INSTITUTO CAJAL

SEMINARIO PRESENCIAL

Viernes, 21 de octubre de 2022
12:30 h. Instituto Cajal (CSIC) Madrid

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Oligodendroglia during developmental and disease: insights from single-cell and spatial omics

Abstract

Oligodendroglia (OLG) mediate myelination of neurons, a process that allows efficient electrical impulse transmission in the central nervous system (CNS). Oligodendrogenesis has been shown to occur in at least three waves during mouse CNS development. By performing single cell transcriptomics, we have previously shown that these mouse waves undergo a process of transcriptional convergence before birth, attenuating the expression of patterning transcription factors. We have now extended this analysis to post-natal stages and aging in mouse, using single cell and spatial transcriptomics and epigenomics, including technologies as Nano-Cut&Tag and spatial CUT&Tag, that allow to probe histone modifications genome-wide at a single cell and spatial level, respectively.

An autoimmune response against oligodendroglia and myelin triggers demyelination in multiple sclerosis (MS). We have previously identified disease-specific OLG populations in a mouse model of MS, characterized by the expression of immune genes. Assessing chromatin accessibility and the transcriptome simultaneously at the single cell level, we found that immune genes exhibit a primed chromatin state in mouse and human OLG in a non-disease context, compatible with rapid transitions to immune-competent states in MS. This primed chromatin state could reflect epigenetic memory from previous cellular states during development. Moreover, MS susceptibility single-nucleotide polymorphisms (SNPs) overlap with open chromatin regions in mouse and human OLG, suggesting that susceptibility for MS may involve OLG.

Affiliation and short bio

Dr Gonçalo Castelo-Branco is a Professor of Glial Cell Biology at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet, Stockholm, Sweden.

Dr. Castelo-Branco received his PhD in Medical Biochemistry in 2005, working on development of dopaminergic neurons and neural stem differentiation. He completed post-doctoral fellowships first at the Karolinska Institutet and then at the University of Cambridge, United Kingdom, working in neural and pluripotent stem cells and chromatin.

Dr. Castelo-Branco started his research group in 2012, focusing on the molecular mechanisms regulating the epigenomic states of oligodendrocyte lineage cells in neuroinflammatory and demyelinating diseases such as multiple sclerosis (MS), using technologies such as single cell transcriptomics and epigenomics, among others. The long-term goal of his group is to build a solid platform of convergent knowledge and know-how on the epigenetics of (re)myelination and neuroinflammation, which will allow to establish innovative regenerative strategies for neuroinflammatory diseases such as MS.

Dr. Castelo-Branco has received many prestigious awards and grants, including the European Research Council Consolidator Grant, the Swedish Society for Medical Research (SSMF) 100 years Jubileum Prize, the Royal Swedish Academy of Sciences Göran Gustafsson Prize 2021 in Medicine and the Hans Wigzell prize 2022.

Related publications with the topic:

Epigenomic priming of immune genes implicates oligodendroglia in multiple sclerosis susceptibility
Meijer M, Agirre E, Kabbe M, Van Tuijn Ca, Heskol A, Zheng C, Mendanha Falcão A, Bartosovic M, Kirby L, Calini D, Johnson Mr, Corces Mr, Montine Tj, Chen X, Chang Hy, Malhotra D, Castelo-branco G
Neuron 2022;110(7):1193-1210.e13

Single-cell CUT&Tag profiles histone modifications and transcription factors in complex tissues.
Bartosovic M, Kabbe M, Castelo-Branco G
Nat Biotechnol 2021 April

Altered human oligodendrocyte heterogeneity in multiple sclerosis
Sarah Jäkel, Eneritz Agirre, Ana Mendanha Falcão, David van Bruggen, Ka Wai Lee, Irene Knuesel, Dheeraj Malhotra, Charles ffrench-Constant, Anna Williams and Gonçalo Castelo-Branco.
Nature. 2019 Feb;566(7745):543-547.

Disease-specific oligodendrocyte lineage cells arise in multiple sclerosis.
Falcão AM, van Bruggen D, Marques S, Meijer M, Jäkel S, Agirre E, *et al*
Nat. Med. 2018 12;24(12):1837-1844

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