

Name: Nicolas H. Thomä

Current Position: Senior Group Leader in Structural Biology
Friedrich Miescher Institute for Biomedical Research
Maulbeerstrasse 66
CH-4058 Basel
Switzerland

Education:
1994 - 1998 PhD at the University of Cambridge (United Kingdom) with
Prof. P. Leadlay and P. Evans
1993 - 1994 Undergraduate in Biochemistry Natural Science Tripos
University of Cambridge (United Kingdom)
1991 - 1993 Undergraduate in Biochemistry and Molecular Biology
University of Hamburg (Germany)

Employment History:
2012 - present Senior Group Leader, Friedrich Miescher Institute
2006 - 2012 Junior Group Leader (tenure-track), Friedrich Miescher Institute
2001 - 2006 Postdoctoral Fellow in Crystallography with Prof. N. Pavletich at
Memorial Sloan Kettering Cancer Center, New York (USA).
1998 - 2001 Postdoctoral Fellow in Enzymology and Biophysics with Profs. R.
Goody and S. Schlichting at the Max-Planck-Institute for Molecular
Physiology, Dortmund (Germany)

Institutional Responsibilities: Senior Group Leader in Structural Biology
Strategic Committee member advising the FMI Director
FMI Diversity and Inclusion Committee
Founder and Steering Committee Member of the joint Novartis-FMI
Cryo-EM imaging center
Member of the PhD Committee
Member of the Imaging Facility Committee
Member of the Protein Analysis Facility Committee
Chaired and was a member of numerous FMI Group Leader
hiring Committees

Teaching (Uni. Basel):
2019-2015 G5 Translational Control and Post-Translational Protein
Modifications (Co-organizer)
2019-2011 G4 Chromatin and Epigenetics
2018-2008 Dynamics and maintenance of the Genome: DNA
Replication, Repair, Recombination

Scientific Reviewer: *Journals:* Nature, Nature Structural Molecular Biology, Science,
Cell, Molecular Cell, Biochemistry, Journal of Molecular Biology,
Structure etc..
Funding bodies: SNSF, Swiss Cancer League, ERC, Cancer UK.

Board Memberships: CRUK Grant Review Board (United Kingdom), and chair of the
Monte Rosa Therapeutics AG Scientific Advisory Board (Basel)

Prizes & Awards:
2020 Awarded ERC Advanced Grant
2019 [Ted-X Basel talk](#)
2017 - 2018 Appointed Novartis Scholar

2015	Elected EMBO member
2015	Awarded ERC Advanced Grant
2014	Elected Academia Europaea member
2012	Novartis Leading Scientist Award
2011	Member Network of Excellence EpiGeneSys
2010	Awarded ERC consolidator grant
2002 – 2005	Awarded Human Frontiers Science Program Long-Term Fellowship
1999 – 2001	Awarded EMBO Long-Term Fellowship
1995 – 1998	Awarded PhD scholarship by Studienstiftung des Deutschen Volkes

Collaborative network history:

I have coordinated several collaborative grant projects with various laboratories, and I am an active member in the Ubicode EU ITN Network, and was previously part of the EU Network EpiGenesys.

Mentoring:

Since joining the FMI, I have successfully led a research laboratory of 12 -15 people on average, and trained 6 PhD students and 18 postdoctoral fellows; of these 8 are currently in leadership roles in academia or industry. I am also mentoring several junior group leaders at the FMI.

Organization of conferences:

Keystone meeting on the ubiquitin system and its relation to drug discovery (2020 (postponed) and 2022), organizer of Cold Spring Harbor Ubiquitin Meeting (2021-2027).

Publications in international peer reviewed journals (2008 - 2022 only):

A full list of publications can be found [here](#).

The CRL4^{DCAF1} cullin-RING ubiquitin ligase is activated following a switch in oligomerization state. Mohamed WI, Schenk AD, Kempf G, Cavadini S, Basters A, Potenza A, Abdul Rahman W, Rabl J, Reichermeier K, Thomä NH. **EMBO J.** 2021 Nov 15;40(22):e108008.

