CURRICULUM VITAE

1. PERSONAL INFORMATION

Name: Piergiorgio Percipalle, PhD, Associate Professor
[redacted]

2. SCIENTIFIC INTERESTS

Nuclear actin and myosin, gene expression regulation (transcription, assembly of ribonucleoprotein complexes, mRNA transport and localization), cell fate and identity

3. PhD EXAMINATION

1995/01/27, Philosophy Doctor (PhD)
International School for Advanced Studies, Trieste Italy
Laboratory of Protein Structure and Function, International Centre for Genetic Engineering and Biotechnology, Trieste, Italy
Area: Molecular analysis of protein-DNA interactions in vitro and in vivo
Supervisor: Prof. Sandor Pongor

4. PHD RESEARCH TRAINING

1991/01 - 1995/01
PhD training laboratory
Protein Structure and Function, International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

5. POSTDOCTORAL WORK

1995/02/01 – 1998/08/31
MRC Laboratory of Molecular Biology, Structural Studies Division, Cambridge UK
Supervisor: Dr Daniela Rhodes
Area: Molecular mechanisms of nucleocytoplasmic transport

1998/09/01 – 2001/12/31
Department of Cell and Molecular Biology, Karolinska Institute, Stockholm Sweden
Supervisor: Prof. Bertil Daneholt
Area: Transcriptional and post-transcriptional regulation of gene expression

6. CURRENT POSITION

2010/01/01 - present
Associate Professor, Department of Cell and Molecular Biology, Karolinska Institute.

I spend most of the time in research and teaching activities and I am also involved in administration.

Research budget supported since 2003 by competitive grants awarded by Swedish Research Council (Vetenskapsrådet) and Swedish Cancer Research Society (Cancerfonden).

7. PREVIOUS POSITIONS

2004/01/01- 2009/12/31
Principal Investigator supported by an external grant from the Swedish Research Council, Department of Cell and Molecular Biology, Karolinska Institute, Stockholm Sweden - Budget supported by grants from Swedish Research Council and Swedish Cancer Research Society.

2002/01/01- 2003/12/31
Researcher and team leader, Department of Cell and Molecular Biology, Karolinska Institute, Stockholm Sweden - Budget supported by grants from Swedish Research Council and Swedish Cancer Research Society.

Sabbatical stays

2009 May-Aug
Sabbatical stay, Institute of Molecular and Cell Biology, Agency for Science, Technology, and Research (A*STAR) 61 Biopolis Drive, Proteos, Singapore 138673
Affiliation: Laboratory of Dr. Robert C. Robinson
Project: Identification of the nuclear actin proteome by a combination of affinity chromatography, mass spectrometry and SILAC - stable isotope labelling with amino acids in cell culture

8. SUPERVISION

Doctoral students who have graduated under my direct supervision

Ales Obrdlik, June 2010 (current position: postdoc, EMBL, Heidelberg)
Chandrasekhar Raju, June 2011 (current position: postdoc, UCSF, San Francisco, USA)
Aishe Sarshad, June 2014 (current position: postdoc, NIH, Bethesda, USA)

Main supervisor of doctoral students currently working in my lab

Bader Al-Muzzaini, registered Feb. 2012, graduation expected in 2016

Co-supervisor of doctoral students

Varsha Prakash (main supervisor: Dr. Theresa Vincent, Karolinska Institute)
Fosco Giordano (main supervisor: Dr. Lena Ström, Karolinska Institute)

External mentor of doctoral students

Manizheh Izadi (main supervisor: Dr. Jorge Ruas, Karolinska Institute)

Postdocs (names and years)

Present
Magnus Hansson (2014 -)
Ghasem Nurani (2014 -)
Kari-Pekka Skarp (joining in 2015 -)

Past
Alexander Kukalev (2003-2006)
Emilie Louvet (2006-2010)
Nanaho Fukuda (2008-2013)
Galina Bartish (2013)

9. INDIVIDUAL AWARDS AND DISTINCTION

Awards
2006: The Svedberg Prize, awarded by The Swedish Society for Biochemistry and Molecular Biology (SFBM) and The Royal Swedish Academy of Sciences
2006: The UNESCO Prize "Città di Trapani"
2003: 6-year award as Senior Investigator (Rådforskare), Swedish Research Council (Vetenskapsrådet). Area of expertise, "Functional Architecture of the Cell Nucleus"
2000: Blanceflor-Ludovisi research fellowship
1998: EC Marie Curie post-doctoral research fellowship (1998-2000)
1995: EMBO long-term postdoctoral research fellowship (1995-1997)

10. SERVICE TO THE PROFESSION

Organization of international conferences

2015 Member of organizing committee, Wenner Gren Symposium **"Nuclear dynamics: design and principles"**, Stockholm, approved for August 2015

Co-organizers: Prof. Neus Visa and Ann-Kristin Östlund (Stockholm University), Prof. Maria Vartiainen (University of Helsinki, Finland)

2014 Member of organizing committee, Special Interest Subgroup "**Nucleoskeletal Dynamics in Signaling and Gene Expression**", American Society for Cell Biology 2014 Meeting, Philadelphia,

