CURRICULUM VITAE (01/03/2024)

I. Personal Information

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Nationality:	German

II. Biosketch

As Group Leader of the Single Cell Genomics group at the Centro Nacional de Análisis Genómico (CNAG) Dr. Heyn joins computational, technical and biological knowledge to establish and apply best practices in single-cell and spatial research. His group combines collaborative research, technology development activities and follows an independent research line of translational/clinical cancer research. Dr. Heyn published 120 articles, including 107 original research articles, 10 Reviews and 3 book chapters. His papers have been cited 17,975x, resulting in an h-index of 59 (Google Scholar). Dr. Heyn was listed among the top Highly Cited Researchers in 2022 (Clarivate). The EU (ERC and H2020) and the Chan Zuckerberg Initiative support Dr. Heyn's role in the Human Cell Atlas (HCA) Project, where he leads the atlas of the B-cell lineage and contributes to the immune cell, pancreas and kidney atlases. He is co-chairing the Standards and Technology Working Group of the HCA and hosted the 2019 Annual Meeting in Barcelona. Dr. Heyn is also scientific co-chair and working group leader of the SpatioTemporal Omics Consortium (STOC). National and international, public and private (pharma partners) funding supports his work to determine the plasticity and dynamics of immune cells in cancer and inflammation. Dr. Heyn previously contributed to several national and international research consortia, including the European Epigenome (BLUEPRINT) and the Cancer Genome Atlas (TCGA) Projects.

General quality indicators of scientific production

Number of peer-reviewed publications:	120
Total citations:	17,975
Citations last 5 years (2019-2024):	11,930
Active funding:	8.1M EUR
PhD thesis supervised:	8 (5 ongoing)

III. Research Experience

2023-present	Centro Nacional de Análisis Genómico (CNAG), Barcelona, Spain **Group Leader** Research group: Single Cell Genomics
2016-2023	Centro Nacional de Análisis Genómico, Centre for Genomic Regulation (CNAG-CRG), Barcelona, Spain **Team Leader** Research group: Single Cell Genomics
2015-2016	Cancer Epigenetics and Biology Program (PEBC), Bellvitge Institute for Biomedical Research (IDIBELL), Spain **Miguel Servet Researcher** Research group: Cancer Epigenetics (Dr. Manel Esteller)
2009-2015	Cancer Epigenetics and Biology Program (PEBC), Bellvitge Institute for Biomedical Research (IDIBELL), Spain **Juan de la Cierva Postdoctoral Fellow** Research group: Cancer Epigenetics (Dr. Manel Esteller)

IV. Education

2005-2009	Hannover Medical School, Hanover, Germany **Doctor of Science** Mentor: Prof. Brigitte Schlegelberger, Dr. Carmela Beger
2003-2005	University of Bremen, Bremen, Germany **Degree in Biology** Mentor: Prof. Jörn Bullerdiek
2002-2003	University of Glasgow, Glasgow, United Kingdom **Erasmus Student** Mentor: Prof. Jeremy Mottram
1999-2002	University of Bremen, Bremen, Germany **Undergraduate Student**

V. Publications (* Authors contributed equally; [1] Corresponding author)

10 Key publications

Massoni-Badosa R, Aguilar-Fernández S, Nieto JC, Soler-Vila P, (…), Martin-Subero JI[1], **Heyn H[1]**. An atlas of cells in the human tonsil. **Immunity** 2024, 57(2):379-399.e18.

De Rop FV, Hulselmans G, Flerin C, Soler-Vila P, (…), Aerts S[1], **Heyn H[1]**. Systematic benchmarking of single-cell ATAC-sequencing protocols. **Nature Biotechnology** 2023, doi: 10.1038/s41587-023-01881-x.

Moffitt JR, Lundberg E, **Heyn H[1]**. The emerging landscape of spatial profiling technologies. **Nature Reviews Genetics** 2022; 23(12):741-759.