BANP opens chromatin and activates CpG-island-regulated genes. Grand RS, Burger L, Gräwe C, Michael AK, Isbel L, Hess D, Hoerner L, Iesmantavicius V, Durdu S, Pregnolato M, Krebs AR, Smallwood SA, Thomä NH, Vermeulen M, Schübeler D. **Nature.** Jul 7. doi: 10.1038/s41586-021-03689-8.

Reading the chromatinized genome.

Michael AK, Thomä NH. **Cell.** 2021 Jul 8;184(14):3599-3611. doi: 10.1016/j.cell.2021.05.029. Epub 2021 Jun

Haven't got a glue: Protein surface variation for the design of molecular glue degraders. Kozicka Z, Thomä NH. **Cell Chem Biol.** 2021 Apr 28:S2451-9456(21)00202-6 (invited review).

Structural mechanism of cGAS inhibition by nucleosomes

Pathare G, Decout, A, Glück S, Cavadini S, Makasheva K, Hovius R, Kempf G, Weiss J, Kozicka Z, Guey B, Melenc P, Fierz B, Thomä NH*, Ablasser A.* **Nature** 2020 Sep 10. doi: 10.1038/s41586-020-2750-6 (*co-corresponding author)

Rational discovery of molecular glue degraders via scalable chemical profiling.

Mayor-Ruiz C, Bauer S, Brand M, Kozicka Z, Siklos M, Imrichova H, Kaltheuner IH, Hahn E, Seiler K, Koren A, Petzold G, Fellner M, Bock C, Müller AC, Zuber J, Geyer M, Thomä NH, Kubicek S, Winter GE. **Nat Chem Biol.** **2020** Nov;16(11):1199-1207. doi: 10.1038/s41589-020-0594-x.

The CDK inhibitor CR8 acts as a molecular glue degrader that depletes cyclin K
Słabicki S, Kozicka Z, Petzold G, Li Y, Manojkumar M, Bunker R, Donovan KA, Sievers QL, Koeppl J, Suchyta D, Sperling AS, Fink E, Gasser JA, Wang LR, Corsello SM, Sellar RS, Jan M, Gillingham D, Scholl C, Fröhling S, Golub TR, Fischer ES, Thomä NH*, Ebert BL.* **Nature.** **2020** Sep;585(7824):293-297. doi: 10.1038/s41586-020-2374-x. (*co-corresponding author)

Structural insights into Fe-S protein biogenesis by the CIA targeting complex
Kassube S, Thomä NH. **Nat Struct Mol Biol.** **2020** Aug;27(8):735-7420

Mechanisms of OCT4-SOX2 motif readout on nucleosomes
Michael AK, Grand RS, Isbel L, Cavadini S, Kozicka Z, Kempf G, Bunker RD, Schenk AD, Graff-Meyer A, Pathare GR, Weiss J, Matsumoto S, Burger L, Schübeler D*, Thomä NH*. **Science** **2020** Jun 26;368(6498):1460-1465
(*co-corresponding author)

Live Analysis and Reconstruction of Single-Particle Cryo-Electron Microscopy Data with CryoFLARE Schenk AD, Cavadini S, Thomä NH, Genoud C. **J Chem Inf Model.** **2020** Apr 10.

FANally...A Structure Emerges of the Fanconi Anemia Core Complex
Aguirre JD, Thomä NH. **Trends Biochem Sci.** **2020** Apr;45(4):275-276. Epub 2020 Jan 24.

PIKES Analysis Reveals Response to Degradation and Key Regulatory Mechanisms of the CRL4 Network
Reichermeier KM, Straube R, Reitsma JM, Sweredoski MJ, Rose CM, Moradian A, den Besten W, Hinkle T, Verschuere E, Petzold G, Thomä NH, Wertz IE, Deshaies RJ, Kirkpatrick DS. **Mol Cell.** **2020** Mar 5;77(5):1092-1106.n

Taking the Brakes Off Targeted Protein Degradation
Kozicka Z, Petzold G, Thomä NH. **Cell Chem Biol.** **2020** Jan 16;27(1):16-18.

