BIOGRAPHICAL SKETCH

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NAME: TAN, SONG

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

POSITION TITLE: Professor of Biochemistry & Molecular Biology

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 MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	B.A.	05/1985	Physics
University of Cambridge, Cambridge, UK	Ph.D.	12/1989	Molecular Biology
ETH-Zürich, Zürich, Switzerland	Post doc	09/1992	Structural Biology

A. Personal Statement

My laboratory is interested in how the cell interacts with its genomic information packaged as chromatin, and in particular, how the nucleosome unit of chromatin is recognized by cellular proteins. We study how chromatin proteins and histone modification enzymes act on their nucleosome substrate. We combine biochemical and structural approaches in our investigations to provide high-resolution structural descriptions of chromatin enzymes in complex with the nucleosome. We determined the first crystal structure of a chromatin protein bound to the nucleosome (RCC1/nucleosome, 2010) and the first crystal structure of a chromatin enzyme bound to the nucleosome (PRC1 ubiquitylation module/nucleosome, 2014). We have used X-ray crystallography for most of our studies to date, but from Aug 2015 to July 2016, I was a Visiting Scientist at the MRC Laboratory of Molecular Biology in Cambridge, U.K. learning cryoelectron microscopy. I plan to combine cryoelectron microscopy and X-ray crystallography to determine structures of challenging chromatin enzymes in complex with their nucleosome substrate.

To handle the technical complexities of our projects, we have developed new methods and technologies. Many of the macromolecules we work with are multicomponent complexes, and we have developed polycistronic expression systems to coexpress protein complexes in *E. coli*. We have distributed the pST39 and pST44 polycistronic expression systems to over 400 laboratories around the world, requested mostly by structural biology groups who have used the plasmids to prepare and determine the structures of more than 20 protein complexes. We recently created and made available to more than 400 laboratories two plasmids that produce 100 bp and 1 kb DNA ladders upon digestion with restriction enzymes at a fraction of the cost of commercial DNA ladders.

B. Positions and Honors

Positions and Employment

1992 - 1998 Project Leader (Oberassistent), ETH-Zurich, Zurich
1998 - 2004 Assistant Professor, Penn State University, University Park, PA
2004 - 2011 Associate Professor, Penn State, University Park, PA
2011 - Professor, Penn State University, University Park, PA
2015 - 2016 Visiting Scientist, MRC Laboratory of Molecular Biology, Cambridge, UK (sabbatical)

Other Experience and Professional Memberships

2003 - 2003	Ad Hoc Reviewer, Department of Energy Genomes to Life Study Section
2003 - 2003	Ad Hoc Reviewer, NIH BBCB Biophysical Chemistry Study Section
2003 - 2003	Co-Organizer, Penn State Summer Symposium on Chromatin Structure and Function
2004 - 2004	Ad Hoc Reviewer, American Cancer Society Genetic Mechanisms in Cancer Peer Review Committee
2005 - 2005	Ad Hoc Reviewer, NIH MSFC Molecular Structure and Function Study Section
2005 - 2008	Reviewer, American Cancer Society Genetic Mechanisms in Cancer Peer Review Committee
2006 - 2006	Ad Hoc Reviewer, NIH MGC Molecular Genetics Study Section
2007 -	Editorial Board Member, Protein Expression and Purification
2007 - 2007	Reviewer, NIH Special Emphasis P41 Research Resource Scientific Review Group
2007 - 2007	Co-Organizer, Penn State Summer Symposium on Chromatin and Epigenetic Regulation of Transcription
2008 - 2008	Vice-Chair, American Cancer Society Genetic Mechanisms in Cancer Peer Review Committee
2008 - 2008	Ad Hoc Reviewer, NIH NRSA Genes, Genomics & Genetics Study Section
2009 - 2009	Ad Hoc Reviewer, NIH NIGMS P01 Program Project Grant
2009 - 2009	Expert Reviewer, NIH Transformative R01 Grant
2009 - 2009	Ad Hoc Reviewer, NIH BCMB-B Biological Chemistry & Macromolecular Biophysics Special Emphasis Panel
2009 - 2009	Chair, American Cancer Society Genetic Mechanisms in Cancer Peer Review Committee
2010 - 2010	Co-Editor, Current Opinion in Structural Biology
2010 - 2014	Reviewer, NIH MSFB Molecular Structure and Function Study Section
2011 - 2011	Co-Organizer, Penn State Summer Symposium on Chromatin and Epigenetic Regulation of Transcription
2012 - 2012	Co-Editor, Current Opinion in Structural Biology
2013 - 2013	Ad Hoc Member, American Cancer Society Council for Extramural Grants
2015 - 2015	Reviewer, NIH NCI Lab of Biochemistry and Molecular Biology site visit
2015 - 2015	Co-Organizer, Penn State Summer Symposium on Chromatin and Epigenetic Regulation of Transcription
2015 - 2019	Member, American Cancer Society Council for Extramural Grants
2016 - 2017	Co-Chair, French HCERES evaluation team of IGBMC (Inst. of Genetics, Mol. & Cell Biology)
2017	Ad Hoc Reviewer, NIH MSFC Molecular Structure and Function Study Section
2018	Member, Academic Program Review Committee, U Arizona Dept of Mol. & Cell. Biology

