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Renal protection through CBS/H_2S pathway in mammalian hibernation: A natural model of hypothermic organ preservation during cold ischemia and reperfusion

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Background: Hibernation represents the most radical example of hypometabolism among mammalian species and is characterized by repetitive cycles of cooling (torpor) and rewarming, which resembles several clinically relevant conditions such as deep hypothermia, organ storage for transplantation, major surgery and ischemia-reperfusion. Therefore mechanisms applied by hibernators to undergo hibernation without reperfusion injury or other ill effects may have potential application to human medicine. Recently, we have shown that cultured hamster cells are protected from cooling induced apoptotic cell death by an increased production of endogenous H2S through upregulation of cystathionine-β-synthase (CBS). This study aimed at investigating the role of CBS enzyme and H2S in the induction of torpor and kidney preservation during hibernation.

Method: Male Syrian golden hamsters (*Mesocricetus auratus*) were housed in cages in a climate controlled chamber at 5°C under dim red light to induce torpor. Movement of all animals was continuously monitored with passive infrared detectors. Osmotic mini-pumps filled with saline or CBS inhibitor aminooxyacetic acid (AOAA; 100 mg/kg/day) were implanted i.p. during torpor following a bolus injection of AOAA (70 mg/kg) under 2.5% isoflurane anesthesia. At 4 days following implantation of pumps, hamsters which re-entered torpor were aroused by handling for 4 hours and euthanized under pentobarbital anesthesia. Blood samples were taken and kidney of the hamsters was obtained. Summer euthermic hamsters served as controls.

Results: Torpid hamsters were aroused during pump implantation. In contrast to saline infusions, infusion of AOAA prevented hamsters from re-entry into torpor. Infusion of AOAA also induced excess renal damage as indicated by high expression of kidney injury marker as well as changes in renal morphology. In contrast, renal morphology was well preserved during hibernation in the saline and non-hibernating summer control groups.

Conclusion: Our data show that CBS/H2S pathway is essential in entrance into torpor and preservation of kidney morphology and function during hibernation. These findings might be relevant for a number of clinical conditions such as therapeutic hypothermia or organ preservation for transplantation medicine.

Biography

George J Dugbartey is pursuing his PhD at University Medical Center Groningen, Netherlands and will finish in December 2014 after which he intends to do a Postdoctoral research in renal transplantation. He has just submitted four research papers to reputed journals and awaiting reviewers' feedback, and currently writing two review papers.

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