DNA damage detection in nucleosomes involves DNA register shifting
Matsumoto S, Cavadini S, Bunker RD, Potenza A, Rabl J, Yamamoto J, Grand RS, Schenk AD, Schübeler D, Iwai S, Sugawara K, Kurumizaka H, Thomä NH. **Nature** **2019** Jul;571(7763):79-84.

Structural basis of BRCC36 function in DNA repair and immune regulation
Rabl J, Bunker RD, Schenk AD, Cavadini S, Gill ME, Rahman WA, Andrés-Pons A, Luijsterburg M, Ibrahim A, Branigan E, Aguirre JD, Marceau AH, Guérillon C, Bouwmeester T, Hassiepen U, Peters AHFM, Renucci M, Gelman L, Rubin SM, Mailand N, van Attikum H, Hay RT, Thomä NH. **Mol Cell** **2019** Aug 8;75(3):483-497.

Defining the human C2H2 zinc finger degrome targeted by thalidomide analogs through CRBN
Sievers QL, Petzold G, Bunker RD, Renneville A, Słabicki M, Liddicoat BJ, Abdulrahman W, Mikkelsen T, Ebert BL*, Thomä NH*. **Science.** **2018** Nov 2;362(6414). (*co-corresponding author)

Regulatory control of DNA end resection by Sae2 phosphorylation

Cannavo E, Johnson D, Andres SN, Kissling VM, Reinert JK, Garcia V, Erie DA, Hess D, Thomä NH, Enchev RI, Peter M, Williams RS, Neale MJ, Cejka P. *Nature Comms.* 2018 Oct 1;9(1):4016.

Shepherding DNA ends: Rif1 protects telomeres and chromosome breaks

Fontana GA, Reinert JK, Thomä NH, Rass U. *Microb Cell.* 2018 May 17;5(7):327-343.

Activity-dependent neuroprotective protein recruits HP1 and CHD4 to control lineage-specifying genes

Ostapcuk V, Mohn F, Carl SH, Basters A, Hess D, Iesmantavicius V, Lampersberger L, Flemr M, Pandey A, Thomä NH, Betschinger J, Bühler M. *Nature.* 2018 May;557(7707):739-743.

Rif1 maintains telomeres and mediates DNA repair by encasing DNA ends

Mattarocci S, Reinert JK, Bunker RD, Fontana GA, Shi T, Klein D, Cavadini S, Faty M, Shyian M, Hafner L, Shore D, Thomä NH*, Rass U. *Nature Struct Mol Biol.* 2017 Jul;24(7):588-595. *co-corresponding author.

Targeted protein degradation: You can glue it too!

Walczak MJ, Petzold G, Thomä NH. *Nat Chem Biol.* 2017 Apr 13;13(5):452-453.

Cullin-RING ubiquitin E3 ligase regulation by the COP9 signalosome

Cavadini S, Fischer ES, Bunker RD, Potenza A, Lingaraju GM, Goldie KN, Mohamed WI, Faty M, Petzold G, Beckwith RE, Tichkule RB, Hassiepen U, Abdulrahman W, Pantelic RS, Matsumoto S, Sugawara K, Stahlberg H, Thomä NH. *Nature.* 2016 Mar 31;531(7596):598-603.

Structural basis of lenalidomide-induced CK1 α degradation by the CRL4(CRBN) ubiquitin ligase

Petzold G, Fischer ES, Thomä NH. *Nature.* 2016 Apr 7;532(7597):127-30. H

SPLINTS: small-molecule protein ligand interface stabilizers

Fischer ES, Park E, Eck MJ, Thomä NH. *Curr Opin Struct Biol.* 2016 Apr;37:115-22. doi: 10.1016/j.sbi.2016.01.004. Epub 2016 Jan 30. Review.

Structural basis of pyrimidine-pyrimidone (6-4) photoproduct recognition by UV-DDB in the nucleosome

Osakabe A, Tachiwana H, Kagawa W, Horikoshi N, Matsumoto S, Hasegawa M, Matsumoto N, Toga T, Yamamoto J, Hanaoka F, Thomä NH, Sugawara K, Iwai S, Kurumizaka H. *Science Rep.* 2015 Nov 17;5:16330.