Honors

1981	4th place, Westinghouse Science Talent Search
1985	Presidential Scholar, Cornell University
1985	Churchill Scholarship (declined), Winston Churchill Foundation
1985	Marshall Scholarship, Marshall Aid Commemoration Commission
1985	NSF Graduate Fellowship, US National Science Foundation
2001	Pew Scholar in Biomedical Sciences, Pew Charitable Trust
2002	Tershak Outstanding Faculty Teaching Award, Penn State University
2014	C.I. Noll Award for Excellence in Teaching, Penn State Eberly College of Science
2015	Faculty Scholar Medal, Penn State University
2015	Fellow of American Association for the Advancement of Science

C. Contributions to Science

MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/107rpjaDEGAAk/bibliography/46229419/public/?sort=date&direction=ascending

1. My laboratory has determined atomic structures showing how chromatin proteins interact with their nucleosome substrate. Despite the abundance of biochemical, genetic and genomic studies for how hundreds of chromatin factors interact with the nucleosome complex of histones and DNA to regulate gene expression, we lacked a molecular understanding of how such chromatin proteins recognized the nucleosome. Our crystal structure of the RCC1 chromatin protein bound to the nucleosome in 2010 provided the first atomic description of a chromatin protein/nucleosome complex. In 2014, we published the first crystal structure of a chromatin enzyme and the first structure of a multisubunit protein complex, the PRC1 ubiquitylation module, bound to its nucleosome substrate. These structures, together with other crystallographic studies from other laboratories, have defined the Arginine anchor paradigm in which a chromatin protein uses an arginine side chain to bind to the acidic patch on the nucleosome histone dimer. Our PRC1/nucleosome complex structure also showed how a chromatin enzyme can specifically act on the nucleosome not through specific interactions with a histone peptide but through global recognition of the nucleosome surface. This structure also provided the first crystal structure of a RING domain E3 ubiquitin ligase in complex with its E2 ubiquitin conjugating enzyme and its substrate.
    a. Makde RD, England JR, Yennawar HP, Tan S. (2010) Structure of RCC1 chromatin factor bound to the nucleosome core particle. **Nature**, 467(7315):562-566. PMCID: PMC3168546.
    b. Makde RD, Tan S. (2013) Strategies for crystallizing a chromatin protein in complex with the nucleosome core particle. **Anal Biochem**, 442(2):138-145. PMCID: PMC3799870.
    c. McGinty RK, Henrici RC, Tan S. (2014) Crystal structure of the PRC1 ubiquitylation module bound to the nucleosome. **Nature**, 514(7524):591-596. PMCID: PMC4215650.
    d. Sun, J, Paduch, M, Kim, S, Kramer, RM, Barrios, AF, Lu, V, Luke, J, Usatyuk, S, Kossakoff, AA, Tan. S. (2018) Structural basis for activation of SAGA histone acetyltransferase Gcn5 by partner subunit Ada2. **PNAS**, 115(40):10010-10015, PMCID: PMC6176591

