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Heat-sensing Protein Switches and Uses Thereof

TRPV1 is a membrane protein ion channel that is activated at elevated temperatures. TRPV1 is modulated by various physical and chemical stimuli such as mild voltage, endogenous lipids, small proteins and pH in addition to high temperature and capsaicin. Due to its sensitivity to some noxious stimuli, TRPV1 is an excellent therapeutic target especially for pain. However, the modulation mechanisms of TRPV1 are not well understood and/or controversial. The ability to control expression and function of the thermosensor of TRPV1 is the key to developing protein-based temperature switches.

Researchers at the Biodesign Institute of Arizona State University have constructed and characterized a membrane protein sensing domain, isolated from the TRPV1 protein, that changes conformational structure as a function of temperature, specifically between room temperature and slightly above physiological temperature. Milligrams of pure protein can be generated for development of artificial ways to regulate biology, such as in synthetic biology by fusing this domain to other proteins which could in turn be turned on or off as a function of temperature.

This technology is the first isolation of a protein-based temperature switch in this temperature range and offers a simplified, conformational state-specific drug screening platform in addition to other applications.

Potential Applications

- Drug screening
- Protein based temperature switch used to regulate pathways and signaling cascades in vivo
- Synthetic biology – engineering protein-based temperature switches
- Constructing chimeras with other proteins that are not currently thermosensitive
- Developing state specific therapeutics – could lead to more specific and potent drug discovery in pain, inflammation, diabetes, etc.
- Generating structural activity relationships - useful for refining lead compounds
- Basic science/research

Benefits and Advantages

- Simplified, conformational state-specific screening platform
- The sensing domain changes conformation structure as a function of temperature
- 2 mg/L pure protein generation

- Able to fine tune the conformation state of a target to increase efficacy of screening and development

For more information about the inventor(s) and their research, please see [Dr. Van Horn's laboratory webpage](#)