Functional regulation of the DNA damage-recognition factor DDB2 by ubiquitination and interaction with xeroderma pigmentosum group C protein

Matsumoto S, Fischer ES, Yasuda T, Dohmae N, Iwai S, Mori T, Nishi R, Yoshino K, Sakai W, Hanaoka F, Thomä NH, Sugawara K. *Nucleic Acids Res.* 2015 Feb 18;43(3):1700-13. doi: 10.1093/nar/gkv038. Epub 2015 Jan 27.

Structure of the DDB1-CRBN E3 ubiquitin ligase in complex with thalidomide

Fischer ES, Böhm K, Lydeard JR, Yang H, Stadler MB, Cavadini S, Nagel J, Serluca F, Acker V, Lingaraju GM, Tichkule RB, Schebesta M, Forrester WC, Schirle M, Hassiepen U, Ottl J, Hild M, Beckwith RE, Harper JW, Jenkins JL, Thomä NH. *Nature.* 2014 Aug 7;512(7512):49-53.

Crystal structure of the human COP9 signalosome

Lingaraju GM, Bunker RD, Cavadini S, Hess D, Hassiepen U, Renatus M, Fischer ES, Thomä NH. *Nature*. 2014 Aug 14;512(7513):161-5.

Rif1 controls DNA replication timing in yeast through the PP1 phosphatase Glc7

Mattarocci S, Shyian M, Lemmens L, Damay P, Altintas DM, Shi T, Bartholomew CR, Thomä NH, Hardy CF, Shore D. *Cell Rep*. 2014 Apr 10;7(1):62-9. J

Structural and mechanistic insight into Holliday-junction dissolution by topoisomerase III α and RMI1

Bocquet N, Bizard AH, Abdulrahman W, Larsen NB, Faty M, Cavadini S, Bunker RD, Kowalczykowski SC, Cejka P, Hickson ID, Thomä NH. *Nature Struct Mol Biol*. 2014 Mar;21(3):261-8.

Rif1 and Rif2 shape telomere function and architecture through multivalent Rap1 interactions

Shi T, Bunker RD, Mattarocci S, Ribeyre C, Faty M, Gut H, Scrima A, Rass U, Rubin SM, Shore D, Thomä NH. *Cell*. 2013; 53(6):1340-53.

An N-terminal acidic region of Sgs1 interacts with Rpa70 and recruits Rad53 kinase to stalled forks

Hegnauer AM, Hustedt N, Shimada K, Pike BL, Vogel M, Amsler P, Rubin SM, van Leeuwen F, Guénolé A, van Attikum H, Thomä NH, Gasser SM. *EMBO J*. 2012 Sep 12;31(18):3768-83.

Detecting UV-lesions in the genome: The modular CRL4 ubiquitin ligase does it best!

Scrima A, Fischer ES, Lingaraju GM, Böhm K, Cavadini S, Thomä NH. *FEBS Lett*. 2011; 585:2818-25. Invited Review.

The molecular basis of CRL4DDB2/CSA ubiquitin ligase architecture, targeting, and activation

Fischer ES, Scrima A, Böhm K, Matsumoto S, Lingaraju GM, Faty M, Yasuda T, Cavadini S, Wakasugi M, Hanaoka F, Iwai S, Gut H, Sugasawa K, Thomä NH. *Cell*. 2011 Nov 23;147(5):1024-39.

Determinants and dynamics of genome accessibility

Bell O, Tiwari VK, Thomä NH, Schübeler D. *Nature Rev Genet*. 2011 Jul 12;12(8):554-64. doi: 10.1038/nrg3017. Review.

Histone methylation by PRC2 is inhibited by active chromatin marks

Schmitges FW, Prusty AB, Faty M, Stützer A, Lingaraju GM, Aiwazian J, Sack R, Hess D, Li L, Zhou S, Bunker RD, Wirth U, Bouwmeester T, Bauer A, Ly-Hartig N, Zhao K, Chan H, Gu J, Gut H, Fischle W, Müller J, Thomä NH. *Mol Cell*. 2011 May 6;42(3):330-41.