2. We have characterized the solution interactions between chromatin proteins and the nucleosome to complement our crystallographic studies. We determined through biochemical approaches that the RCC1 chromatin protein employs an arginine residue in the switchback loop region of its β-propeller domain to bind to the nucleosome. Our studies of the Piccolo NuA4 histone acetyltransferase identified the minimal complex and, in particular, an Esa1 Tudor/chromo barrel loop region and the Epl1 Enhancer of Polycomb A (EpcA) basic region critical for nucleosome activity. We used nucleosome binding and histone demethylase assays to establish that the LSD1/CoREST histone demethylase requires DNA beyond the nucleosome core particle for robust activity. We combined crystallographic information with biochemical data to develop a structural model for how the Set8 histone methylase binds to its nucleosome substrate. These studies have defined regions of chromatin protein/enzymes and surfaces of the nucleosome that mediate their interactions.
    a. England JR, Huang J, Jennings MJ, Makde RD, Tan S. (2010) RCC1 uses a conformationally diverse loop region to interact with the nucleosome: a model for the RCC1-nucleosome complex. **J Mol Biol**, 398(4):518-529. PMCID: PMC2895563.
    b. Huang J, Tan S. (2013) Piccolo NuA4-catalyzed acetylation of nucleosomal histones: critical roles of an Esa1 Tudor/chromo barrel loop and an Epl1 enhancer of polycomb A (EPcA) basic region. **Mol Cell Biol**, 33(1):159-169. PMCID: PMC3536312.
    c. Kim SA, Chatterjee N, Jennings MJ, Bartholomew B, Tan S. (2015) Extranucleosomal DNA enhances the activity of the LSD1/CoREST histone demethylase complex. **Nucleic Acids Res**, 43(10):4868-4880. PMCID: PMC4446439.
    d. Girish TS, McGinty RK, Tan S. (2016) Multivalent interactions by the Set8 histone methyltransferase with Its nucleosome substrate. **J Mol Biol**, 428(8):1531-1543. NIHMSID: 766194.

3. I have developed technologies for producing recombinant protein complexes for biophysical and biochemical studies. Prior work had relied on creating specialized coexpression vectors specific for individual projects. I created general polycistronic expression vectors that coexpress up to 4 proteins in *E. coli*. My laboratory has distributed the pST39 and pST44 polycistronic expression systems to over 400 laboratories around the world, requested mostly by structural biology groups who have used the plasmids to prepare and determine the structures of more than 20 protein complexes. We also performed a systematic comparison of affinity tags for protein purification and incorporated the most effective affinity tags into our polycistronic expression vector system.
    a. Tan S. (2001) A modular polycistronic expression system for overexpressing protein complexes in *Escherichia coli*. **Protein Expr Purif**, 21(1):224-234. PubMed PMID: 11162410.
    b. Tan S, Kern RC, Selleck W. (2005) The pST44 polycistronic expression system for producing protein complexes in *Escherichia coli*. **Protein Expr Purif**, 40(2):385-395. PubMed PMID: 15766881.
    c. Lichty JJ, Malecki JL, Agnew HD, Michelson-Horowitz DJ, Tan S. (2005) Comparison of affinity tags for protein purification. **Protein Expr Purif**, 41(1):98-105. PubMed PMID: 15802226.
    d. Selleck W, Tan S. (2008) Recombinant protein complex expression in *E. coli*. **Curr Protoc Protein Sci**, Chapter 5:Unit 5.21. PMCID: PMC2582387.