Nieto P, Elosua-Bayes M, Trincado JL, Marchese D, (…), **Heyn H[1]**. A single-cell tumor immune atlas for precision oncology. **Genome Research** 2021, 31(10):1913-1926.

Rubio-Perez C, Planas-Rigol E, Trincado JL, Bonfill-Teixidor E, (…), **Heyn H[1]**, Seoane J[1]. Immune cell profiling of the cerebrospinal fluid enables the characterization of the brain metastasis microenvironment. **Nature Communications** 2021, 12(1):1503.

Elosua-Bayes M, Nieto P, Mereu E, Gut I, **Heyn H[1]**, SPOTlight: seeded NMF regression to deconvolute spatial transcriptomics spots with single-cell transcriptomes. **Nucleic Acids Research** 2021, Feb 5:gkab043.

Rozenblatt-Rosen O, Shin JW, Rood JE, Hupalowska A, Human Cell Atlas Standards and Technology Working Group, Regev A, **Heyn H[1]**, Building a high-quality Human Cell Atlas, **Nature Biotechnology** 2021, 39(2):149-153.

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Mereu E, Lafzi A, Moutinho C, Ziegenhain C, (…), **Heyn H[1]**, Benchmarking Single-Cell RNA Sequencing Protocols for Cell Atlas Projects, **Nature Biotechnology** 2020, 38(6):747-755.

Salzer M, Lafzi A, Berenguer-Llergo A, Youssif C, Castellanos A, (…), **Heyn H[1]**, Aznar Benitah S[1], Identity Noise and Adipogenic Traits Characterize Dermal Fibroblast Aging, **Cell** 2018, 175(6):1575-1590.e22

Publication List (last 5 years).
Full list: Google Scholar

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Massoni-Badosa R, Aguilar-Fernández S, Nieto JC, Soler-Vila P, Elosua-Bayes M, Marchese D, Kulis M, Vilas-Zornoza A, Bühler MM, Rashmi S, Alsinet C, Caratù G, Moutinho C, Ruiz S, Lorden P, Lunazzi G, Colomer D, Frigola G, Blevins W, Romero-Rivero L, Jiménez-Martínez V, Vidal A, Mateos-Jaimez J, Maiques-Diaz A, Ovejero S, Moreaux J, Palomino S, Gomez-Cabrero D, Agirre X, Weniger MA, King HW, Garner LC, Marini F, Cervera-Paz FJ, Baptista PM, Vilaseca I, Rosales C, Ruiz-Gaspà S, Talks B, Sidhpura K, Pascual-Reguant A, Hauser AE, Haniffa M, Prosper F, Küppers R, Gut IG, Campo E, Martin-Subero JI[1], **Heyn H[1]**. An atlas of cells in the human tonsil. **Immunity** 2024, 57(2):379-399.e18.

Rueda AD, Salvador-Martínez I, Sospedra-Arrufat I, Alcaina-Caro A, Fernández-Miñán A, Burgos-Ruiz AM, Cases I, Mohedano A, Tena JJ, **Heyn H**, Lopez-Rios J, Nusspaumer G., The cellular landscape of the endochondral bone during the transition to extrauterine life. **Immunology & Cell Biology** 2024, 102(2):131-148.

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Garrido-Trigo A, Corraliza AM, Veny M, Dotti I, Melón-Ardanaz E, Rill A, Crowell HL, Corbí Á, Gudiño V, Esteller M, Álvarez-Teubel I, Aguilar D, Masamunt MC, Killingbeck E, Kim Y, Leon M, Visvanathan S, Marchese D, Caratù G, Martin-Cardona A, Esteve M, Panés J, Ricart E, Mereu E, **Heyn H**, Salas A. Macrophage and neutrophil heterogeneity at single-cell spatial resolution in human inflammatory bowel disease. **Nature Communications** 2023. 26;14(1):4506.

