

1991-1996 Postdoctoral fellow, Medical Research Council, Centre for Protein Engineering, Cambridge, UK
1997-2001 Scientific staff, Medical Research Council Laboratory of Molecular Biology, Cambridge, UK
2001-2006 Staff Scientist, Laboratory of Molecular Biology, NIDDK, NIH, Bethesda MD, USA
2006-2017 Tenure track investigator, Membrane Protein Structure and Function Unit, NINDS, NIH, USA
2017- Staff Scientist, Laboratory of Cell Biology, NCI, NIH, Bethesda MD, USA

Other Experience and Professional Memberships

2001-present Founder and chair of the NIH Membrane Protein Interest Group, see http://sigs.nih.gov/MPIG/Pages/default.aspx
2001-present Grant and Journal reviewer (ad hoc)
2004-2009 Member of the Scientific Advisory Committee for the Membrane Protein Structure Initiative (Mpsi) of the United Kingdom's BBSRC funded Structural Proteomics of Rational Targets (SPoRT) initiative
2007-2015 Member of the Scientific Advisory Committee for the New York Consortium on Membrane Protein Structure (NYCOMPS) at the New York Structural Biology Center
2004-2011 NIH Study Section member (ad hoc): NIH Special Emphasis Panel PA-02-060 'Structural Biology of Membrane Proteins' (2004); NIH Technology Development Special Emphasis Panel ZRG1

F14A 20L (2006); NIH Special Emphasis Panel RM-07-003 'Membrane Protein Production and Structure Determination' RO1 Roadmap Initiative (2007); NIH Special Emphasis Panel ZRG1 BCMB-P50 R RFA-RM-08-019 'Centers for Innovation in Membrane Protein Production for Structure Determination' Roadmap Initiative (2009); NIH Member Conflict Special Emphasis Panel 'Biological Chemistry and Macromolecular Biophysics' 2011/05 ZRG1 BCMB-B (02) M (2011)

2019 Deutsche Forschungsgemeinschaft (DFG) Sonderforschungsbereich (SFB) Funding Proposal 2020-2023 Collaborative Research Center 1423 Leipzig University, Germany (2019)

Session chair at conferences: Gordon Research Conferences, Keystone Symposia, Membrane Protein Interest Group and Structural Biology Interest Group postdoc symposia at NIH

PhD Thesis Defense "Opponent", Stockholm University, Sweden, 2 September 2011

PhD Thesis Examiner, Johns Hopkins University, Baltimore MD, USA, 4 May 2015

Honors

C. Contribution to Science

1. My early work addressed methods development for the recombinant production, purification, and characterization of G protein-coupled receptors. * Corresponding author.
    a. Grisshammer R*, Duckworth R, and Henderson R (1993) Expression of a rat neurotensin receptor in Escherichia coli. Biochem. J. 295, 571-576; PMCID: PMC1134918
    b. Grisshammer R*, Little J, and Aharony D (1994) Expression of rat NK-2 (neurokinin A) receptor in E. coli. Receptors and Channels 2, 295-302
    c. Hänninen A-L, Bamford DH, and Grisshammer R* (1994) Expression in Escherichia coli of rat neurotensin receptor fused to membrane proteins from the membrane-containing bacteriophage PRD1. Biol. Chem. Hoppe-Seyler 375, 833-836
    d. Popp MP, Grisshammer R, Hargrave PA, and Smith WC* (1996) Ant opsins: Sequences from the Saharan silver ant and the carpenter ant. Invertebrate Neuroscience 1, 323-329
    e. Tucker J, and Grisshammer R* (1996) Purification of a rat neurotensin receptor expressed in Escherichia coli. Biochem. J. 317, 891-899; PMCID: PMC1217569
    f. Calandra B, Tucker J, Shire D, and Grisshammer R* (1997) Expression in Escherichia coli and characterization of the human central CB1 and peripheral CB2 cannabinoid receptors. Biotechnology Letters 19, 425-428
    g. Grisshammer R*, and Tucker J (1997) Quantitative evaluation of neurotensin receptor purification by immobilized metal affinity chromatography. Protein Expression and Purification 11, 53-60
    h. Grisshammer R*, Averbeck P, and Sohal AK (1999) Improved purification of a rat neurotensin receptor expressed in Escherichia coli. Biochemical Society Transactions 27 (6), 899-903
    i. Fassio A, Evans G, Grisshammer R, Bolam JP, Mimmack M, and Emson PC* (2000) Distribution of the neurotensin receptor NTS1 in the rat CNS studied using an amino-terminal directed antibody. Neuropharmacology 39, 1430-1442
    j. Grisshammer R*, and Hermans E (2001) Functional coupling with $G\alpha q$ and $G\alpha_{i1}$ protein subunits promotes high-affinity agonist binding to the neurotensin receptor NTS-1 expressed in Escherichia coli. FEBS Letters 493, 101-105
    k. Kunji ERS, Spudich EN, Grisshammer R, Henderson R, and Spudich JL* (2001) Electron crystallographic analysis of two-dimensional crystals of sensory rhodopsin II: A 6.9 Å projection structure. J. Mol. Biol. 308, 279-293
    l. Weiß HM*, and Grisshammer R (2002) Purification and characterization of the human adenosine A2a receptor functionally expressed in Escherichia coli. Eur. J. Biochem. 269, 82-92
    m. Daniels DA*, Sohal AK, Rees S, and Grisshammer R* (2002) Generation of RNA aptamers to the G-protein-coupled receptor for neurotensin, NTS-1. Analytical Biochemistry 305, 214-226
    n. Grisshammer R*, Grunwald T, and Sohal AK (2002) Characterization of an antibody Fv fragment that binds to the human, but not to the rat neurotensin receptor NTS-1. Protein Expression and Purification 24, 505-512
    o. White JF, Trinh LB, Shiloach J, and Grisshammer R* (2004) Automated large-scale purification of a G-protein-coupled receptor for neurotensin. FEBS Letters 564, 289-293
    p. Niebauer RT, White JF, Fei Z, and Grisshammer R* (2006) Characterization of monoclonal antibodies directed against the rat neurotensin receptor NTS1. Journal of Receptors and Signal Transduction 26, 395-415