4. Undergraduates in my laboratory and I have created two plasmids (pPSU1 & pPSU2) that produce 100 bp and 1 kb DNA ladders when digested with inexpensive restriction enzymes. Unlike most currently available DNA ladders, the 100 bp ladder fragments migrate appropriately on both agarose and polyacrylamide gels. 100 ml of E. coli cultures for the two plasmids is sufficient to prepare 100 bp or 1 kb DNA ladders for 1 000 lanes. The plasmids enable DNA ladders to be produced for less than a penny a lane, 50x less than commercial equivalents. The pPSU1 and pPSU2 plasmids are available without licensing restrictions to nonprofit academic users through the Addgene plasmid repository and have already been distributed to more than 270 laboratories in 34 countries around the world.
    a. Henrici, R.C., Pecen, T.J., Johnston, J.L., Tan, S. (2017) The pPSU plasmids for generating DNA molecular weight markers. **Scientific Reports**, 7:2438.

5. During my postdoctoral training with Tim Richmond at the ETH-Zurich in Switzerland, I performed biochemical and structural characterization of multiple gene regulation protein/DNA or protein/protein complexes including the TFIIA/TBP/DNA and TFIIF general transcription complexes, and the MATα2/MCM1/DNA and the serum response factor SRF/DNA specific DNA-binding complexes. These studies provided structural insights into the role of DNA bending in how individual and multiple transcription factors interact with DNA.
    a. Pellegrini L, Tan S, Richmond TJ. (1995) Structure of serum response factor core bound to DNA. **Nature**, 376(6540):490-498. PubMed PMID: 7637780.
    b. Tan S, Hunziker Y, Sargent DF, Richmond TJ. (1996) Crystal structure of a yeast TFIIA/TBP/DNA complex. **Nature**, 381(6578):127-151. PubMed PMID: 8610010.
    c. Tan S, Richmond TJ. (1998) Crystal structure of the yeast MATα2/MCM1/DNA ternary complex. **Nature**, 391(6668):660-666. PubMed PMID: 9490409.
    d. Gaiser F, Tan S, Richmond TJ. (2000) Novel dimerization fold of RAP30/RAP74 in human TFIIF at 1.7 A resolution. **J Mol Biol**, 302(5):1119-1127. PubMed PMID: 11183778.

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

Ongoing Research Support

R35 GM127034-01 Tan (PI) 09/01/2018-08/31/2023

Structural studies of chromatin complexes

The goal of this project is to understand how histone modification enzymes function on their nucleosome substrates through X-crystallography and cryoelectron microscopy structure determination of chromatin enzyme/nucleosome complexes.

Role: PI

T32 GM125592 Pugh (PI) 07/01/2018-06/30/2023

Eukaryotic Gene Regulation (EGR) Predoctoral Training Program

Predoctoral training program to train future generation of scientists in experimental, molecular and computational sciences applied towards understanding mechanisms of eukaryotic gene regulation.

Role: Faculty

NIH S10OD025145-01 Yennawar (PI) 09/13/2018-09/12/2019

TA Instruments Low Volume AutoAffinity ITC

Funds used to procure TA instruments automated ITC equipment for characterizing protein-ligand interactions

Role: Co-PI

TSF SAP 4100077246 Tan (PI) 7/1/2017 – 12/31/2020

Biomolecular Structure Characterization to Advance Biomedicine

Pennsylvania Dept. of Health Tobacco CURE Fund

The major goal of this project is to determine structures of biomedically important macromolecular complexes by cryoelectron microscopy.

Role: PI

Completed Research Support

R01 GM111651-01 Tan (PI) 08/01/2014-07/31/2019

Molecular interactions of histone ubiquitylation enzymes with the nucleosome

The goal of this project is to determine how the Ran small GTPase interacts with both the Regulator of Chromosomal Condensation 1 (RCC1) protein and the nucleosome using biochemical and crystallographic approaches.

Role: PI

R01 GM088236-05A1 Tan (PI) 08/01/2009-07/31/2019

Structural Basis for RCC1 Directed Recruitment of Ran GTPase to Chromatin

The goal of this project is to determine how histone ubiquitylation enzymes bind to the nucleosome and promote post-translational modification of histone tails through crystallographic and biochemical approaches.