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De Rop FV, Hulselmans G, Flerin C, Soler-Vila P, Rafels A, Christiaens V, González-Blas CB, Marchese D, Caratù G, Poovathingal S, Rozenblatt-Rosen O, Slyper M, Luo W, Muus C, Duarte F, Shrestha R, Bagdatli ST, Corces MR, Mamanova L, Knights A, Meyer KB, Mulqueen R, Taherinasab A, Maschmeyer P, Pezoldt J, Lambert CLG, Iglesias M, Najle SR, Dossani ZY, Martelotto LG, Burkett Z, Lebofsky R, Martin-Subero JI, Pillai S, Sebé-Pedrós A, Deplancke B, Teichmann SA, Ludwig LS, Braun TP, Adey AC, Greenleaf WJ, Buenrostro JD, Regev A, Aerts S[1], **Heyn H[1]**. Systematic benchmarking of single-cell ATAC-sequencing protocols. **Nature Biotechnology** 2023. doi: 10.1038/s41587-023-01881-x

Blanco-Carmona E, Narayanan A, Hernandez I, Nieto JC, Elosua-Bayes M, Sun X, Schmidt C, Pamir N, Özduman K, Herold-Mende C, Pagani F, Cominelli M, Taranda J, Wick W, von Deimling A, Poliani PL, Rehli M, Schlesner M, **Heyn H[1]**, Turcan Ş[1]. Tumor heterogeneity and tumor-microglia interactions in primary and recurrent IDH1-mutant gliomas. **Cell Reports Medicine** 2023 Oct 20:101249. doi: 10.1016/j.xcrm.2023.101249.

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Cañellas-Socias A, Cortina C, Hernando-Momblona X, Palomo-Ponce S, Mulholland EJ, Turon G, Mateo L, Conti S, Roman O, Sevillano M, Slebe F, Stork D, Caballé-Mestres A, Berenguer-Llergo A, Álvarez-Varela A, Fenderico N, Novellasdemunt L, Jiménez-Gracia L, Sipka T, Bardia L, Lorden P, Colombelli J, **Heyn H**, Trepat X, Tejpar S, Sancho E, Tauriello DVF, Leedham S, Attolini CS, Batlle E. Metastatic recurrence in colorectal cancer arises from residual EMP1+ cells. **Nature** 2022; Nov;611(7936):603-613.

Beucher A, Miguel-Escalada I, Balboa D, De Vas MG, Maestro MA, Garcia-Hurtado J, Bernal A, Gonzalez-Franco R, Vargiu P, **Heyn H**, Ravassard P, Ortega S, Ferrer J. The HASTER lncRNA promoter is a cis-acting transcriptional stabilizer of HNF1A. **Nature Cell Biology** 2022; Oct;24(10):1528-1540.

Nadeu F, Royo R, Massoni-Badosa R, Playa-Albinyana H, Garcia-Torre B, Duran-Ferrer M, Dawson KJ, Kulis M, Diaz-Navarro A, Villamor N, Melero JL, Chapaprieta V, Dueso-Barroso A, Delgado J, Moia R, Ruiz-Gil S, Marchese D, Giró A, Verdaguer-Dot N, Romo M, Clot G, Rozman M, Frigola G, Rivas-Delgado A, Baumann T, Alcoceba M, González M, Climent F, Abrisqueta P, Castellví J, Bosch F, Aymerich M, Enjuanes A, Ruiz-Gaspà S, López-Guillermo A, Jares P, Beà S, Capella-Gutierrez S, Gelpí JL, López-Bigas N, Torrents D, Campbell PJ, Gut I, Rossi D, Gaidano G, Puente XS, Garcia-Roves PM, Colomer D, **Heyn H**, Maura F, Martín-

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Álvarez-Varela A, Novellasdemunt L, Barriga FM, Hernando-Momblona X, Cañellas-Socias A, Cano-Crespo S, Sevillano M, Cortina C, Stork D, Morral C, Turon G, Slebe F, Jiménez-Gracia L, Caratù G, Jung P, Stassi G, **Heyn H**, Tauriello DVF, Mateo L, Tejpar S, Sancho E, Stephan-Otto Attolini C, Batlle E. Mex3a marks drug-tolerant persister colorectal cancer cells that mediate relapse after chemotherapy. **Nature Cancer** 2022; Sep;3(9):1052-1070.