Co-organizer: Prof. Richard Anderson (University of Wisconsin)

2011 Member of organizing committee, Wenner Gren Symposium **"Actin and actin-associated proteins from gene to polysomes"**, Stockholm, September 2011

Co-organizers: Prof. Neus Visa and Ann-Kristin Östlund (Stockholm University), Prof. Thoru Pederson (UMASS, Medical School, Worcester, USA)

Editorial tasks

2013-2014 Guest Editor for a special issue of "Seminars Cell and Developmental Biology" on RNA Biogenesis (Vol 32, August 2014, ISSN 1084-9521)

2014 Guest Associate Editor, PLOS Genetics

2010-present Appointed member of the editorial board, "Nucleus" (Landes Biosciences)

Commissions of trust

2006 - Appointed reviewer for the Swedish Research Council evaluation board for research funding in the area of cell and molecular biology (6 years)
2007 - Ad hoc reviewer for Swedish Research Council, areas of Biochemistry and Biophysics, Sub-atomic Physics and for post-doctoral grants
2007 - Ad hoc reviewer for Norwegian Research Council, area of functional genomics
2008 - Ad hoc reviewer for the Swiss Research Council
2008 - Ad hoc reviewer for Cancer Research UK
2010 - Ad hoc reviewer for the Czech Science Foundation
2011 - Ad hoc reviewer for BBSRC, UK
2010-present - Reviewer for the Lundbeck Foundation, Denmark
2014 - Ad hoc reviewer for Wellcome Trust, UK
2015 - Ad hoc reviewer for BBSRC, UK

Ad hoc reviewer for the following journals:

Reviewer for many scientific journals, including Nature Cell Biology, Nature Rev Mol Cell Biol, Nature Methods, Nature Protocols, PLOS Genetics, Journal of Biological Chemistry, Journal of Cell Biology, Molecular Systems Biology, Mol Cell Proteomics, Experimental Cell Research, Nucleic Acids Research, Journal of Cell Sciences, PLOS One, Cytoskeleton

University, medical school and departmental committees

2010 - present Member of departmental seminars committee, Department of Cell and Molecular Biology, Karolinska Institute
2010 - 2012 Evaluation committee for the Karolinska Institute Doctoral (KID) Program for funding of graduate students
2009 - 2011 Appointed member of the departmental advisory board
2010 - present Ad hoc member of more than 10 PhD students admission committees
2005 - 2008 Appointed member of the department environmental working group

Service on dissertation committees

2014 Opponent, PhD student defense of Joseph Dopie (supervisor: Maria Vartiainen), University of Helsinki, Finland
2011 External examiner, PhD student defense of Michael A. Johnson (supervisor: Beric Henderson), University of Sydney, Australia

2005 - 2014 Member of 8 mid-term evaluation boards and 13 PhD dissertation committees, KI; member of 3 PhD dissertation committees, Stockholm University; member of 1 PhD dissertation committee, Uppsala University

Selected invited lectures and participations in national and international conferences

Invited speaker, 2015 ASTAR Bioinformatics Institute, Singapore
Invited speaker, 2014 Annual Meeting of the American Society for Cell Biology, December 2014, Philadelphia, USA
Invited speaker, 2014 Institute of Biotechnology, University of Helsinki, Finland
Invited speaker, 2014 Faculty of Biology, Ney York University, NY, USA
Invited speaker, 2013 Ecole Polytechnique, Paris, France
Invited speaker, 2011 Annual Meeting of the American Society for Cell Biology, 3-7 December 2011, Denver, USA
Invited speaker, International Centre for Genetic and Biotechnology, Feb 2011, Trieste, Italy
Invited speaker, University of Bergen, Department of Biosciences, Dec 2010, Bergen, Norway
Invited speaker, 2008 Annual Meeting of the American Society for Cell Biology, 13-17 December 2008, San Francisco, USA
Invited speaker, Workshop on Computational Systems Biology Approaches to Analysis of Genome Complexity and Regulatory Gene Networks 19 – 26 Nov 2008, National University of Singapore and Bioinformatic Institute, Singapore
Invited speaker, 33rd FEBS Congress, 28 June – 3 July 2008, Athens, Greece
Invited speaker, The 3rd Symposium "Nuclear structure and function", 17 Dec 2007, Centre for Biochemistry and Cell Biology, Nottingham University, UK
Speaker, The 20th Wilhelm Bernhard Workshop, International Conference on the Cell Nucleus, St. Andrews, 27 – 31 August, 2007
Invited speaker, Conference on "Computational methods in biomolecular structures and interaction networks", 9 Jul – 3 Aug 2007, Institute for Mathematical Sciences, National University of Singapore and Genome Institute of Singapore
Invited speaker, Czech Academy of Science, Institute of Experimental Medicine, Prague, January 2007
Invited speaker, Biozentrum, University of Basel, Basel 31 October 2006
Invited speaker, The 29th Annual Meeting of the German Society for Cell Biology, Braunschweig, 29 March – 1 April, 2006
Invited speaker at the Symposium "Figuring out life: Application of mathematics to medicine", 28-29 Nov 2005, Institute for Mathematical Sciences, National University of Singapore, Singapore
Invited speaker, Department of Biomedical Sciences, National University of Singapore, Singapore, 24 Nov 2005
Speaker at the EMBO/FEBS Conference on "Nuclear Structure and Dynamics", La Grande Motte, 24 –28 Sept, 2005
Invited speaker, German Cancer Research Centre, Heidelberg, 8 Sept 2005
Speaker, EMBO/FEBS Workshop on "The functional Organization of the Cell Nucleus", Prague, 18 – 21 April, 2002
Speaker, FASEB Summer Research Conference on "Post-transcriptional Control of Gene Expression: Effectors of mRNA Decay", Tucson, 6 – 11 July, 2002
Speaker, EMBO Workshop on "Signal-regulated nuclear transport", Strasburg, 11 – 14 August, 2001

