TITLE.- "Computational and biophysical approaches to identify Fascin allosteric inhibitors as novel antimetastatic drugs"

ABSTRACT.- Fascin, a F-Actin binding protein, is specifically over-expressed in almost all metastatic cancer where its implication in processes of migration and invasion of tumor cells is clearly demonstrated. It is the main responsible for the cross-linking of individual Actin filaments, packaging it in the form of clusters or bundles. Fascin has a flexible and dynamic conformational structure, capable of going under conformational changes in its structure, which makes it a good candidate to experiment some type of allosteric modulation.[1] In order to identify the conformations and most relevant allosteric sites, we have implemented a detailed study of the conformational properties of Fascin. Combining both biophysical techniques with advanced computational methodologies (molecular dynamics simulations or analysis of normal modes of vibration)[2] we to address the search for allosteric inhibitors of Fascin. Additionally, we have implemented a high-throughput image-based screening assay which relies on the F-Actin bundling property. This image-based assay will be essential for the screening of wide microbial extract libraries. Exploring greater chemical and structural diversity, providing new opportunities for the identification of Fascin inhibitors.

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