

Researchers discover way to block body's response to cold

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Researchers at St. Joseph's Hospital and Medical Center in Phoenix, Arizona, in collaboration with Amgen Inc. and several academic institutions, have discovered a way to block the body's response to cold using a drug. This finding could have significant implications in treating conditions such as stroke and cardiac arrest.

The research, led by Andrej Romanovsky, MD, PhD, Director of the <u>Systemic Inflammation</u> Laboratory (FeverLab), which is a part of St. Joseph's Trauma Research program, was published in the Feb. 8 issue of the *Journal of Neuroscience*. The groundbreaking discovery has also been highlighted in Scientific American.

Lowering the body's temperature is an effective way to treat certain conditions because of the body's decreased need for <u>oxygen</u> at low temperatures. However, natural defense mechanisms to maintain a steady temperature – such as shivering, vasoconstriction and heat generation by brown adipose tissue – can make it difficult to lower body temperature in unanesthetized patients. Dr. Romanovsky and his team believe they have discovered a pharmacological method to inhibit these natural defense mechanisms.

Their research focuses on the TRPM8 (transient receptor potential melastatin-8 channel) receptor, a protein responsible for the sensation of feeling cold, and on M8-B, a drug that acts as a TRPM8 antagonist. Dr. Romanovsky's team discovered that M8-B inhibited multiple cold-defense mechanisms in mice and rat models. This TRPM8-antagonist-



induced hypothermia is the first example of a change in the deep body temperature of an animal occurring as a result of the documented pharmacological blockade of temperature signals at the thermoreceptor level.

"Humans have used the same mechanisms to defend themselves against cold since the days of the caveman," says Dr. Romanovsky. "Our study is significant because it is the first time we have been able to block the body's natural defense mechanisms using a selective pharmacological antagonist. We believe that this approach will be used in the future to induce mild therapeutic hypothermia in unanesthetized patients, as well as to maintain deep body temperature, and perhaps the activity of some thermoeffectors, at desired levels."

Dr. Romanovsky also believes that this finding is the beginning of thermopharmacology, a new discipline that uses drugs to block temperature signals that the body receives from the environment and thus to alter body temperature for treating specific conditions.

Provided by St. Joseph's Hospital and Medical Center

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