Structural basis of UV DNA-damage recognition by the DDB1-DDB2 complex

Scrima A, Konícková R, Czyzewski BK, Kawasaki Y, Jeffrey PD, Groisman R, Nakatani Y, Iwai S, Pavletich NP*, Thomä NH*. *Cell*. 2008 Dec 26;135(7):1213-23. (*co-corresponding author)

Extramural Funding:

01-01-2020 60 month ERC senior grant ~2.45 mio CHF

01-01-2020 36 month Swiss Cancer League project grant ~350 k CHF

01-07-2019 36 month Sinergia Grant (w. D. Gillingham; T. Halazonetis) ~1.2 mio CHF

01-08-2019 36 month UBIcode, EU consortium, ~120 k CHF
01-07-2018 48 month SNF project grant ~1.0 mio CHF
01-01-2016 36 month Gebert Rüf, Rare Disease, ~400 k
01-01-2016 60 month ERC senior grant ~2.3 mio CHF
01-01-2016 36 month Sinergia grant (w. D. Shore; T. Halazonetis) ~1.2 mio CHF
01-06-2013 24 month Swiss Cancer League ~330 k CHF
01-10-2012 36 month SNF project grant ~450 k CHF
01-01-2011 60 month ERC young investigator grant ~1.5 mio €
01-11-2010 36 month AICR project grant ~350 k CHF
01-01-2007 24 month Marie-Curie European Reintegration Grant ~80k €
01-01-2009 12 month OncoSuisse project grant ~1.2 k CHF
01-12-2008 36 month SNF project grant ~2.5k CHF
01-07-2008 24 month OncoSuisse project grant ~1.8 k CHF

Research Focus:

My lab pursues an interdisciplinary approach aimed at dissecting the roles of macromolecular machines in genome biology. Driven by structural biology, we use a wide range of genetic, chemical biology and complex biochemical reconstitution techniques to study protein function in genome maintenance and transcription. The lab focuses on chromatin in DNA repair, replication and transcription examining how proteins are able to decode and process DNA when encapsulated in chromatin. We are also interested in how chromatin and the ubiquitin transferase systems interplay.

In recent years we increasingly focused on understanding how proteins can be re-programmed by small molecules to carry out neo-morphic functions, and how this insight can be used to develop novel drugs.

Leadership experience:

At my host institute, the FMI, I have experience in leadership roles since starting as a junior group leader in 2006. Most importantly, I have driven the successful reshaping of Cancer Biology & Growth Control division towards Quantitative Biology, being the most senior member in the unit. In the process, I chaired multiple hiring committees and shaped the discussion between my division, the FMI and the Scientific Advisory Board. I have been actively involved in the management of the institute, most notably as member of its Strategic Committee under director Susan Gasser. As member of the recently created FMI Diversity and Inclusion committee, I also take an active role in the FMI's current drive towards improving the gender imbalance at the institute on the group-leader level member. I am a member of the oversight committee for the EM facility, the PhD selection committee as well as the mass-spectrometry committee, and I have co-organized the FMI annual meeting twice, which hosts nearly 300 participants. I am also the co-organizer of the Keystone (2020, 2021) and Cold Spring Harbor ubiquitin meetings (2021-2027). In addition, I serve on a grant review board of CRUK, and I chair the scientific advisory board of Monte Rosa Therapeutics, a biotech company in Basel.

My research in chemical biology and ubiquitin ligase biology was acknowledged by a Novartis Leading Scientist Award in 2012. I then initiated and drove efforts on ubiquitin ligase reprogramming at Novartis, starting in 2014. This work led to the Novartis targeted protein degradation effort, where I was a steering committee member together with the President of Novartis Institutes of BioMedical Research (NIBR), and the Heads of Chemistry, Oncology and Chemical biology from 2016-2018. This effort oversaw more than 150 researchers. In addition, I drove and supervised the establishment of the first Titan Krios EM structure facility in the pharmaceutical industry, setting up of a highly productive EM facility shared between the FMI and NIBR.