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Rodríguez-Ubreva J, Arutyunyan A, Bonder MJ, Del Pino-Molina L, Clark SJ, de la Calle-Fabregat C, Garcia-Alonso L, Handfield LF, Ciudad L, Andrés-León E, Krueger F, Català-Moll F, Rodríguez-Cortez VC, Polanski K, Mamanova L, van Dongen S, Kiselev VY, Martínez-Saavedra MT, **Heyn H**, Martín J, Warnatz K, López-Granados E, Rodríguez-Gallego C, Stegle O, Kelsey G, Vento-Tormo R, Ballestar E. Single-cell Atlas of common variable immunodeficiency shows germinal center-associated epigenetic dysregulation in B-cell responses. **Nature Communications** 2022; Apr 1;13(1):1779.

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2021

Perez-Zsolt D, Muñoz-Basagoiti J, Rodon J, Elosua-Bayes M, Raïch-Regué D, Risco C, Sachse M, Pino M, Gumber S, Paiardini M, Chojnacki J, Erkizia I, Muñiz-Trabudua X, Ballana E, Riveira-Muñoz E, Noguera-Julian M, Paredes R, Trinité B, Tarrés-Freixas F, Blanco I, Guallar V, Carrillo J, Blanco J, Telenti A, **Heyn H**, Segalés J, Clotet B, Martinez-Picado J, Vergara-Alert J, Izquierdo-Useros N., SARS-CoV-2 interaction with Siglec-1 mediates trans-infection by dendritic cells. **Cell and Molecular Immunology** 2021; 18(12):2676-2678.

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Nieto P, Elosua-Bayes M, Trincado JL, Marchese D, Massoni-Badosa R, Salvany M, Henriques A, Nieto J, Aguilar-Fernández S, Mereu E, Moutinho C, Ruiz S, Lorden P, Chin VT, Kaczorowski D, Chan CL, Gallagher R, Chou A, Planas-Rigol E, Rubio-Perez C, Gut I, Piulats JM, Seoane J, Powell JE, Batlle E, **Heyn H[1]**. A single-cell tumor immune atlas for precision oncology. **Genome Research** 2021; 31(10):1913-1926.

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VI. Research Projects (last 5 years)

2022-2026 SERPENTINE trial: Metastatic colorectal cancer, combinatory PDL1 and CTLA4 inhibitors.
Funding agency: AstraZeneca
PI: Holger Heyn; Amount: **1,615,157** €

2019-2025 Single-cell genomics to comprehensively understand healthy B-cell maturation and transformation to chronic lymphocytic leukemia (BCLL@las)
Funding agency: European Commission (ERC Synergy 2017)
PI: Holger Heyn
Amount: **4,042,622** € (Total: 8,333,331 €)

2019-2025 Decision on optimal combinatorial therapies in IMIDs using systems approaches (DocTIS; SEP-210574908)
Funding agency: European Commission (SC1-BHC-02-2019)
PI/WP Leader: Holger Heyn
Amount: **1,065,750** € (Total: 6,260,050 €)

2023-2025 CLLSYSTEMS-(Epi)Genomic and microenvironment interactions driving evolution in chronic lymphocytic leukemia. Targets for clinical intervention (HR22-00172).
Funding agency: La Caixa Foundation
PI: Holger Heyn;
Amount: **379,398.10** €

2023-2025 AngioHeArt-Understanding and promoting the growth and regenerative functions of blood vessels in heart disease (HR22-00316).
Funding agency: La Caixa Foundation
PI: Holger Heyn;
Amount: **162,360.00** €

2021-2024 Nueva inmunoterapia contra el cáncer: bloqueo de la reprogramación lipídica basada en el mapeo de transcriptomas de metástasis: LipIMMUNE. (PLEC2021-007654)
Funding agency: Ministerio de Ciencia e Innovación (MCIN)
PI: Holger Heyn; Amount: **591,011** €