q. Ho JTC, White JF, Grisshammer R, and Hess S* (2008) Analysis of a G protein-coupled receptor for neurotensin by liquid chromatography–electrospray ionization–mass spectrometry. Anal. Biochem. 376, 13-24; PMCID: PMC2628288
r. Xiao S, White JF, Betenbaugh MJ, Grisshammer R*, Shiloach J* (2013) Transient and stable expression of the neurotensin receptor NTS1: A comparison of the baculovirus-insect cell and the T-REx-293 expression systems. PLoS One, 8, e63679, PMCID: PMC3656039

2. My next set of publications addressed functional aspects of NTSR1 signaling.
   a. White JF, Grodnitzky J, Louis JM, Trinh LB, Shiloach J, Gutierrez J, Northup JK, and Grisshammer R* (2007) Dimerization of the class A G protein-coupled neurotensin receptor NTS1 alters G protein interaction. Proc. Natl. Acad. Sci. USA 104, 12199-12204; PMCID: PMC1913548
   b. Inagaki S, Ghirlando R, White JF, Gvozdenovic-Jeremic J, Northup JK, and Grisshammer R* (2012) Modulation of the interaction between neurotensin receptor NTS1 and Gq protein by lipid. J. Mol. Biol. 417, 95-111; PMCID: PMC3294418
   c. Inagaki S, Ghirlando R*, Grisshammer R* (2013) Biophysical Characterization of Membrane Proteins in Nanodiscs. Methods 59, 287-300; PMCID: PMC3608844
   d. Inagaki S, Ghirlando R, Vishnivetskiy SA, Homan KT, White JF, Tesmer JJG, Gurevich VV, Grisshammer R* (2015) G protein-coupled receptor kinase 2 (GRK2) and 5 (GRK5) exhibit selective phosphorylation of the neurotensin receptor *in vitro*. Biochemistry 54, 4320-4329; PMCID: PMC4512254
   e. Heitkamp T, Grisshammer R, Börsch M* (2018) Towards monitoring conformational changes of the GPCR neurotensin receptor 1 by single-molecule FRET. Conference Proceedings of SPIE Photonics West (International Society for Optics and Photonics), 27 January – 1 February 2018 in San Francisco, USA. Proc SPIE Int Soc Opt Eng. 2018 Jan-Feb;10498, Epub 2018 Feb 23; PMCID: PMC6044442