Role: PI

U01 GM094588 Tan (PI) 07/01/2013-06/30/2015

University of Chicago (NIH/NIGMS)

Chaperone-enabled studies of epigenetic regulation enzymes

Subcontract to produce recombinant histone acetyltransferase complexes and to perform crystallization studies of such HAT complexes in complex with custom synthetic antigen binders.

BIOGRAPHICAL SKETCH

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NAME: Armache, Jean-Paul

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

POSITION TITLE: Assistant Professor of Biochemistry and Molecular Biology

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 MM/YYYY	FIELD OF STUDY
Technical University of Lodz (Poland)	M.S.	12/2006	Computer Science
Ludwig-Maximilians-Universität (University of) Munich (Germany)	Ph.D.	05/2011	Chemistry and Pharmacy
University of California San Francisco (USA)	Postdoctoral	03/2019	Biochemistry and Biophysics

A. Personal Statement

My research interests are centered on understanding the mechanisms and functions of ATP-dependent chromatin remodeling complexes and their place in genome maintenance. Efficient and tightly controlled DNA and histone repositioning, exchange and ejection are necessary for assuring gene expression and silencing, as well as DNA repair. Revealing the three-dimensional structures at different stages of these processes thus has a great impact in biomedical research, life sciences and possibly, nanoscale engineering. In the last year, I have participated in two chromatin-oriented studies (Armache et al., **Elife** 2019 and Valencia-Sanchez et al. **Mol. Cel**. 2019), where electron cryo-microscopy was used to solve structures of SNF2h and Dot1L, respectively, attached to nucleosomes at near-atomic resolution. Since 2007 I have used cryo-EM to answer a number of questions in the field of translation, membrane trafficking and chromatin using structural biology.
In my own lab at Penn State University, I continue using cryo-EM to pursue structures of dynamic DNA ATP-dependent remodeling enzymes as well as work on developing novel hardware for cryo-EM optimization.

B. Positions and Honors

Positions and Employment

2007 – 2011 Graduate Student, Ludwig-Maximilians-Universität Munich, Munich, Germany
2011 – 2013 Postdoctoral Scholar, Ludwig-Maximilians-Universität Munich, Munich, Germany
2013 – 2019 Postdoctoral Scholar, University of California San Francisco, San Francisco, CA, USA
2019 – Assistant Professor, Pennsylvania State University, University Park, PA, USA

Honors

2011 Römer Award, Ludwig-Maximilians-Universität Munich, Munich, Germany

C. Contributions to Science

1. During my graduate studies at Ludwig-Maximilians-Universität Munich, I focused on determining high-resolution structures of eukaryotic and archaeal ribosomes. The first structure was a 5.5 Å cryo-EM reconstruction of a *T. aestivum* ribosome (Armache et al. **PNAS** 2010a, Armache et al. **PNAS** 2010b), which allowed us to localize and model many eukaryote-specific rRNA and r-proteins. We furthered eukaryotic translation studies by obtaining a structure of human ribosome at 4.5-5Å, revealing the additional layer and increased complexity of rRNA and r-proteins in comparison to lower eukaryotes (Anger et al. **Nature** 2013). The same year, we also published a study of evolutionary branching of r-proteins based on their binding to defined RNA motifs (Armache et al. **NAR** 2013).