2021-2024 Fenotipado celular espacial de tumores para oncología digital personalizada (Ref. PID2020-115439GB-I00)
Funding agency: Ministerio de Ciencia e Innovación (MCIN)
PI: Holger Heyn; Amount: **314,600** €

2020-2023 T cell exclusion during cancer immune evasion and immunotherapy failure: cell types, transcriptional programs and biomechanics (772/C/2019)
Funding agency: La Marató de TV3 Foundation
PI: Holger Heyn
Amount: **133,125** €

2021-2023 Charting SARS-CoV-2 entry factors in human tissues (reference 202112-31)
Funding agency: La Marató TV3 Foundation
PI: Holger Heyn; Amount: **200,000** €

2019-2022 Developing tools and standards for integration of multidimensional HCA data (HCA3-0000000191)
Funding agency: Chan-Zuckerberg Initiative (Human Cell Atlas project)
PI: Holger Heyn
Amount: **237,029** €

2020-2021 Human Cell Atlas of the Pancreas (ESPACE; 874710)
Funding agency: European Commission (SC1-BHC-31-2019)
PI/WP Leader: Holger Heyn
Amount: **907,436** € (Total: 4,962,495 €)

Clinical Trials:

Phase II, Open-Label Study of preliminary efficacy of Durvalumab (MEDI4736) in Combination with Cediranib in Patients with Metastatic Uveal Melanoma. (CEDUVEAL-M; GEM-1805)
Funding agency: Spanish Multidisciplinary Melanoma Group (2019-001045-40)
PI: Jose María Piulats (Role: Partner).

Phase II, Open-Label Study of Tislelizumab in Combination with CBDCA+Paclitaxel as neoadjuvant therapy in Patients with Ovarian Cancer.
Funding agency: BeiGene
PI: Jose María Piulats (Role: Partner)

Phase II, Open-Label Study of preliminary efficacy of AloCelyvir in Patients with Metastatic Uveal Melanoma (PULSE).
Funding agency: ISCIII
PI: Jose María Piulats (Role: Partner)

SERPENTINE trial: Metastatic colorectal cancer, combinatory PDL1 and CTLA4 inhibitors.
Funding: AstraZeneca
PI: Holger Heyn and Elena Elez (VHIO)

VII. Scientific Activities

Scientific Co-founder:
As Scientific Co-founder of Omniscope, Dr. Heyn brings high-resolution profiling technologies to clinical application, developing advanced diagnostics and therapeutics tools. Omniscope is a Systems Immunology company providing solutions to detect diseases for interceptive medicine and to develop next-generation cell therapies. Reading the immune system as universal sensor of diseases, we envision Omniscope's technologies to enable modern medicine and to disrupt current practices in health care. Website: Omniscope.ai

Scientific Advisory Board:
Genome Biology (ISSN: 1474-760X)
Clinical Epigenetics (ISSN: 1868-7083)
MiRXES (Singapore, mirxes.com)
Nanostring (Seattle, US, nanostring.com)
National Genomics Infrastructure (SciLifeLab, Sweden)
Single Cell Core (VIB, Belgium)
PERSIST-SEQ (IMI2 project)
4D-HEALING (ERACoSysMed; H2020)

Research Grant Reviewer:
ERC Advanced and Consolidator Grants (EU), NRC (Norway), The European Hematology Association (EHA), The Research Foundation Flanders (FWO, Belgium), VIB Grand Challenge Program (Belgium), The Israel Science Foundation (ISF, Israel), etc.

Journal Reviewer:
Nature, Science, Nature Genetics, Nature Biotechnology, Nature Reviews Genetics, Nature Medicine, Nature Reviews Clinical Oncology, Genome Research, Genome Biology, Nature Communications, PLoS Genetics, Aging Cell, Cancer Research, Bioinformatics, Clinical Cancer Research, Clinical Epigenetics, Briefings in Functional Genomics, International Journal of Epidemiology, Epigenomics, PLoS Computational Biology, Epigenetics, etc.

