



Christine Mayr, MD, PhD

Cancer Biology and Genetics Program
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EDUCATIONAL BACKGROUND

PhD in Immunology, *magna cum laude* 2001
Humboldt University, Berlin, Germany

MD 2000
Free University, Berlin, Germany

RESEARCH EXPERIENCE & RESIDENCY

Postdoctoral Fellow 2005-2009
Whitehead Institute/Massachusetts Institute of Biology, Cambridge, MA
Laboratory of David P. Bartel

Residency 2004-2005
Technical University, Munich, Germany
Institute of Human Genetics
Director: Thomas Meitinger

Postdoctoral fellow 2002-2004
Ludwig-Maximilians University, Munich, Germany
Department of Hematology/Oncology
Laboratory of Michael Hallek

Residency 2000-2002
Ludwig-Maximilians University, Munich, Germany
Department of Hematology/Oncology
Director: Wolfgang Hiddemann

Graduate Student 1996-2000
Humboldt University, Berlin, Germany, Department of Internal Medicine, Charité
Free University, Berlin, Germany, Department of Molecular Biology and Biochemistry
Laboratories of Burkhardt F. Klapp and Werner Reutter

POSITIONS AND EMPLOYMENT

Member 2019-present
Cancer Biology and Genetics Program
Memorial Sloan Kettering Cancer Center, New York, NY

Professor, Gerstner Sloan Kettering Graduate School of Biomedical Sciences, New York 2019-present
Professor of Biochemistry and Molecular Biology 2019-present
Professor of Computational Biology and Medicine 2019-present
Weill Cornell Medical College, New York, NY

Assistant Member 2009-2015
Associate Member 2015-2019
Cancer Biology and Genetics Program
Memorial Sloan Kettering Cancer Center, New York, NY

HONORS & AWARDS

Member of the Editorial Board of <i>Cell</i>	2020
Louise and Allston Boyer Young Investigator Award for Basic Research	2019
Contributing member of F1000prime	2018
NIH Director's Pioneer Award	2016
Pershing Square Sohn Prize for Young Investigators in Cancer Research	2015
Selected as 'Cell Scientist to watch' by Journal of Cell Science	2015
Science Signaling Breakthrough of the year 2013	2014
Damon Runyon-Rachleff Innovation Award	2013
Sidney Kimmel Scholar Award	2011
MSKCC Special Projects Award	2010
Whitehead Postdoc Association Educational Award	2008
Post-doctoral fellowship from the Deutsche Forschungsgemeinschaft (DFG), Germany	2006
Merit Award of the American Society of Clinical Oncology (ASCO)	2004
Post-doctoral fellowship from the Deutsche Krebshilfe (German Cancer Aid), Germany	2002

GRANT REVIEW ACTIVITIES & CONFERENCES

Co-organizer, International Titisee Conference, RNA as a driving force in cellular organization	2022
Boehringer Ingelheim Fonds ad hoc reviewer	since 2022
Mathers Foundation Advisory Panel	since 2021
Pershing Square Sohn Cancer Research Alliance Scientific Review Council member	since 2021
Co-organizer, Cell Symposia, Biological Assemblies: Phase Transitions and more	2021
NIGMS, MGB Study Section ad hoc reviewer	2019
NHGRI, ENCODE Special Emphasis Panel ad hoc reviewer	2016
NCI, Collaborative Research in Cancer Biology ad hoc reviewer	2013
DoD Idea Development Award ad hoc reviewer	2013
DoD Idea Development Award ad hoc reviewer	2012

TEACHING

BCMB Core Course, From genes to cells – mRNA 3' end processing	since 2010
MD-PhD Frontiers in Biomedical Science I – Cytoplasmic condensates	since 2010
GSK Core Course – Secretory Pathway	since 2020
GSK Core Course – RNA biology	since 2022

RESEARCH INTERESTS

My lab studies the functions of mRNAs that go beyond their role as templates for protein synthesis. We study how mRNAs regulate protein complex assembly and investigate assembly and biological functions of constitutively expressed cytoplasmic condensate networks such as TIS granules and the FXR1 network.

We take a multi-disciplinary approach and use molecular biology and biophysics, biochemistry and chemical biology, high-resolution imaging, and computational methods to study how RNA regulates protein activity. We found that RNA binding to intrinsically disordered regions (IDRs) of proteins changes the conformational states of the IDRs and allows binding of specific protein interactors which in turn regulate downstream pathways.

