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Suspended animation protects against lethal hypothermia, study shows (w/ Video)

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How is it that some people who apparently freeze to death, with no heart rate or respiration for extended periods, can be brought back to life with no long-term negative health consequences? New findings from the laboratory of cell biologist Mark B. Roth, Ph.D., of Fred Hutchinson Cancer Research Center, may help explain the mechanics behind this widely documented phenomenon.

Reporting online ahead of the July 1 print issue of *Molecular Biology of the Cell,* Roth, a member of the Hutchinson Center's Basic Sciences Division, and colleagues show that two widely divergent model organisms - yeast and nematodes, or garden worms - can survive hypothermia, or potentially lethal cold, if they are first put into a state of suspended animation by means of anoxia, or extreme oxygen deprivation .

Roth and colleagues found that under normal conditions, yeast and nematode embryos cannot survive extreme cold. After 24 hours of exposure to temperatures just above freezing, 99 percent of the creatures expire. In contrast, if the organisms are first deprived of oxygen and thus enter a state of anoxia-induced suspended animation, 66 percent of the yeast and 97 percent of the nematode embryos will survive the cold. Once normal growth conditions are resumed - upon rewarming and reintroduction of oxygen - the organisms will reanimate and go on to live a normal lifespan.

A better understanding of the potentially beneficial, symbiotic relationship between low oxygen and low temperatures may one day lead to the development of improved techniques for extending the shelf life of human organs for transplantation, Roth said.

A time-lapse video of anoxia-induced suspended animation in a nematode. The video, courtesy of the Roth lab, depicts a 10-hour experiment shot at 175x real time.

"We have found that extension of survival limits in the cold is possible if oxygen consumption is first diminished," he said. "Our experiments in yeast and nematodes suggest that organs may last longer outside the body if their oxygen consumption is first reduced before they are made cold."

Roth's laboratory studies the potential clinical benefits of metabolic flexibility - from anoxia-induced reversible suspended animation to metabolic hibernation brought on by exposure to agents such as hydrogen sulfide. The ultimate goal of this work is to find ways to temporarily lower metabolism - like dialing down a dimmer switch on a lamp - as a means to "buy time" for patients in trauma situations, such as victims of heart attack or blood-loss injury, by reducing their need for oxygen until definitive medical care can be given.

Roth first got the idea to study the link between anoxia-induced suspended animation and hypothermia from documented cases in which humans have managed to make complete recoveries after apparently freezing to death. Widely publicized cases include Canadian toddler Erica Nordby, who in the winter of 2001 wandered outside clad only in a diaper. Her heart had stopped beating for two hours and her body temperature had plummeted to 61 degrees Fahreneit before she was discovered, rewarmed and resuscitated. Another incident that made headlines was that of a Japanese man, Mitsutaka Uchikoshi, who in 2006 fell asleep on a snowy mountain and was found by rescuers 23 days later with a core body temperature of 71 degrees Fahrenheit. He, too, was resuscitated and made a full recovery.

"There are many examples in the scientific literature of humans who appear frozen to death. They have no heartbeat and are clinically dead. But they can be reanimated. Similarly, the organisms in my lab can be put into a state of reversible suspended animation through oxygen deprivation and other means. They appear dead but are not. We wondered if what was happening with the organisms in my laboratory was also happening in people like the toddler and the Japanese mountain climber. Before they got cold did they somehow manage to decrease their oxygen consumption? Is that what protected them? Our work in nematodes and yeast suggests that this may be the case, and it may bring us a step closer to understanding what happens to people who appear to freeze to death but can be reanimated," Roth said.

The mechanism by which anoxia-induced suspended animation protects against extreme cold has to do with preventing the cascade of events that lead to biological instability and, ultimately, death. For example, suspended animation preserves the integrity of cell-cycle control by preventing an organism's cells from dividing in an error-prone fashion. During suspended animation, the cell cycle is reversibly halted. Upon reanimation, the cycle resumes as normal.

"When an organism is suspended its biological processes cannot do anything wrong," Roth said. "Under conditions of extreme cold, sometimes that is the correct thing to be doing; when you can't do it right, don't do it at all."

Provided by Fred Hutchinson Cancer Research Center

hypothermia-video.html