Elucidating the role of chromatin remodelers in cytokinesis

Patrizio Dimitri, Dipartimento di Biologia e Biotecnologie "Charles Darwin", Sapienza Università, Roma, Italy and Istituto Pasteur Italia-Fondazione Cenci Bolognetti - via dei Sardi, 70. patrizio.dimitri@uniroma1.it

Cytokinesis is the crucial final step of cell division. After chromosome segregation is completed, the actomyosin contractile ring drives the constriction of the plasma membrane. As a consequence, two daughter cells are generated still connected by a cytoplasmic bridge that contains the so-called midbody (MB), a mitotic structure that was first described around a century ago by Walther Flemming. Cytokinesis failure results in tetraploid and polyploid cells which in turn can give rise to genomic instability which is hallmark of cancer. Thus, the identification of new factors required for proper cytokinesis have a relevant impact on carcinogenesis.

The results of our studies have shown that proteins of SRCAP and p400/Tip60 chromatin remodeling complexes localize at MB during cell cycle progression. Remarkably, the main function of those complexes is to govern the deposition of the H2A variant into chromatin, thus such a bulky association with the MB is unexspeted. This PhD project will investigate the possibility that chromatin remodeling proteins are functionally relevant in cell division. In particular, the project will use functional genomic and proteomic approaches to study the effect of knock down of genes encoding SRCAP and p400/Tip60 proteins on cytokinesis and to characterize their network of interactions. In addition the project will study the localization dependencies between key MB players and chromatin remodelers in human cells. By identifying new factors required for proper cytokinesis we expect to clarify a yet poorly understood scenario in which chromatin remodelers, cell division and carcinogenesis can be closely interlinked.

Selected publications