Speaker, Cold Spring Harbor Laboratory Conference on "Dynamic Organization of Nuclear Function", Cold Spring Harbor, 13 – 17 Sept, 2000

Memberships

Member of the American Society for Cell Biology

11. TEACHING ACTIVITIES

Formal Pedagogical Training

In 2005 I was awarded the academic title of Associate Professor of Cell Biology. The formal requirements are a minimum number of peer-reviewed scientific publications in the field and formal pedagogic training offered by Karolinska Institute, along with relevant examinations. Diplomas and certificates are available on request.

Direct supervision of current and past group members

I have supervised 6 postdoctoral fellows (3 are former lab members), 4 PhD students (three of them have already graduated in 2010, 2011 and 2014, respectively), 6 undergraduate students (BSc or MSc students) and 1 medical student all from 10 different nationalities (including Japanese, Italian, French, German, Swedish, Russian, Indian, Dutch, Iranian and Saudi).

Teaching

• Undergraduate teaching

2008-present	Lecturer of Cell Biology in the Karolinska Institute Biomedical Research School
2005-2007	Lecturer of Cell Biology in the Karolinska Institute Medical School
2003-2004	Lecturer of Cell Biology in the Karolinska Institute Biomedical Research School
2003-2004	Lecturer of Cell Biology in the Royal Institute of Technology (KTH, Kungliga Tekniska Högskolan)

• Graduate teaching

2006-2012	Organizer and main lecturer of elective course for graduate students, "Molecular localization by immunofluorescence and confocal microscopy" (27 Nov - 8 Dec 2006, 15-26 February 2010, 18-30 October 2010, 21 Nov - 2 Dec 2011), Department of Cell and Molecular Biology, Karolinska Institute, Stockholm
24-30 Nov 2010	Lecturer, Joint Karolinska Institute-RIKEN course for graduate students, Functional Organization of the Cell Nucleus, Yokohama, Japan
2004-2006	Organizer and lecturer in Core Curriculum course, "The Cell Nucleus – Part I", mandatory for PhD students, Department of Cell and Molecular Biology, Karolinska Institute
8-16 April 2003	Organizer and main lecturer of elective course for graduate students, "*In vivo* Analysis of Protein-Protein Interactions", Department of Cell and Molecular Biology, Karolinska Institute, Stockholm

15-25 Nov 2004 Organizer and main lecturer of elective course for graduate students, "Experimental Methods in Cell and Molecular Biology", Department of Cell and Molecular Biology, Karolinska Institute, Stockholm

18-23 Nov 2005 Lecturer in the course on "Bioinformatics for molecular medicine and cell biology with advanced current topics", National University of Singapore, Department of Biological Sciences, Singapore

Course development and the administration of education

2005 - 2006 Appointed member of the Course Advisory Board (kursråd) for medical students at the Karolinska Institute, Stockholm

Pedagogic work and teaching material

For undergraduates, I am involved in the preparation of exam questions.

Among the main tasks in the organization of courses for graduate students, I have prepared several types of compendia including course description, literature and collections of experimental protocols.

Assessment of pedagogic activities

In general, I have received very good evaluations from graduate and undergraduate students who have followed my courses. For a formal evaluation of my pedagogic activities, a certificate can be obtained from Dr. Matti Nikkola, Dean of Graduate and Undergraduate Studies, Department of Cell and Molecular Biology, Karolinska Institute.

LIST OF PEER REVIEWED PUBLICATIONS

Annotations are provided for those publications which are most relevant for my present and future research activities. The asterisk (*) denotes corresponding/senior authorship.

1) Al-Muzzaini B, Sarshad AA, Corcoran M, Östlund A-K, Percipalle P*. (2014) Nuclear myosin 1 contributes to a chromatin landscape compatible with RNA polymerase II transcription activation. BMC Biology, final revision

Using ChIP-Seq in combination with molecular analyses, here we investigated the global association of nuclear myosin 1 (NM1) with the mammalian genome. We show that NM1 binds to both intergenic and genic regions with occupancy peaks at class II gene promoters, correlating with distributions of RNA Polymerase II (Pol II) and active epigenetic marks. We show that NM1 synergizes with polymerase-associated actin to maintain active Pol II at gene promoters. NM1 also co-localizes with the nucleosome remodeler SNF2h at class II promoters where they assemble together with WSTF as part of the B-WICH complex. A high resolution micrococcal nuclease (MNase) assay and quantitative real time PCR shows that this mechanism is required for local chromatin remodeling. Following B-WICH assembly, NM1 mediates physical recruitment of the histone acetyl transferase PCAF and the histone methyl transferase Set1/Ash2 to maintain and preserve H3K9acetylation and H3K4trimethylation for active transcription. We propose a novel genome-wide mechanism where myosin synergizes with Pol II-associated actin to link the polymerase machinery with permissive chromatin for transcription activation.