In cells, RNA-dependent assembly of protein complexes occurs in TIS granules but not in the cytosol. In vitro, these protein complexes only form in the presence of RNA. Mechanistically, we identified the sequence and structural motifs of a new and widespread RNA-binding domain in IDRs of transcription factors and enzymes – protein classes that are not known to bind to RNA. Using NMR, we observed an RNA-dependent conformational change in the IDRs of transcription factors, such as MYC. More generally, we found that the IDR RNA-binding domains often overlap with hotspots of recurrent missense mutations in cancer, suggesting that these regions are functionally important. We propose that protein activity regulation by RNA will play regulatory roles similar in scale and scope to post-translational modifications.

Going forward, we will study the molecular mechanism and functional scope of RNA-induced protein activity regulation through changes in IDR conformations. We will develop novel methodology to monitor RNA-dependent conformational changes in proteins and develop new and robust tools to rationally manipulate the activity of transcription factors and enzymes through RNA. This will establish RNA as widespread regulator of protein conformations and protein activity.

PUBLICATIONS

(**) My five most significant publications.

MANUSCRIPTS IN PREPARATION

Horste EL, Zhen G, Fansler MM, Chen X, Lee FCY, Ule J, **Mayr C**. Cytoplasmic location of translation controls protein output. *In preparation*.

Luo Y, Pratihata S, Horste EL, Al-Hashimi HM, **Mayr C. Assembly of MYC protein complexes is regulated by RNA-induced conformation changes of its disordered region. *In preparation*.

Chen X, **Mayr C. Enzymatic activity regulation through FXR1 network-induced conformational changes. *In preparation*.

Zhen G, Kwon B, **Mayr C**. Nucleosome-depleted regions define bi-directional transcription termination zones in yeast. *In preparation*.

PREPRINTS

Fansler MM, Zhen, G, **Mayr C**. Quantification of alternative 3'UTR isoforms from single cell RNA-seq data with scUTRquant. bioRxiv (2021); doi: <https://doi.org/10.1101/2021.11.22.469635>.

PUBLISHED PAPERS

Kwon B, Fansler MM, Patel ND, Lee J, Ma W, **Mayr C**. Enhancers regulate 3' end processing activity to control alternative 3'UTR isoforms. *Nature commun* 13, 2709 (2022).

Mitschka S, Fansler MM, **Mayr C**. Generation of 3'UTR knockouts using CRISPR/Cas9-mediated genome editing. *Methods in Enzymology* 655, 724-754 (2021).

Mitschka S, **Mayr C**. Endogenous p53 expression in human and mouse is not regulated by its 3'UTR. *eLife* 10:e65700 (2021).

Ma W, Zhen G, Xie W, **Mayr C**. *In vivo* reconstitution finds multivalent RNA-RNA interactions as drivers of mesh-like condensates. *eLife*, 10:e64252 (2021).

Previous version on bioRxiv; doi: <https://doi.org/10.1101/2020.02.14.949503>

-Highlighted by preLights

Lee SH, **Mayr C. Gain of additional BIRC3 protein functions through 3'UTR-mediated protein complex formation. *Mol Cell* 74, 701-712 (2019).

Ma W, **Mayr C. A membraneless organelle associated with the endoplasmic reticulum enables 3'UTR-mediated protein-protein interactions. *Cell* 175, 1492-1506 (2018).

-Previewed in *Developmental Cell*

-Highlighted in *Nature Reviews Molecular Cell Biology*

McMaster ML*, Berndt SI*, Zhang J*, Slager SL*, , Fansler MM, **Mayr C**, ... , Chanock SL*, Rothman N*, V Joseph*, Goldin LR*, Skibola CF*, Caporaso ME*. Two high-risk susceptibility loci at 6p25.3 and 14q32.13 for Waldenström macroglobulinemia/lymphoplasmacytic lymphoma. *Nat Commun* 9:4182 (2018).

Lee SH*, Singh I*, Tisdale S, Abdel-Wahab O, Leslie CS, **Mayr C**. Widespread intronic polyadenylation inactivates tumor suppressor genes in leukemia. *Nature* 561, 127-131 (2018).

-Highlighted in *Nature Reviews Cancer*

-Highlighted in *Cancer Discovery*

-Highlighted in *Trends in Cancer*

Singh I, Lee SH, Sperling AS, Samur MK, Tai YT, Fulciniti M, Munshi NC, **Mayr C***, Leslie CS*. Widespread intronic polyadenylation diversifies immune cell transcriptomes. *Nat Commun* 9:17169:1716 (2018).