    a. **Armache JP**, Jarasch A, Anger AM, Villa E, Becker T, Bhushan S, Jossinet F, Habeck M, Dindar G, Franckenberg S, Marquez V, Mielke T, Thomm M, Berninghausen O, Beatrix B, Söding J, Westhof E, Wilson DN, Beckmann R. (2010) Cryo-EM structure and rRNA model of a translating eukaryotic 80S ribosome at 5.5-A resolution. **Proc Natl Acad Sci USA**. Nov 16;107(46):19748-53 (PMID: 20980660)
    b. **Armache JP**, Jarasch A, Anger AM, Villa E, Becker T, Bhushan S, Jossinet F, Habeck M, Dindar G, Franckenberg S, Marquez V, Mielke T, Thomm M, Berninghausen O, Beatrix B, Söding J, Westhof E, Wilson DN, Beckmann R. (2010) Localization of eukaryote-specific ribosomal proteins in a 5.5-Å cryo-EM map of the 80S eukaryotic ribosome. **Proc Natl Acad Sci USA**. Nov 16;107(46):19754-9 (PMID: 20974910)
    c. Anger AM, **Armache JP**, Berninghausen O, Habeck M, Subklewe M, Wilson DN, Beckmann R. (2013) Structures of the human and Drosophila 80S ribosome. **Nature**. May 2;497(7447):80-5 (PMID: 23636399)
    d. **Armache JP**, Anger AM, Márquez V, Franckenberg S, Fröhlich T, Villa E, Berninghausen O, Thomm M, Arnold GJ, Beckmann R, Wilson DN. (2013) Promiscuous behaviour of archaeal ribosomal proteins: implications for eukaryotic ribosome evolution. (2013) **Nucleic Acids Res**. Jan;41(2):1284-93 (PMCID: PMC3553981)

2. On my postdoctoral training in Yifan Cheng's laboratory at UCSF, I determined a structure of Transient Receptor Potential cation channel, subfamily A, member 1 (TRPA1), an important detector of noxious chemical agents encountered in our environment or produced endogenously during tissue injury or drug metabolism (Paulsen et al. **Nature** 2015). The full-length structure of TRPA1, solved in the presence of pharmacophores, including a potent antagonist, revealed extensive coiled-coil assembly domain stabilized by polyphosphate co-factors and a highly integrated nexus that converges on a TRP-like allosteric domain

    a. Paulsen CE, **Armache JP**, Gao Y, Cheng Y, Julius D. (2015) Structure of the TRPA1 ion channel suggests regulatory mechanisms. **Nature**. Apr 23;520(7548):511-7 (PMID: 25855297)

3. In addition, I participated in studies aimed at pushing the envelope on cryo-EM technology. To this end, we studied a novel lipid scaffold technology for membrane proteins (Frauenfeld et al. **Nat Methods** 2016). I also participated in a study that developed a new and improved, state-of-the-art motion correction software (Zheng et al. **Nat. Methods** 2017) that allowed for a large quality and resolution improvement.

    a. Frauenfeld J, Löving R**, Armache JP**, Sonnen AF, Guettou F, Moberg P, Zhu L, Jegerschöld C, Flayhan A, Briggs JA, Garoff H, Löw C, Cheng Y, Nordlund P. A (2016) A saposin-lipoprotein nanoparticle system for membrane proteins. **Nat Methods**. Apr;13(4):345-51 (PMID: 26950744)
    b. Zheng SQ, Palovcak E**, Armache JP**, Verba KA, Cheng Y, Agard DA. (2017) MotionCor2: anisotropic correction of beam-induced motion for improved cryo-electron microscopy. **Nat Methods**. Apr;14(4):331-332 (PMID: 28250466)

4. During my postdoctoral training, I also solved cryo-EM structures of SNF2h-nucleosome complexes with ADP-BeFx that captured two reaction intermediates. In one structure, a number of histone residues was disordered. Some of those distortions are expected to limit the assembly of a SNF2h dimer, while others most likely promote DNA translocation. The second structure, at high-resolution, showed a 2bp translocation, as a representation of an elemental translocation step and revealed novel interactions that promote binding and remodeling (Armache et al. 2019 **Elife**).

    a. **Armache JP**, Gamarra N, Johnson SL, Leonard JD, Wu S, Narlikar GN, Cheng Y (2019) Cryo-EM structures of remodeler-nucleosome intermediates suggest allosteric control through the nucleosome. **Elife**. Jun 18; 2019 (PMID: 31210637)

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/jean-paul.armache.1/collections/58367513/public/

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