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PRESS RELEASE

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HIBERNATING SQUIRRELS MAY HOLD SECRETS OF PREVENTING DAMAGE FROM STROKE IN HUMANS

Researchers at the University of Minnesota Duluth have begun to identify genes that play an important role in controlling how the heart functions in hibernating animals. The discovery of these genes, reported today (Wednesday 21 July) at BioScience2004 in Glasgow, may someday help doctors prevent tissue damage resulting from reduced blood flow, causing conditions such as stroke in humans. Other benefits may also include extending the preservation time of organs used for transplantation.

"Hibernating mammals provide a unique system for identifying molecules that are important in controlling brain and heart function under suboptimal conditions of body temperature, oxygen consumption and fuel supply," said Dr Matthew Andrews. In a state of deep hibernation, body temperature hovers a few degrees above $0^{o}C$, oxygen consumption holds at 1/30 to 1/50 of the aroused condition, and heart rate can be as low as three to 10 beats per minute, compared to 200-300 beats per minute when the animal is active.

Dr Andrews reported that there is an increase in two important proteins in the heart when thirteen-lined ground squirrels begin to hibernate. These proteins are biological catalysts called enzymes and remain at a high level throughout the hibernating period when metabolism and body temperature are greatly reduced.

Tissues of hibernating squirrels can survive with a minimum supply of oxygen using fat as their main source of fuel. In humans, however, a lack of oxygen and carbohydrate such as glucose can cause severe damage to organs. The brain is the most susceptible tissue and stroke is a common consequence.

“Hibernation in mammals is accompanied by a decrease in cardiac output and brain blood flow that is similar in magnitude to stroke,” said Dr Andrews. “Yet the brain and other tissues of hibernators are naturally protected from the damage this could cause.”

“By identifying genes that are expressed in natural hibernators, such as ground squirrels, we hope to apply hibernation strategies for the purposes of improving human health. Hibernators have a slower metabolism, less oxygen demand, and as a result are protected from tissue damage. With respect to donated organs, this reduced oxygen demand may lengthen the time these organs can be stored prior to transplantation.

Both proteins that Dr Andrews has identified are important for switching from carbohydrate metabolism to fat metabolism. One is an enzyme called PTL that supplies energy to the heart cell by burning fat. Researchers did not know that it played a part in heart functions or that it could be active at low temperatures.

“We found that both human and ground squirrel PTL perform remarkably well at temperatures as low as 0^{o}C,” he said. “This may be crucial in keeping the heart functioning at extreme temperatures.”

The other protein is PDK4, which prevents the burning of carbohydrates. Carbohydrate is a major fuel source for brain functions. Because hibernating ground squirrels do not eat for four to five months, the animals have to keep their usage of carbohydrates to a minimum,

as any consumption could not be replaced.

Recognising the importance of hibernation studies to human health, the National Human Genome Research Institute of the National Institutes of Health plans to insert thirteen-lined ground squirrel genes into artificial chromosomes so that the entire genome is available for sequencing. Such a ground squirrel genome project would allow Dr. Andrews and his team to isolate any gene that may be important for surviving the physiological extremes of hibernation.

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