INTERNAL FRICTION AS A KEY PARAMETER GOVERNING THE TEMPERATURE SENSITIVITY OF TRP CHANNELS

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The ability of organisms to sense ambient and body temperature is crucial for survival. In the modern concept, six thermo-activated transient receptor potential channels (thermo-TRP) are the molecular basis of the thermosensation. These channels show outstanding temperature sensitivity and can be directly activated by temperature from noxious cold to noxious heat. However, the mechanism that underlies the extreme temperature sensitivity of the TRP channels remains largely unknown. Thermo-activation is associated with large changes in standard-state enthalpy and entropy between states: positive for heat- and negative for cold-activated channels [1]. The molecular source of such enthalpy changes is still unrevealed. In particular, it has been suggested that the channels transitions between states are accompanied by large changes in molar heat capacity [2]. According to this concept, every thermos-TRP is both heat- and cold-activated. But there are no experimental data that prove the existence of different modes for the same channel. The electron-conformational model has explained temperature effects in RyR channels [3] focusing on a specific role played by internal friction. We adapted this model for the thermos-TRPs to show that considering the protein dynamics can take advantages for the understanding of thermo-activation mechanism. We show that the channel conformational dynamics is mostly determined by internal friction that has an Arrhenius like temperature dependence. Furthermore, mutations in the channel structure can affect the protein viscosity causing sensitivity losing. This suggestion gets along with the results of protein foldings and enzyme conformational dynamics modeling. In particular, it has been shown that the protein viscosity is essential to interpret temperature dependencies of folding rates [4]. We argue that internal friction can be the key parameter to describe channel activation induced by temperature. The model approach is shown to nicely reproduce experimental data available.

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References

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