2) Sarshad AA, Corcoran M, Al-Muzzaini B, Borgonovo-Brandter L, Von Euler A, Lamont D, Visa N, Percipalle P*. (2014) Glycogen synthase kinase (GSK) 3β phosphorylates and protects nuclear myosin 1c from proteasome-mediated degradation to activate rDNA transcription in early G1 cells. PLoS Genet 10(6): e1004390. doi:10.1371/journal.pgen.1004390

In this study, we conducted a genome-wide screen and demonstrated that GSK3β is selectively coupled to the rDNA transcription unit. GSK3β specifically phosphorylates serine 1020 in the NM1 C-terminus and suppresses NM1 degradation through the ubiquitin-proteasome system, facilitates NM1 association with the rDNA chromatin and consequently, transcription activation at G1. We therefore propose a novel and fundamental role for GSK3β as essential regulator of rRNA synthesis and cell cycle progression through direct regulation of the actomyosin complex across the rDNA transcription unit.

3) Percipalle P*. (2014) New insights into co-transcriptional sorting of mRNA for cytoplasmic transport during development. Sem Cell Dev Biol 32: 55-62 (doi: 10.1016/j.semcdb.2014.03.009)

In this review we propose a working model on how actin may mediate co-transcriptional assembly of ribonucleoprotein (RNP) complexes. Since actin is not an RNA binding protein, the hypothesis is that it is tethered to the nascent transcript by the RNA binding hnRNP CBF-A/hnrnpab. We hypothesize that this mechanism promotes a translationally silent state of the newly synthesized transcript. This in turn sorts the transcript for cytoplasmic transport and localization vs immediate translation.

4) Percipalle P*. (2014) mRNA biogenesis, from the gene to polysomes. Sem Cell Dev Biol 32:1 (doi: 10.1016/j.semcdb.2014.04.028)

This is an editorial article that was submitted to introduce the issue on RNA biogenesis that I guest-edited for Seminars in Cell and Developmental Biology. It provides a broad view on the pathway that leads to the production of mRNA molecules and their transit from gene to polysomes where they are ultimately translated.

5) Sarshad AA, Percipalle P*. (2014) New insight into role of myosin motors for activation of RNA polymerases. Int Rev Cell Mol Biol. 2014;311:183-230. doi: 10.1016/B978-0-12-800179-0.00004-0.

In this review/book chapter, we discuss how actin-based myosin motors are believed to function in the context of RNA polymerase mediated transcription. We place these recent observations in the context of what is broadly known about myosin function in the cytoplasm. We also anticipate the emerging importance of genome-wide studies to investigate how and why motor proteins interact with the genome.

6) Fukuda N, Fukuda T, Sinnamon J, Raju CS, Izadi M, Czaplinski K, Percipalle P* (2013) The transacting factor CBF-A targets protamine 2 mRNA 3'UTR via the A2RE/RTS cis-acting element to regulate stage-specific translation during mouse spermatogenesis. PLoS Genet 9: e1003858

During eukaryotic gene expression, a fraction of newly exported mRNA molecules is transported to the cellular periphery for translation. The underlying mechanisms are not fully understood even though they likely affect specialized functions in many cell types including oligodendrocyets, neurons and germ cells. In previous work, we discovered that the heterogeneous nuclear ribonucleoprotein CBF-A, interacts with a conserved sequence, the RNA trafficking sequence (RTS), located in the untranslated region of transported mRNAs. This interaction facilitates transport of myelin basic protein mRNA (Raju et al., 2008) and dendritic mRNAs in oligodendrocytes and neurons (Raju et al., 2011), respectively. In this study we investigated whether RTS-recognition by CBF-A coordinates transport and localized translation of the Protamine 2 mRNA in spermatogenic cells. In this study, we show that during spermatogenesis the Protamine 2 mRNAs is synthesized and kept in a silent form to be translated at later stages. We show that by interacting with the RTS of the Protamine 2 mRNA both CBF-A isoforms, p37 and p42, contribute to regulate the transcript at the translational level. In a CBF-A knockout mouse model, we demonstrate that the interplay between the CBF-A isoforms in translation regulation of the Protamine 2 mRNA and other testicular transcripts has an impact on spermatogenesis.