Berkovits BD, **Mayr C. Alternative 3'UTRs act as scaffolds to regulate membrane protein localization. *Nature* 522, 363-367 (2015).

-Highlighted in *Nature Reviews Molecular Cell Biology*

Lianoglou S, Garg V, Yang JL, Leslie CS, **Mayr C**. Ubiquitously transcribed genes use alternative polyadenylation to achieve tissue-specific expression. *Genes Dev* 27, 2380-2396 (2013).
-Selected by Science Signaling as one of the Breakthroughs of 2013
-Recommended by the Faculty of 1000

Mayr C, Bartel DP. Widespread shortening of 3'UTRs by alternative cleavage and polyadenylation activates oncogenes in cancer cells. *Cell* 138, 673-684 (2009).
-Highlighted in Nature
-Highlighted in Nature Reviews Genetics
-Designated as "Exceptional" by the Faculty of 1000

Pallasch CP, Patz M, Park YJ, Hagist S, Eggle D, Claus R, Debey-Pascher S, Schulz A, Frenzel L, Claasen J, Kutsch N, Krause G, **Mayr C**, Rosenwald A, Plass C, Schultze JL, Hallek M, Wendtner CM. miRNA deregulation by epigenetic silencing disrupts suppression of the oncogene PLAG1 in chronic lymphocytic leukemia. *Blood* 114, 3255-3264 (2009).

Wang ET, Sandberg R, Luo S, Khrebtkova I, Zhang L, **Mayr C**, Kingsmore SF, Schroth GP, Burge CB. Alternative isoform regulation in human tissue transcriptomes. *Nature* 456,470-476 (2008).
-Designated as "Exceptional" by the Faculty of 1000

Wiesner M, Zentz C, **Mayr C**, Wimmer R, Hammerschmidt W, Zeidler R, Moosmann A. Conditional immortalization of human B cells by CD40 ligation. *PLoS ONE* 3, e1464 (2008).

Bund D, **Mayr C**, Kofler DM, Hallek M, Wendtner CM. CD23 is recognized as tumor-associated antigen (TAA) in B-CLL by CD8+ autologous T lymphocytes. *Exp Hematol* 35, 920-930 (2007).

Zhou B, Wang S, **Mayr C**, Bartel DP, Lodish HF. miR-150, a microRNA expressed in mature B and T cells, blocks early B cell development when expressed prematurely. *Proc Natl Acad Sci U S A* 104, 7080-7085 (2007).

Mayr C, Hemann MT, Bartel DP. Disrupting the pairing between let-7 and Hmga2 enhances oncogenic transformation. *Science* 315, 1576-1579 (2007).
-Highlighted in Science as Editor's Choice
-Highlighted in Nature Reviews Cancer
-Highlighted in Journal of the American Chemical Society

Bund D, **Mayr C**, Kofler DM, Hallek M, Wendtner CM. Human Ly9 (CD229) as novel tumor-associated antigen (TAA) in chronic lymphocytic leukemia recognized by autologous CD8+ T cells. *Exp Hematol* 34, 860-869 (2006).

Mayr C, Bund D, Schlee M, Bamberger M, Kofler DM, Hallek M, Wendtner CM. MDM2 is recognized as a tumor-associated antigen in CLL by CD8+ autologous T lymphocytes. *Exp Hematol* 34, 44-53 (2006).

Mayr C, Speicher MR, Kofler DM, Buhmann R, Busch R, Strehl J, Hallek M, Wendtner CM. Chromosomal translocations are associated with poor prognosis in chronic lymphocytic leukemia. *Blood* 107, 742-751 (2006).

Mayr C, Kofler DM, Büning H, Bund D, Hallek M, Wendtner C-M. Transduction of CLL cells by CD40 ligand (CD40L) enhances an antigen specific immune recognition by autologous T cells. *Blood* 106, 3223-3226 (2005).

Mayr C, Bund D, Schlee M, Moosmann A, Kofler DM, Hallek M, Wendtner C-M. Fibromodulin as a novel tumor-associated antigen (TAA) in chronic lymphocytic leukemia (CLL) which allows expansion of specific CD8+ autologous T lymphocytes. *Blood* 105, 1566-1573 (2005).

Kofler DM, Büning H, **Mayr C**, Bund D, Baumert J, Hallek M, Wendtner CM. Engagement of the B-cell antigen receptor (BCR) allows efficient transduction of ZAP-70 positive B-CLL cells by recombinant adeno-associated virus (rAAV) vectors. *Gene Ther* 11, 1416-1424 (2004).

