Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

# Master project 2024-2025

## Personal Information


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## Project

# Computational genomics

**Project Title:**

Function and specificity of human histone H1 variants in the organization and control of the genome.


**Keywords:**

Chromatin, histones, genomics, transposable elements, ChIP-seq



**Summary:**

Histone H1 participates in the stabilization of DNA around the core histone octamer that constitutes the nucleosome, in the spacing between adjacent nucleosomes, in nucleosome mobility, and in further levels of chromatin compaction. As a consequence, H1 is seen as a chromatin structural protein that might be involved in DNA compaction, heterochromatin formation and stabilization, and in the regulation of nuclear processes such as transcription, replication, DNA repair, etc. Nonetheless, in mammalians, histone H1 is not a single protein but an evolutionary diverse gene family that comprises up to seven members in somatic cells. Although considered for long time H1 variants to be redundant, we and others have described structural and functional differences between variants that include their distribution within the genome and nuclei, and diverse consequences upon depletion of particular H1 variants. We have recently described that H1 variants show distinct abundances among different repetitive and transposable elements (TE), with an enrichment of H1 variants that are located within high GC regions (H1X and H1.4) at TE that have incorporated recently into the human genome along its evolution. These variants may be involved in the repression of these TE. In parallel, we have found that depletion of these variants causes transcription from cryptic promoters. On the other hand, variants enriched within low GC DNA (H1.2, H1.3, H1.5 and H1.0) are enriched at TE incorporated early in evolution, are preferentially located at peripheral heterochromatin and may have a role in maintaining heterochromatin identity and tethering to nuclear lamina. Our hypothesis is that histone H1 participates in the repression of such elements by participating in heterochromatin maintenance, and does this in a variant-specific manner. Besides, depletion of multiple H1 variants induces and interferon response in some cell types that could be used to induce immunoresponse against tumors. We propose to study the involvement of histone H1 variants: 1. In the repression of cryptic transcription. 2. In the control of transposable elements. 3. In maintaining heterochromatin identity and the organization of nuclear compartments. 4. In preventing the viral mimicry phenomenon that may induce an interferon response in tumor cells, and its consequences in cancer progression and sensitivity to immunotherapy. We investigate the occupancy of H1 variants genome-wide by ChIP-seq (NGS) and the consequences of altering H1 levels on gene expression (RNA-seq) and chromatin organization (ATAC-seq, DNA methylation, hiC, etc), with an extensive use of Genomics and Bioinformatics.


**References:**


1. (3/3) Salinas-Pena M*, Serna-Pujol N*, Jordan A (2024) Genomic profiling of six human somatic histone H1 variants denotes that H1X accumulates at recently incorporated transposable elements. Nucleic Acids Research 52:1793-1813. 2. (3/3) Salinas-Pena M, Rebollo E, Jordan A (2023) Imaging analysis of six human histone H1 variants reveals universal enrichment of H1.2, H1.3, and H1.5 at the nuclear periphery and nucleolar H1X presence. eLife peer-reviewed preprint October 10, 2023; doi 10.7554/eLife.91306.1. 3. (15/17) Pascal C, Zonszain J, Hameiri O, Tammer L, Ben-Salmon S, Roy VR, Eid M, Levy T, Rabe'a SA, Gargi C, Shalev N, Elbaz L, Hakim T, Lev-Maor G, Jordan A, Meshorer E, Ast G (2023) Human histone H1 variants impact splicing outcome by controlling RNA polymerase II elongation rate. Molecular Cell 83:3801-17. 4. (9/11) Fernández-Justel JM, Santa-María C, Martín-Vírgala S, Ramesh S, Ferrera-Lagoa A, Salinas-Pena M, Isoler-Alcaraz J, Maslon MM, Jordan A, Cáceres JF, Gómez M. (2022) Histone H1 regulates non-coding RNA turnover on chromatin in a m6A-dependent manner. Cell Reports. 40:111329. 5. (6/6) Serna-Pujol N, Salinas-Pena

M, Mugianesi F, Le Dily F, Marti-Renom MA, Jordan A (2022) Coordinated changes in gene expression, H1 variant distribution and genome 3D conformation in response to H1 depletion. Nucleic Acids Research 50:3892-3910. 6. (8/8) Serna-Pujol N, Salinas-Pena M, Mugianesi F, Lopez-Anguita N, Torrent-Llagostera F, Izquierdo-Bouldstridge A, Marti-Renom MA, Jordan A (2021) TADs enriched in histone H1.2 strongly overlap with the B compartment, inaccessible chromatin and AT-rich Giemsa bands. FEBS Journal 288: 1989-2013. 7. (3/4) Ponte I, Andrés M, Jordan A, Roque A (2021) Towards understanding the regulation of histone H1 somatic subtypes with OMICs. Journal of Molecular Biology 433: 166734. 8. (13/13) Izquierdo-Bouldstridge A*, Bustillos A*, Bonet-Costa C, Aribau P, Garcia D, Dabad M, Esteve-Codina A, Pascual L, Peiro S, Esteller M, Murtha M, Millán-Ariño Ll, Jordan A (2017) Histone H1 depletion triggers an interferon response in cancer cells via activation of heterochromatic repeats. Nucleic Acids Research 45(20):11622-42. 9. (3/3) Millán-Ariño Ll, Izquierdo-Bouldstridge A, Jordan A (2016) Specificities and genomic distribution of somatic mammalian histone H1 subtypes. BBA Gene Regulatory Mechanisms 1859(3):510-19. 10. (9/9) Millán-Ariño Ll, Islam A, Izquierdo-Bouldstridge A, Mayor R, Terme JM, Luque N, Sancho M, López-Bigas N, Jordan A (2014) Mapping of six somatic linker histone H1 variants in human breast cancer cells uncovers specific features of H1.2. Nucleic Acids Research 42:4474-4493.

**Expected skills:**

Strong motivation for research. Background or interest in Biologgy/Biomedicine and Epigenetics. The student will work in analyzing high-throughput genomic data such as ChIP-seq, RNA-seq, ATAC-seq and hi-C. To do so, experience in handling aligners, peak calling softwares, differential gene expression analysis and statistics tests will be an advantage. In addition, programming skills in R, Python and/or Perl are also desirable.

**Possibility of funding:**

To be discussed

**Possible continuity with PhD:**

Yes