7) Sarshad A, Sadeghifar F, Louvet E, Mori R, Böhm S, Vintermist A, Fomproix N, Östlund A-K, Percipalle P* (2013) Nuclear myosin 1 facilitates chromatin modifications required to activate rRNA gene transcription and cell cycle progression. PLoS Genetics 9: e1003397

In this study we show evidence that nuclear myosin 1c (NM1), by interacting with polymerase-associated actin and chromatin, has an essential structural role connecting the RNA polymerase I with the rDNA chromatin. We also show that NM1 facilitates assembly of the chromatin remodeling complex WICH and recruitment of the HAT PCAF for histone acetylation. Whether NM1 binds to actin or to the chromatin remodelling complex depends on the motor function of the myosin. We demonstrate that this mechanism is important for

transcription activation and cell cycle progression at the exit of mitosis. In this study we also start discussing the idea that NM1 is a proliferative factor which is one of the main points of my future research activities.

8) Percipalle P* (2013) Co-transcriptional nuclear actin dynamics. Nucleus 4: 43-52

In this review article I discuss how actin is implicated throughout the RNA polymerase II transcriptional cycle. I focus on the importance of actin in assembly of the pre-initiation complex, and later on in the establishment of transcription-competent polymerase during promoter clearance. I also bring forward the novel and testable hypothesis that actin undergoes co-transcriptional polymerization through a treadmilling mechanism.

9) Obrdlik A, Percipalle P* (2011) The F-actin severing protein cofilin-1 is required for RNA polymerase II transcription elongation. Nucleus 2: 72-79 [Faculty of 1000, exceptional interest]

In this study we showed for the first time that the F-actin severing protein cofilin involved in the regulation of actin polymerization by treadmilling is also required for RNA polymerase II transcription elongation. We found that cofilin ineteracts with the RNA polymerase II machinery by directly targeting the polymerase-bound actin. We demonstrated that in cells where the cofilin gene was silenced by RNAi, protein coding genes were found to be devoid of actin and RNA polymerase II. Since we found that cofilin is excluded from the gene promoter by chromatin immunoprecipitation, in view of the known function of cofilin in the treadmilling of actin polymers we proposed that controlled actin polymerization accompanies the elongating polymerase during synthesis of nascent mRNA transcripts.

10) Raju C, Fukuda N, Lopez-Iglesias C, Göritz C, Visa N, Percipalle P* (2011). In neurons, activity dependent association of dendritically transported mRNA transcripts with the transacting factor hnRNP CBF-A is mediated by A2RE/RTS elements. Mol Biol Cell 22: 1864-1877

We discovered that in oligodendrocytes the actin-binding hnRNP CBF-A binds the RNA trafficking sequence (RTS) in the 3'UTR of the myelin basic protein (MBP) mRNA (see below Raju et al., 2008). In the present study we demonstrate that CBF-A binds to the conserved RTS in the UTR of certain dendritic transcripts. In hippocampal neurons RTS recognition by CBF-A occurs co-transcriptionally and leads to the establishment of a transport-competent configuration of the transcripts that are transported to synapses in a manner that is dependent on post-synaptic receptor stimulation. Follow up to these discoveries is the observation that CBF-A binds also to the conserved RTS in the UTR of the protamine 2 mRNA in spermatogenic cells and this mechanism has a huge impact on sperm cells development (see Fukuda et al. 2013).

11) Percipalle P*, Louvet E (2011) In vivo run-on assays to monitor nascent precursor RNA transcripts. Meth Mol Biol 809: 519-533

12) Vintermist A, Böhm S, Sadeghifar F, Louvet E, Mansén A, Percipalle P, Östlund Farrants A-K. (2011) The chromatin remodelling complex B-WICH changes the chromatin structure and recruits histone acetyl-transferases to active rRNA genes. PLOS One 6: e19184

13) Visa N, Percipalle P* (2010) Nuclear functions of actin. Cold Spring Harb Perspect Biol doi: 10.1101/cshperspect.a000620

In this review we discuss how actin cooperates with a number of nuclear proteins, including heterogeneous nuclear ribonucleoproteins (hnRNPs) and nuclear myosin species, to regulate transcription during gene expression. This review article is also part of a book entitled "The Nucleus", edited by D. Spector and T. Misteli.

14) Obrdlik A, Louvet E, Kukalev A, Naschekin D, Kiseleva E, Fahrenkrog B, Percipalle P* (2010) Nuclear myosin 1 is in complex with mature rRNA transcripts and associates with the nuclear pore basket. FASEB J 24: 146-157 [Highlighted in Simon and Wilson, 2011, Nature Rev Mol Cell Biol]

This article shows for the first time that actin and myosin play a role during processing of newly synthesized rRNA transcripts. We found that they are specifically required during maturation of the 36S precursor rRNA into the 28S transcript, an important step that is propaedeutic to the formation of the large ribosomal subunit. We also show evidence that actin and NM1 remain incorporated in the large ribosomal subunit and accompany it to the basket of the nuclear pore complex. Our findings here suggest that during rRNA biogenesis, an actomyosin complex is not only required co-transcriptionally during the synthesis of precursor rRNA (see Fomproix and Percipalle, 2004; Percipalle et al., 2006; Percipalle and Östlund Farrants, 2006) but it is also required posttranscriptionally to facilitate assembly of export competent ribosomal subunits.

