Mathematical modelling of centriole number dynamics in proliferating cancer cells

Marco António Dias Louro*[1]

[1]Instituto Gulbenkian de Ciência – Portugal

Abstract

Abnormally high centriole numbers are a hallmark of cancer cells. This phenomenon known as centriole amplification correlates with increased aggressiveness and poorer prognosis in several cancer types. However, it has been observed that centriole number varies extensively within tumours, between different types of cancers, and along cancer development. Thus, elucidating the role of centrosome amplification as a putative cancer biomarker would benefit from a quantitative characterisation of this heterogeneity. We develop mathematical models of centriole number dynamics grounded on classical mutation-selection balance theory, which conceptually resembles the proximal interaction between centriole overproduction and proliferative defects. Using a model selection approach, we find that models assuming a uniform cost of extra centrioles best describes data from a diverse panel of human cell lines. We highlight how using these models to classify different cell lines and to obtain accurate parameter estimates requires combined optimisation of both experimental and computational protocols. Finally, we explore how these models may be extended and how centriole biogenesis and post-mitotic segregation may constrain adaptation in the context of cancer evolution.

*Speaker