Katedry genetiky a biochémie PriF UK
a občianske združenie *NATURA*

Vás pozývajú na 130. prednášku v rámci Kuželových seminárov:

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COMPENSATORY EVOLUTION TO IMPAIRED MICROTUBULE DYNAMICS: WHY ARE TUBULINS DIFFERENT?

ktorá sa uskutoční **2. októbra 2024** (streda) o **13:30**
v miestnosti **CH1-222** Prírodovedeckej fakulty UK

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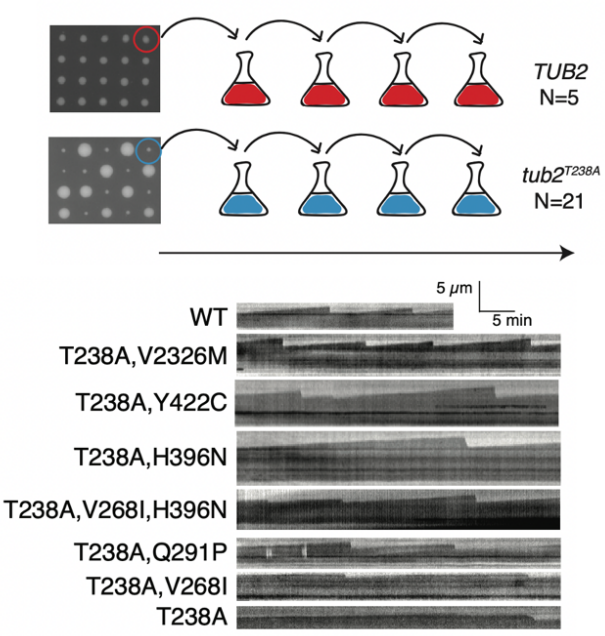
Andrea Ciliberto graduated in biology from the University of Florence in 1995, using cellular automata to simulate dividing cells. He did his PhD in Genetics in Pavia (2000) with a theoretical and experimental work addressing mitotic patterns in early sea urchin development. He then worked as a post-doc with John Tyson at Virginia Tech on different cell cycle models (2000-2003). His second post-doc was in Budapest, with Bela Novak, where he further developed models with non-linear differential equations to study problems related with cell replication (2003-2005). In 2005, he started his own group at IFOM, in Milan where in 2013 he was tenured principal investigator. In Milan he leads a group that combines models and experiments to study mechanisms of resistance to drugs that alter microtubule dynamics.



Synopsis of the lecture: Tubulins form microtubules that are essential components of the cytoskeleton. In mitosis, they play a key role for chromosome segregation. In the clinics, many tubulin binding agents are used to treat cancer patients. A major drawback of these drugs is the emergence of resistance to treatment. Here, we ask how cells cope with tubulin mutants that dramatically alter microtubule dynamics. We performed evolution experiments using both mutants that destabilize or hyperstabilize tubulins. The first mimic drugs such as vinca alkaloids, the second taxans. Our results show that in a hundred generations cells acquire compensatory mutations that restore full viability. With a combination of cell biology, genetic sequencing and biophysical studies, we find that cells follow predictable evolutionary paths, which involve both acquisition of extra chromosomes and point mutations. Mutations restore microtubule dynamics to different degrees, but they all rescue cellular growth, unveiling a role of the mitotic checkpoint in buffering genetic variability. Finally, we show significant overlapping between compensatory mutations found in yeast and those detected in cancer patients.

Selected publications:

1. Pavani M, Chiroli E, Cancrini C, Gross F, Bonaiuti P, Villa S, Giavazzi F, Matafora V, Bachi A, Fava LL, Lischetti T, **Ciliberto A.** (2023). Triap1 upregulation promotes escape from mitotic-slippage-induced G1 arrest. *Cell Reports* 42(3): 112215.
2. Pavani M, Bonaiuti P, Chiroli E, Gross F, Natali F, Macaluso F, Póti Á, Pasqualato S, Farkas Z, Pompei S, Cosentino Lagomarsino M, Rancati G, Szüts D, **Ciliberto A**. (2021). Epistasis, aneuploidy and functional mutations underlie evolution ot resistance to induced microtubule depolymerization. *The EMBO Journal* 40(22): e108225.
3. Bonaiuti P, Chiroli E, Gross F, Corno A, Vernieri C, Stefl, M, Cosentino Lagomarsino M, Knop M, **Ciliberto A**. (2018). Cells escape an operational mitotic checkpoint through a stochastic process. *Current Biology* 28: 28-37.
4. Gross, F, Bonaiuti, P, Hauf, S., **Ciliberto A**. (2018). Implications of alternative routes to APC/C inhibition by the mitotic checkpoint complex, *PLoS Computational Biology* 14(9): e1006449.
5. Vernieri C, Chiroli E, Francia V, Gross F, **Ciliberto A**. (2013). Adaptation to the spindle checkpoint is regulated by the interplay between Cdc28/Clbs and PP2ACdc55, *Journal of Cell Biology* 202: 765-778.