15) Percipalle P*, Obrdlik A (2009) "RNA immunoprecipitation: a method to study chromatin-associated nascent RNA transcripts. Methods Mol Biol 567: 215-235

16) Ameyar-Zazoua M, Souidi M, Fritsch L, Robin P, Thomas A, Hamiche A, Percipalle P, Ait-Si-Ali S, Harel-Bellan A. (2009) Physical and functional interaction between Heterochromatin Protein 1 alpha and the RNA binding protein hnRNP U. J Biol Chem. 284: 27974-27979

17) Louvet E, Percipalle P* (2009) The role of actin and myosin in gene transcription. Int Rev Cell Mol Biol 272: 107-147

18) Percipalle P* (2009) The long journey of actin and actin-associated proteins from gene to polysomes. Cell Mol Life Sci 66: 2151-2165

In this review article I discuss the discovery that actin is a key regulator of RNP biogenesis. Based on our discoveries that actin is occupies transcription sites in an RNA-dependent manner (see Percipalle et al., 2001) and actin is directly involved in mRNA synthesis (Kukalev et al., 2005), I propose testable models on how actin can be involved in transcription regulation and in the co-transcriptional assembly of nascent RNP particles. I also discuss for the first time the possibility that signalling mechanisms regulate the basal functions of actin in the cell nucleus.

19) Percipalle P*, Raju CS, Fukuda N (2009) Actin-associated hnRNP proteins as transacting factors in the control of mRNA transport and localization. RNA Biology 6: 171-174

Following up our discovery that the actin binding hnRNP protein CBF-A interacts with the RNA trafficking sequence in the 3'UTR of the myelin basic protein mRNA in oligodendrocytes (see Raju et al., 2008), in this review article we start speculating on how the actin-CBF-A interaction may be important in assembly transport competent RNPs.

20) Kukalev AS, Lobov IB, Percipalle P, Podgornaya OI. (2009) SAF-A/hnRNP U localization in interphase and metaphase. Cytogenet Genome Res. 124: 288-297

21) Vincent T, Kukalev A, Andäng M, Pettersson R, Percipalle P* (2008) RAS-dependent inhibition of RNA polymerase I transcription by the glycogen synthase kinase (GSK) 3□. Nat Oncogene 27: 5254-5259

In this article we present the first evidence that upon oncogenic H-RAS transformation the glycogen synthase kinase GSK 3 β accumulates into nucleoli and targets RNA polymerase I-specific transcription factors to repress synthesis of rRNA. We found that this inhibitory mechanism also led to a delay in the cell cycle progression and decresed cell growth and proliferation. We concluded that GSK3 β functions as tumour suppressor in transformed cells (see also the recent insightful review article by Drygin et al., 2010 where our work is placed in context of tumour development). We now know that GSK3 β also has a basal regulatory function in RNA polymerase I transcription in non-transformed cells (see Sarshad et al., 2014).

22) Obrdlik A, Kukalev A, Louvet E, Östlund Farrants A-K, Caputo L, Percipalle P* (2008) The histone acetyl transferase PCAF associates with actin and hnRNP U for efficient RNA polymerase II transcription. Mol Cell Biol 28: 6342-6357

In this study we showed for the first time that actin interacts with the hnRNP protein hnRNP U to recruit the histone acetyl transferase (HAT) PCAF. This mechanism occurs after promoter clearance and it is required for histone H3K9 acetylation, which in turn leads to the establishment of permissive chromatin for transcription activation.

23) Raju CS, Göritz C, Nord Y, Hermanson O, Lopez-Iglesias C, Visa N, Catselo-Branco G, Percipalle P* (2008) In cultured oligodendrocytes the A/B type hnRNP CBF-A accompanies MBP mRNA bound to mRNA trafficking sequences. Mol Biol Cell 19: 3008-3019

In this primary research article we demonstrate that the actin binding hnRNP CBF-A is a novel transacting factor required for trafficking of the myelin basic protein mRNA in mouse oligodendrocytes. CBF-A performs its functionby specifically targeting the RNA trafficking sequence (RTS) in the 3'UTR of the MBP mRNA. The interaction occurs co-transcriptionally and CBF-A accompanies the MBP mRNA transcript from gene to myelin compartment in mouse oligodendrocytes. We have been able to show that the role of CBF-A for RTS dependent trafficking is conserved in neurons and spermatogenic cells where it has an impact on development (see Raju et al., 2011; Fukuda et al., 2013).

24) Obrdlik A, Kukalev A, Percipalle P* (2007) The function of actin in gene transcription. Histology and Histopathology 22: 1051-1055

25) Percipalle P* (2007) Genetic connections of the actin cytoskeleton and beyond. BioEssays 29: 407-411

26) Percipalle P*, Visa N (2006) Molecular functions of nuclear actin. J Cell Biol, 172: 967-971

In this review article, we proposed for the first time testable models on how actin could be incorporated into nascent RNPs. We discuss the possibility that this mechanism si also mediated by the phosphorylated carboxy-terminal domain of the RNA polymerase II largest subunit. We also discuss how actin in complex with specific hnRNP proteins may facilitate recruitment of HATs (see Percipalle et al., 2003; Kukaklev et al., 2005; Obrdlik et al., 2008) to set a chromatin configuration compatible with transcription activation/elongation.

