

Structure and functions of transient receptor potential channel TRPA1

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Transient receptor potential (TRP) channels are a large superfamily of nonselective cation channels. TRPA1 is a candidate for mechanically gated transduction channels potentially mediating the sensations of hearing, touch, and some forms of pain. Human TRPA1 is a 127.4 kDa protein comprised of 1119 amino acids. Like other TRPs also TRPA1 has six predicted membrane-spanning domains (S1 to S6) and the pore between S5 and S6. In this work we focus on homology modeling of its for TRPs unusually long N-terminal intracellular region containing 18 predicted ankyrin repeats. Ankyrin repeats have been implicated in protein-protein interactions, provide elasticity and make molecular springs. Also a calcium-binding domain, EF-hand, was indicated at the N-terminus, consisting of 12 residues involved in Ca-dependent activation. Simulations of the dynamic behavior of tree-dimensional all-atom models indicate stability and equilibration, and let us describe structural and functional properties to understand the system. Structural models are build using Modeller, for visual analyzing and energy minimization of the created models Yasara is used, and molecular dynamics simulations are carried out in GROMACS (molecular dynamics simulation package). The general aim is to embed the results of this work later into an all-atom model of the channel the membrane to get a stable tetrameric overall structure of fully functional TRPA1 in its natural environment.

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