Strehl J, Mey U, Glasmacher A, Djulbegovic B, **Mayr C**, Gorschluter M, Ziske C, Schmidt-Wolf IG. High-dose chemotherapy followed by autologous stem cell transplantation as first-line therapy in aggressive non-Hodgkin's lymphoma is superior to conventional chemotherapy in selected patients: a meta-analysis. *Haematologica* 88, 1304-1315 (2003).

Hildebrandt M, Rose M, **Mayr C**, Arck P, Schüler C, Reutter W, Salama A, Klapp BF. Dipeptidyl peptidase IV (DPP IV, CD 26) in patients with mental eating disorders. *Adv Exp Med Biol* 477, 197-204 (2000).

Hildebrandt M, Rose M, **Mayr C**, Schüler C, Reutter W, Salama A, Klapp BF. Alterations in expression and in serum activity of dipeptidyl peptidase IV (DPP IV, CD 26) in patients with hyporectic eating disorders. *Scand J Immunol* 50, 536-541 (1999).

REVIEWS AND COMMENTARIES

- Mitschka S, **Mayr C**. Context-specific regulation and function of mRNA alternative polyadenylation. *Nat Rev Mol Cell Biol*, Jul 7:1-18 (2022).
- Chen X, **Mayr C**. A working model for condensate RNA-binding proteins as matchmakers for protein complex assembly. *RNA* 28, 76-87 (2022).
- Mayr C**. 3'UTRs regulate protein functions by providing a nurturing niche during protein synthesis. *Cold Spring Harb Symp Quant Biol* 84, 95-104 (2019).
- Mayr C**. Protein complexes assemble as they are being made. *Nature* 561, 186-187 (2018).
- Mayr C**. What are 3'UTRs doing? *Cold Spring Harb Perspect Biol*, (2019). epub Sept 4, 2018. Book chapter in *RNA Worlds: New Tools for Deep Exploration* (2018). Edited by Thomas R. Cech, Joan A. Steitz, John F. Atkins.
- Mayr C**. Regulation by 3'-Untranslated Regions. *Annu Rev Genet* 51:171-194 (2017).
- Mayr C**. Evolution and biological roles of alternative 3'UTRs. *Trends Cell Biol* 26, 227-237 (2016).
- Kofler DM, **Mayr C**, Wendtner CM. Current status of immunotherapy in B cell malignancies. *Curr Drug Targets* 7, 1371-1374 (2006).
- Wendtner CM, Kofler DM, **Mayr C**, Bund D, Hallek M. The potential of gene transfer into primary B-CLL cells using recombinant virus vectors. *Leuk Lymphoma* 45, 897-904 (2004).
- Mayr C**, Radzom S, Dreyling M. Neurotoxicity under chemotherapy with high doses of cytarabine. *Arzneimitteltherapie* 19, 296-298 (2001).

INVITED TALKS

KEYNOTE LECTURES

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| Keynote Lecture, VIII National RNA meeting, ptRNA2019, Porto, Portugal | 2019 |
| Keynote Lecture, Macromolecular complexes in mRNA localization, Dusseldorf, Germany | 2018 |
| Keynote Lecture, Gordon Research Seminar, Translation machinery in health and disease, Galveston | 2017 |
| Keynote Lecture, Computational RNA biology Conference, Hinxton, UK | 2016 |
| Keynote Lecture, Spring Meeting 2016, University of Heidelberg | 2016 |

SELECTED SEMINARS (past 5 years)

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| Seminar, University Texas Southwestern, Dallas, TX | 2023 |
| Seminar, Scripps Institute Florida/San Diego | 2023 |
| Seminar, University of Geneva, Switzerland | 2023 |
| RNA biology Symposium, NCI, Bethesda, MD | 2023 |
| Seminar, University of Pittsburgh, PA | 2023 |
| ASBMB meeting, Seattle, WA | 2023 |
| Seminar, University of Rochester, NY | 2023 |
| Seminar, University of California San Francisco, CA | 2023 |
| Seminar, Columbia University, NY | 2023 |
| EMBO Workshop – from functional genomics to systems biology | 2022 |
| Symposium, New Concepts in Organization of the Nucleus, Bethesda, MD | 2022 |
| Workshop on intrinsically disordered proteins, Rockville, MD | 2022 |
| EMBO Workshop on mRNA 3' end processing, Oxford, UK | 2022 |
| 31 st Cancer Course at Jackson Laboratory, Farmington, CT | 2022 |
| EMBO Workshop on RNA localization and local translation, Sant Feliu De Guixols, Spain | 2022 |
| Gordon Research Conference, Post-transcriptional gene regulation, Sunday River, ME | 2022 |
| International Titisee Conference, RNA as a driving force in cellular organization, Freiburg, Germany | 2022 |
| International symposium, RNA: beyond its genetic code, Mainz, Germany | 2022 |
| Annual Lorne Cancer Conference, Lorne, Victoria, Australia | 2022 |
| Cell Symposia, Biological Assemblies: Phase transitions and more. Seville, Spain (virtual) | 2021 |
| Butler Seminar, Princeton University, NJ | 2021 |
| Seminar, Condensate Colloquium Series (virtual) | 2021 |
| 30 th Cancer Course at Jackson Laboratory, Bar Harbor, ME (virtual) | 2021 |
| High Risk High Reward Annual Symposium, NIH, MD (virtual) | 2021 |
| AACR, Annual Meeting, Chair of Educational session on Phase separation (virtual) | 2021 |
| Seminar, University of Sheffield, UK (virtual) | 2021 |