27) Percipalle P*, Östlund Farrants A-K (2006) Chromatin remodelling and transcription: be-WICHed by nuclear myosin 1. Curr. Opin. Cell. Biol. 18: 267-274

In this review article we proposed the first model for the involvement of the actomyosin complex in RNA polymerase I transcription activation. We proposed that nuclear myosin 1 functions as structural switch that is important to recruit the chromatin remodeling complex WICH with the subunits SNF2h and WSTF to the rDNA. This model was proposed based on the papers by Percipalle et (2006) and Fomproix and Percipalle (2004) (see below). The model proved correct, as demonstrated in the recent PLoS Genetics paper (2013) where we indeed found that NM1 is a structural protein connecting polymerase with the chromatin.

28) Percipalle P*, Fomproix N, Cavellan E, Voit R, Reimer G, Krüger T, Thyberg J, Scheer U, Grummt I, Östlund Farrants A-K (2006) The chromatin remodelling complex WSTF-SNF2h interacts with nuclear myosin 1and serves a role in RNA polymerase I transcription. EMBO Reports 7: 525-530

[Faculty of 1000, recommended]

In this paper we discovered that nuclear myosin 1 (NM1) is a component of the multiprotein assembly B-WICH together with the ATPase SNF2h and WSTF. We also showed that NM1 occupies both promters and transcribed sequences across the rDNA transcriptin unit and together with WSTF and SNF2h it is important for the post-initiation phase of RNA polymerase I (pol I) transcription. This study is a continuation of an earlier study (Fomproix and Percipalle, 2004) where we provided the first evidence ever that an actin-myosin interaction is required for pol I transcription. In that paper we showed that NM1 is in actively transcribing nucleolar foci in both interphase and late mitotic cells when transcription is reactivated. Furthermore we demonstrated that actin and NM1 are physically in contact with the pol I machinery.

29) Cavellan E, Asp M, Percipalle P, Östlund Farrants A-K (2006) The chromatin remodelling complex WSTF-SNF2h interacts with several nuclear proteins in transcription. J Biol Chem 281: 16264-16271

30) Percipalle P* (2006) Actin in transcription. Eur J Cell Biol 85S1: 46-47

31) Kukalev A, Nord Y, Palmberg C, Bergman T, Percipalle P* (2005) Actin and hnRNP U cooperate for productive transcription by RNA polymerase II. Nature Struct Mol Biol 12: 238-244

In this primary research article we demonstrated that the interaction between actin and the hnRNP protein hnRNP U is important for transcription by RNA plymerase II. We showed evidence that acti interacts with hnRNP U through a novel actin binding motif. In addition, this study provided first evidence that the actin-hnRNP U complex is physically associated with the hyperphosphorylated form of the RNA polymerase II, further supporting the view that actin and hnRNP U interact to facilitate activation and elongation of nascent mRNA. This paper gives the first glimpse on the direct role of an actin-hnRNP interaction in the RNA polymerase II commitment to transcription elongation.

32) Kukalev A, Podgornaya O, Percipalle P (2004) Fusion of GFP to separate SAF-A/hnRNP U domains confirm computer analysis of the SAF-A domain structure. Chromosome Research 12: 32

33) Fomproix N, Percipalle P* (2004) An actin-myosin complex on actively transcribing genes. Exp Cell Res 294: 140-148 [Highlighted in Grummt I, 2006, Current Opinion in Genetics and Development]

In this primary research article we demonstrated for the first time that an actin-myosin complex localizes to nucleolar transcription sites in both interphase and late mitotic cells when RNA polymerase I is reactivated. We also showed evidence that actin and myosin are in complex with the RNA polymerase I largest subunit and they are necessary for transcription activation. Finally, we show evidence that the role of the actomyosin complex in RNA polymerase I transcription activation is dependent on the myosin ATPase activity. These results opened up the possibility that actin-based myosin motors are required for transcription activation.

34) Percipalle P, Fomproix N, Kylberg K, Miralles M, Björkroth B, Daneholt B, Visa N (2003) An actin-ribonucleoprotein interaction is involved in transcription by RNA polymerase II. Proc. Natl. Acad. Sci. USA 100: 6475-6480

In this study we provided first evidence that an actin-ribonucleoprotein interaction is required for RNA polymerase II transcription. We discovered that in the dipteran Chironomus tentans actin interacts with the hnRNP protein hrp65-2 through a novel actin binding motif that later was found to be conserved in the mammalian hnRNP U protein (see Kukalev et al., 2005).

35) Percipalle P, Jonsson AP, Nashchekin D, Bergman T, Guialis A, Daneholt B (2002) Actin is associated with a specific subset of hnRNP proteins and transferred with mRNA into the cytoplasm. Nucl. Acid Res. 30: 1725-1734

36) Percipalle P, Zhao J, Pope B, Weeds A, Lindberg U, Daneholt B (2001) Actin bound to the hnRNP protein hrp36 accompanies Balbiani ring mRNA from the gene into polysomes. J. Cell Biol. 153: 229-235

In this study we provided in situ evidence for the first time that actin is a bona fide component of ribonucleoprotein (RNP) complexes. We also demonstrated that actin is added co-transcriptionally to nascent transcript and accompanies the mRNA from gene to polysomes bound to a subset of heterogeneous nuclear ribonucleoproteins.