3. My third set of publications addressed structural aspects of NTSR1 signaling including conformational thermo-stabilization methods (in collaboration with Chris Tate, MRC-LMB, Cambridge, U.K.) and computational approaches (in collaboration with Nagarajan Vaidehi, City of Hope, Duarte, CA).
   a. Luca S, White JF, Sohal AK, Filippov DV, v. Boom JH, Grisshammer R*, and Baldus M* (2003) The conformation of neurotensin bound to its G-protein-coupled receptor. Proc. Natl. Acad. Sci. USA 100, 10706-10711; PMCID: PMC196868
   b. Shibata Y, White JF, Serrano-Vega MJ, Magnani F, Aloia AL, Grisshammer R*, and Tate CG* (2009) Thermostabilization of the neurotensin receptor NTS1. J. Mol. Biol. 390, 262-277; PMCID: PMC2696590
   c. White JF, and Grisshammer R* (2010) Stability of the neurotensin receptor NTS1 free in detergent solution and immobilized to affinity resin. PLoS One 5, e12579; PMCID: PMC2935352
   d. White JF, Noinaj N, Shibata Y, Love J, Kloss B, Xu F, Gvozdenovic-Jeremic J, Shah P, Shiloach J, Tate CG, Grisshammer R* (2012) Structure of the agonist-bound neurotensin receptor. Nature 490, 508-513, PMCID: PMC3482300
   e. Shibata Y, Gvozdenovic-Jeremic J, Love J, Kloss B, White JF, Grisshammer R*, Tate CG* (2013) Optimising the combination of thermostabilising mutations in the neurotensin receptor for structure determination. Biochim. Biophys. Acta Biomembranes 1828, 1293-1301; PMCID: PMC3582860
   f. Niesen MJM, Bhattacharya S, Grisshammer R, Tate CG, Vaidehi N* (2013) Thermostabilization of the β_1-adrenergic receptor correlates with increased entropy of the inactive state. The Journal of Physical Chemistry B 117, 7283-7291; PMCID: PMC3718486
   g. Lee S, Bhattacharya S, Grisshammer R, Tate C, Vaidehi N* (2014) Dynamic behavior of the active and inactive states of the adenosine A2a receptor. The Journal of Physical Chemistry B 118, 3355-3365; PMCID: PMC3983344
   h. Bhattacharya S, Lee S, Grisshammer R, Tate CG, Vaidehi N* (2014) Rapid computational prediction of thermostabilizing mutations for G protein-coupled receptors. Journal of Chemical Theory and Computation 10, 5149-5160; PMCID: PMC4230369
   i. Lee S, Bhattacharya S, Tate CG, Grisshammer R, Vaidehi N* (2015) Structural dynamics and thermostabilization of neurotensin receptor 1. The Journal of Physical Chemistry B 119, 4917-4928; PMCID: PMC4564841

j. Krumm BE, White JF, Shah P, Grisshammer R* (2015) Structural prerequisites for G protein activation by the neurotensin receptor. Nature Communications 6, article 7895; PMCID: PMC4515772
k. Krumm BE, Lee S, Bhattacharya S, Botos I, White CF, Du H, Vaidehi N, Grisshammer R* (2016) Structure and dynamics of a constitutively active neurotensin receptor. Scientific Reports 6, 38564; PMCID: PMC5141500
l. Lee S, Mao A, Bhattacharya S, Robertson N, Grisshammer R, Tate CG*, Vaidehi N* (2016) How do short chain non-ionic detergents destabilize GPCRs? Journal of the American Chemical Society 138, 15425-15433; PMCID: PMC5148649
m. Nehmé R, Carpenter B, Singhal A, Strege A, Edwards PC, White CF, Du H, Grisshammer R, Tate CG* (2017) Mini-G proteins: Novel tools for studying GPCRs in their active conformation. PlosOne 12, e0175642; PMCID: PMC5398546
n. Grisshammer R* (2019) Structural and mechanistic insights into the neurotensin receptor. Henry Stewart Talks. Recorded July 2018. To be released 2019.

4. Reviews and Editorials
   a. Grisshammer R*, and Tate CG* (1995) Overexpression of integral membrane proteins for structural studies. Quarterly Reviews of Biophysics 28, 315-422
   b. Tate CG*, and Grisshammer R* (1996) Heterologous expression of G-protein-coupled receptors. Trends in Biotechnology 14, 426-430
   c. Grisshammer R* (1997) The art of the insoluble: Membrane protein isolation. Biotech Link (Link Biotechnology Programmes) 2, 4
   d. Grisshammer R*, White JF, Trinh LB, and Shiloach J (2005) Large-scale expression and purification of a G-protein-coupled receptor for structure determination – an overview. Journal of Structural and Functional Genomics 6, 159-163
   e. Grisshammer R* (2006) Understanding recombinant expression of membrane proteins. Current Opinion in Biotechnology 17, 337-340
   f. Grisshammer R* (2013) Editorial: Why we need many more GPCR structures. Expert Review of Proteomics 10, 1-3; PMCID: PMC4298122
   g. Krumm BE, Grisshammer R* (2015) Invited review: Peptide ligand recognition by G protein-coupled receptors. Frontiers in Pharmacology (Experimental Pharmacology and Drug Discovery) 6:48, PMCID: PMC4360564
   h. Vaidehi N*, Grisshammer R, Tate CG (2016) Invited review: How can mutations thermostabilize G-protein-coupled receptors? Trends in Pharmacological Sciences 37, 37-46, PMCID: PMC4698185
   i. Grisshammer R* (2017) Invited review: New approaches towards the understanding of integral membrane proteins – A structural perspective on G protein-coupled receptors. Protein Science 26, 1493-1504, PMCID: PMC 5521582
   j. Ognjenović J, Grisshammer R, Subramaniam S* (2019) Invited review: Frontiers in cryo electron microscopy of complex macromolecular assemblies. Annual Review of Biomedical Engineering 21, 395-415, PMCID:

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/pubmed?term=Grisshammer%20r

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support
Intramural Research Program of the National Institutes of Health

Completed Research Support
Intramural Research Program of the National Institutes of Health