Kjeldgaard Lecture, University of Aarhus, Denmark (virtual)	2021
Symposium, 100 years of Biophysics, MPI Frankfurt, Germany (virtual)	2021
Seminar, University of Portland, Portland, OR (postponed)	2020
Seminar, Baylor College of Medicine, Houston, TX (virtual)	2020
Seminar, Kitchen table talks, Dewpoint Therapeutics, Boston, MA (virtual)	2020
Seminar, National Cancer Institute, Frederick, VA (virtual)	2020
Seminar, University Texas Galveston, Galveston, TX (postponed)	2020
Seminar, MSK Spotlight, New York, NY (virtual)	2020
Quantitative Biology of the Cancer Cell Symposium, San Francisco, CA	2020
Seminar, Yale University, New Haven, CT	2020
Seminar, Stanford University, Palo Alto, CA	2020
Keystone Symposia, Non-coding RNAs: Mechanism, Function and Therapies, Whistler, Canada	2020
Seminar, Dartmouth College, Hanover, NH	2019
Seminar, Harvard University, Cambridge, MA	2019
Seminar, Mount Sinai School of Medicine, New York, NY	2019
Seminar, Molecular Biology Institute, University of California Los Angeles, Los Angeles, CA	2019
Seminar, Department of Microbiology and Molecular Genetics, University of California Irvine, CA	2019
Seminar, Max Planck Institute of Biochemistry, Martinsried, Germany	2019
Connell Seminar, University of Toronto, Toronto, CA	2019
Seminar, New York University, New York, NY	2019
Seminar, University of Bern, Switzerland	2019
Seminar, ETH Zurich, Switzerland	2019
Seminar, Max Planck Institute of Biophysics, Frankfurt, Germany	2019
FASEB meeting, From unfolded proteins in the ER to disease, Snowmass, CO	2019
3 rd International Conference "The long and the short of non-coding RNAs", Heraklion, Crete	2019
CSHL Symposium, Quantitative Biology addressing RNA Control & Regulation, Cold Spring Harbor, NY	2019
Workshop on Splicing Factor Mutations and RNA Biology in Cancer, Yale University, New Haven, CT	2019
Cell Symposia, Regulatory RNAs, Berlin, Germany	2019
Keystone Symposia, Biomolecular Condensates, Snowbird, UT	2019
Seminar, Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany	2019
Banbury meeting on Phase Separated Assemblies in Cell Biology, Lloyd Harbor, NY	2018
Seminar, Moderna Therapeutics, Cambridge, MA	2018
Biology Colloquium, Massachusetts Institute of Technology, Cambridge, MA	2018
Seminar, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY	2018
EMBL/EMBO symposium, Complex Life of mRNA, Heidelberg, Germany	2018
Symposium, Alternative polyadenylation of mRNAs, Beijing, China	2018
Plenary Lecture, Annual meeting of the Society for Developmental Biology, Portland, OR	2018
Microsymposium on small RNAs, Vienna, Austria	2018
Seminar, University of Wisconsin, Madison, WI	2018
Seminar, Fred Hutchinson Cancer Center, Seattle, WA	2018
Seminar, University of California Santa Cruz, Santa Cruz, CA	2018
Seminar, Salk Institute, San Diego, CA	2018
Barcelona Biomed Plenary Seminar, IRB Barcelona, Barcelona, Spain	2018
Royal Society meeting on translation, Newport Pagnell, UK	2018
Seminar, University of Massachusetts Amherst, Amherst, MA	2018