CRBM external seminar
BIOLuM
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How dividing cells adapt to karyotypic evolution

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Helder Maiato graduated in Biochemistry and holds a PhD in Biomedical Sciences from the University of Porto. He was a visiting PhD student with Bill Earnshaw at the University of Edinburgh (UK) and a Post-doctoral Research Affiliate with Conly Rieder at the New York State Department of Health (USA). At present, he is a Coordinating Investigator at the Institute for Research and Innovation in Health (i3S) where he heads the Chromosome Instability & Dynamics Lab, and is an invited Professor at the Faculty of Medicine of the University of Porto. He is recognized by his work on the role of CLASP proteins in the regulation of microtubule dynamics at kinetochores and the demonstration that kinetochore-driven microtubule organization is a key step in mitotic spindle assembly. More recently, his team uncovered a navigation system for chromosomes and a mitotic error code defined by tubulin detyrosination, as well as the mechanism behind spatial control of nuclear envelope reassembly during mitotic exit by an Aurora B activity gradient. Helder Maiato is currently interested in the spatial, temporal and adaptive mechanisms underlying chromosome segregation fidelity in the context of normal physiology, disease and evolution.

Abstract

Chromosome number among eukaryotic species is highly divergent, ranging from n=1 in haploid males of a primitive Australian ant, to n=ca 224–226 in a diploid blue butterfly, or n=720 in a polyploid fern. Likewise, large variations in chromosome size are also common among eukaryotes. Paradoxically, while karyotypic diversification underlies the emergence of new species, alterations in chromosome number and size within a given species are highly deleterious and have been implicated in cancer evolution, metastasis and drug resistance. Importantly, while significant progress has been made at the level of understanding how karyotypic evolution impacts organism physiology, disease and speciation, much less is known about the impact of karyotypic alterations on fundamental cellular processes. In particular, alterations in chromosome number and size pose significant challenges for cell division and we currently do not know how the cell division machinery adapts to cope with these challenges. To address this problem, we have been exploring natural karyotypic evolution in two related deer species with a very similar genome size and composition, but distinctively divergent chromosome number – 6/7 chromosomes in the female/male Indian muntjac and 46 chromosomes in the Chinese muntjac, as in humans. Here I will elaborate on how we have been using these unique systems for the mechanistic dissection of mitosis in mammals, while investigating how karyotypic alterations may be explored therapeutically in the treatment of human cancers.

Selected publications

1. Almeida, A.C., Soares-de-Oliveira, J., Drpic, D., Cheeseman, L.P., Damas, J., Lewin, H.A., Larkin, D., Aguiar, P., Pereira, A.J., and Maiato, H. (2022) Augmin-dependent microtubule self-organization drives kinetochore fiber maturation in mammals. Cell Reports, 39: 110610
2. Ferreira, L.T., Orr, B., Rajendraprasad, G., Pereira, A.J., Lemos, C., Lima, J.T., Guasch Boldú, C., Ferreira, J.G., Barisic, M. and Maiato, H. (2020) α-tubulin detyrosination impairs mitotic error correction by suppressing MCAK centromeric activity. J. Cell Biol. 219: e201910064. doi: 10.1083/jcb.201910064.
3. Drpic, D., Almeida, A., Aguiar, P., Renda, F., Damas, J., Lewin, H.A., Larkin, D.N., Khodjakov, A., Maiato, H. (2018) Chromosome segregation is biased by kinetochore size. Curr. Biol. 28: 1344-1356.
4.Barisic, M., Sousa, R.S., Tripathy, S.K., Magiera, M.M., Zaytsev, A.V., Pereira, A.L., Janke, C., Grishchuk, E.L., and Maiato, H. (2015) Microtubule detyrosination guides chromosomes during mitosis. Science. 348: 799-803.
5. Afonso, O., Matos, I., Pereira, A.J., Aguiar, P., Lampson, M.A. and Maiato, H. (2014) Feedback control of chromosome separation by a midzone Aurora B gradient. Science, 345: 332-336.