Journal of Molecular Graphics and Modelling

Supplementary Data 4

Deciphering the Three-Domain Architecture in Schlafens and the Structures and Roles of Human Schlafen12 and SerpinB12 in Transcriptional Regulation

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The GTPase-like C-terminal region of hSLFN12 may participate in cytoskeleton interactions and differentiation-related changes in cell morphology

Other potential roles for the GTPase-like domain in schlafens (described in Figure 2 and section 3.5 in the corresponding article) are interacting with the actin cytoskeleton for intercompartmental shuttling and generating differentiation-related changes in cell morphology. Dynamin is part of a network controlling the nucleation of actin from membranes [1]. Cytoskeletal filamentous actin provides a framework for RITS and is also required for RNA polymerase II transcriptional activity [2,3]. Villin, a protein whose expression is stimulated by hSLFN12 and hSerpinB12 [4], bundles, nucleates, caps, and severs actin and induces the growth of microvilli during differentiation, resulting in enterocytes with the ability to absorb nutrients [5,6]. A dynamin homolog, the GTPase Rab11a, has been found to be essential in mice for the correct localization of proteins to the apical microvilli of enterocytes, promoting brush border formation [7]. The hSLFN12 GTPase-like domain could play analogous roles to those observed for dynamin and Rab11a. Very interesting work on human mesenchymal cells has shown that rho GTPase, a homolog of dynamin and the C-terminal domain of hSLFN12, governs the shape of cells during differentiation by controlling actin-myosin tension. In particular, the effects of rho GTPase on cell shape (e.g., round, or flattened and adherent), are sufficient to govern whether cells differentiate into adipocytes versus osteoblasts [8]. Rho GTPase also promotes the differentiation of smooth and skeletal muscle cells [8]. Thus, several GTPases related to hSLFN12 have known activity in actin-related, differentiation-associated shuttling of proteins and changes in cell shape, suggesting additional roles for the GTPase region in hSLFN12.

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