37) Jonsson AP, Aissouni Y, Palmberg C, Percipalle P, Nordling E, Daneholt D, Jörnvall H, Bergman T (2001) Recovery of gel separated proteins for in-solution digestion and mass spectrometry. Anal. Chem. 73: 5370-5377

38) Percipalle P, Butler PJ, Finch JT, Rhodes D (1999) Nuclear Localisation Signal recognition causes release of Importin-α from aggregates in the cytosol. J. Mol. Biol. 292: 263-273

39) Henderson BR, Percipalle P (1997) Interactions between HIV Rev and nuclear import and export factors: The Rev nuclear localisation signal mediates specific binding to human importin-β J. Mol. Biol. 274 (5): 693-707

40) Percipalle P, Clarckson DW, Kent HM, Rhodes D, Stewart M (1997) Molecular interactions between the importinα/β heterodimer and proteins involved in vertebrate nuclear protein import. J. Mol. Biol. 266: 722-732

41) Simoncsits A, Chen J, Percipalle P, Wang S, Toro I, Pongor S (1997) Single-chain repressors containing engineered DNA-binding domains of the phage 434 repressor recognise symmetric or asymmetric DNA operators. J. Mol. Biol. 267: 118-131

42) Percipalle P, Saletti R, Pongor S, Foti S, Zahariev S, Guarnaccia C, Fisichella, S (1997) Synthesis and Mass Spectrometric Characterization of the N-terminal (1-63) DNA-binding Domain of the Bacteriophage 434 Repressor cI. European Mass Spectrometry 3: 151-159

43) Percipalle P, Simoncsits A, Zahariev S, Guarnaccia C, Sanchez R, Pongor S (1995) Rationally designed bipartite repressor analogues as conformational probes to protein-DNA interactions. EMBO J. 14: 3200-3205

This primary research article represents the backbone of my PhD thesis. In this study I rationally designed a subset DNA binding peptides based on the crystal structure of a the bacteriophage 434 repressor, a the helix-turn-helix containing DNA binding protein. Improved DNA binding efficiency was designed by creating bipartite probes. The overall experimental approach comprised an in silico analysis/design based on the model crystal structure, followed by synthesis of the probe by chemical approaches or by recombinant DNA technology and validation of the DNA binding properties by biochemical and biophysical methods.

44) Percipalle P, Saletti R, Pongor S, Foti S, Tossi A, Fisichella S (1994) Structural characterization of synthetic model peptides of the DNA-binding cI434 repressor by elctrospray ionization and fast atom bombardment mass spectrometry. Biological Mass Spectrometry 23: 727-733

45) Percipalle P, Tossi A, Guarnaccia C, Simoncsits A, Zahariev S, Pongor S. (1994) Chemical synthesis of covalently dimerized polypeptides based on the bacteriophage 434 cI repressor. In Peptides 1994 (Proceeding of the 23rd European Peptide Symposium) ESCOM, Netherlands (ed. Maia H.L.S.): 391-392

SUBMITTED MANUSCRIPTS

46) Vincent CT, Dass RA, Obrdlik A, Kaur A, Sarshad A, Percipalle P*,#, Brown AMC# (2015) Wnt5a signaling induces Dvl1 association with ribosomal DNA and represses RNA polymerase I transcription. Submitted
shared senior correspondence

This paper is submitted in its final revised version to Science Signaling. We show for the first time that expression of Wnt5a unleashes a signalling pathway that leads to accumulation of dishevelled 1 (Dvl1) in the nucleolus where it binds to the rDNA transcription unit. This in turn leads to release of the deacetylase sirtuin 7 (SIRT7), disassembly of the RNA polymerase I transcription machinery and down-regulation of rRNA synthesis. These results are compatible with a drop in cell growth and proliferation. They are also relevant in breast cancer development in vivo as loss of Wnt5a signalling enhances tumour growth and Wnt5a-null mammary tumours show enlarged nucleolar organizer regions compared to Wnt5a wild-type tumours. We conclude that in contrast to the oncogenic function of Wnt3, Wnt5a is a tumor suppressor that acts through a novel mechanism mediated by the down-stream effector Dvl1. Importantly, since GSK3β is affected by non-canonical Wnt signalling, these observations suggest that nuclear myosin 1 activity in the context of rRNA synthesis may also be regulated by Wnt. This hypothesis is now one of the questions I will address as part of future investigations.

47) Al-Muzzaini B, Sarshad AA, Rahmanto AS, Hansson M, Von Euler A, Corcoran M, Östlund A-K, Visa N, Percipalle P*. (2015) β-actin activates RNA polymerase I transcription and cell cycle progression through a chromatin-based mechanism. Submitted

Using a combination of genome-wide analysis (ChIP-Seq), cell and molecular analyses, here we provide for the first time loss-of-function evidence of a direct role of β-actin in RNA polymerase I transcription using β-actin knockout mouse embryonic fibroblasts. These actin-based mechanisms are required for transcription activation at the exit of mitosis and have a global impact in cell cycle progression and cellular proliferation.