VIII. Invited Conference Presentations (last 5 year, selected)

Heterogeneity and Evolution in Cancer, CNIO, Madrid, Spain;
"Single Cell Genomics: From Sample to Cell Atlas"
23.-25. September 2019

Charité Single Cell Symposium, Berlin, Germany;
"Towards a High Quality Human Cell Atlas"
21.-22. November 2019

EMBL-EBI Industry Workshop on Single-cell multi-omics analysis, Cambridge, UK;
Keynote Lecture ""Standards and Guidelines for Cell Atlas Projects"
4.-5. December 2019

Euro BioC Conference 2020, Bioconductor Project, Virtual Meeting
Keynote Lecture "A spatially-resolved tumor immune cell atlas for precision immuno-oncology"
14.-18. December 2020

3rd ASEICA Educational Symposium, Virtual Meeting
"Intra-tumor heterogeneity and clonal evolution"
23-25. November 2021

ESMO Virtual Advanced Course on Innovation and Emerging Knowledge in Colorectal Cancer, Virtual Meeting
Keynote Lecture: "Potential of single-cell sequencing in cancer research: focus on CRC"
13.-14. January 2022

The Advances in Genome Biology and Technology 2023 (AGBT), Miami, US
"Spatial Cellular Maps of Inflammatory Bowel Disease by Single-Molecule Imaging"
6.-9. Februar 2023

The Advances in Genome Biology and Technology 2024 (AGBT), Orlando, US
"Spatio-temporal dissection of colorectal cancer initiation using whole transcriptome imaging."
5.-8. Februar 2024

IX. Teaching and Supervisory Activities

Students:

ITN Marie Skłodowska Curie PhD Student. Emanuele Pitino (since 2023) "SIGNATURE: Single Cell in autoimmune diseases" University Pompeu Fabra (UPF), Barcelona, Spain

FPI PhD Student. Paula Nieto (since 2021) "Tumor immune microenvironment dynamics in immuno-therapy". University Pompeu Fabra (UPF), Barcelona, Spain

FPU PhD Student. Laura Jimenez Gracia (since 2020) "Integrative Single-cell Genomics to Unravel Mechanisms and Targets in Autoimmune Pathologies". Barcelona University (UB), Barcelona, Spain

PhD Student. Sergio Aguilar Fernandez (since 2020) "Network analysis of single cell cluster data using multi-omic analyses". University Pompeu Fabra (UPF), Barcelona, Spain

PhD Student. Sonal Rashmi (since 2020) "Integrative multiomic analysis of chronic lymphcytic leukemia at single cell resolution". University Pompeu Fabra (UPF), Barcelona, Spain

PhD Student. Marc Elosua Bayes (2019-2023) "Charting intra-tumoral heterogeneity dynamics through the integration of multi-modal single-cell profiles". University Pompeu Fabra (UPF), Barcelona, Spain

FPI PhD Student. Ramon Massoni (2018-2023) "A highly resolved atlas of the B-cell lineage in health and disease". University Pompeu Fabra (UPF), Barcelona, Spain

ITN Marie Skłodowska Curie PhD Student. Atefeh Lafzi (2016-2020) "Computational Strategies in Single Cell Analysis", SINGEK consortium, Barcelona University (UB), Barcelona, Spain

Master of Science, Lecturer:

Master “Bioinformatics and Omics analysis”. 2012-2016, **University of Vic**, Vic, Spain
Master “Genetics”. 2017, **University of Barcelona**, Barcelona, Spain
Master “Molecular Biology” 2017, **University of Barcelona**, Barcelona, Spain
Master “Translational Medicine”. 2014-2022, **University of Barcelona**, Barcelona, Spain
Master “Epigenetics”. 2018-2022, **University of Barcelona**, Barcelona, Spain
Master “Bioinformatics” 2020-2021, **UPF**, Barcelona, Spain
Master “Bioinformatics” 2020-2021, **ISCIII/CNIO**, Madrid, Spain