Investigating Molecular Mechanisms for Modulating Cytoskeletal Dynamics Using Molecular Dynamics Simulations

M. Preller, *Bonn-Rhein-Sieg University of Applied Sciences, Germany*

In Short

- Deciphering the mechanism for the modula-tion of cytoskeletal dynamics by fungal natu-ral products
- Application of sophisticated simulation tech-niques, which allow to capture biologically relevant timescales and energetic quantifica-tion of the observed effects
- Alterations of the energetic landscape of the actin cytoskeleton as potential therapeutic approaches

The cytoskeleton is an intracellular, highly dynamic, three-dimensional network of interlinked protein filaments, namely microtubules, intermediate filaments, and microfilaments. The latter are composed of actin polymers, which mediate, apart from providing a supporting framework for the structure of the cell, multiple cellular functions. Polymerization/depolymerization of actin filaments and interaction with binding partners is orchestrated by a plethora of actin-binding proteins. Actins are highly abundant and conserved proteins with tissue-specific and subcellular localisations. They play a critical role for processes such as cell motility, active intracellular transport, and generation of protrusive or contractile forces. These processes are essential for animal cells to adapt to their environment by changing their shape, to allow movement, cell division, and exo-/endocytosis (Blanchoin et al. 2014). Hyper- or dysfunction of actin due to mutations in actin isoforms are associated with human diseases, collectively called actinopathies or myopathies (Goebel and Laing 2009). Modulation of actin dynamics holds therefore a huge therapeutic potential. Based on previous work on actin mutations (Viswanathan et al. 2020), we aim to use sophisticated simulation techniques, which allow to capture biologically relevant timescales, together with an energetical quantification to systematically analyze the mechanisms how fungal natural products affect the energy landscape of the proteins, thereby modulate the function and polymerization dynamics of the actin cytoskeleton.

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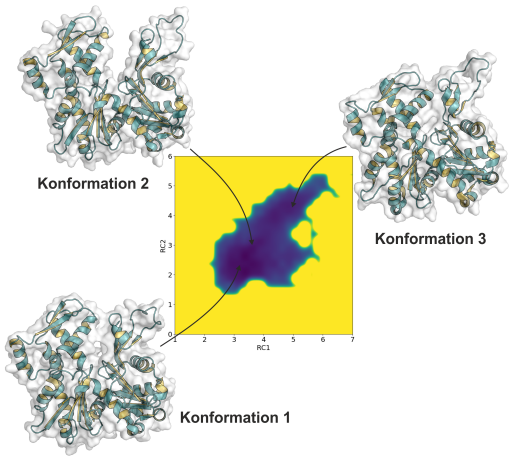

Figure 1: *Natural products might inhibit cytoskeletal dynamics by changing the energy landscape of the proteins.*

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Figure 2: *The NHR logo (in a single text column).*

Figure 3: *The NHR logo. This time across both text columns.*

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More Information

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[3] M.C. Viswanathan, W. Schmidt, P. Franz, M.J. Rynkiewicz, C.S. Newhard, A. Madan, W. Lehman, D.M. Swank, M. Preller, A. Cammarato, *Nat. Commun.* **11**, 2417 (2020). doi: 10.1038/s41467-020-15922-5

Funding

DFG, project number 514177501

DFG Subject Area

201-04