Peroxisome-Proliferator Activated Receptor-Alpha Agonists for Organ Preservation

Published date: Aug. 28, 2016

Technology description

The identification of drugs that would preserve organs would have enormous implications for progress in medicine. For example, effective drugs added to organ preservation solutions could extend the time for extracorporeal survival of grafts prior to transplantation, decrease the incidence of primary graft dysfunction and augment the pool of available donors. Moreover, such drugs may find utility for the prevention and treatment of acute organ failure, for example acute renal failure for which no effective pharmacological agent is currently known. Finally, preservation drugs, if sufficiently efficacious, could allow for the prolonged in situ perfusion of organ systems with solutions to restore organ function or deliver appropriate transfection agents. Our lab has considerable experience in the area of perfusion of rodent kidneys, as well as sterile methods for cell culture. Combining these approaches, we developed a method for perfusing the rat kidney in a rigorously sterile environment such that the kidney can be perfused at 37 degrees C for prolonged periods of time without infection. Using this model system, we can reproducibly induce by 12-hour perfusion at 37 degrees C severe acute tubular necrosis as well as deterioration of the glomerular and renal interstitial elements. Using this relatively inexpensive and convenient model system, we began systematically examining a number of drug classes for possible efficacy. In our screening, the osmotic diuretic mannitol and another pharmacological class (class X drugs) demonstrated promise. Previous studies by other groups have recognized mannitol as an effective drug for improving organ preservation. However, the identification of class X drugs as organ-preserving agents is a novel finding. Accordingly, we engaged a more detailed examination of class X drugs. Also, because mannitol is already employed in some organ preservation solutions and is patented for that purpose, we investigated the interaction between mannitol and class X drugs on kidney preservation. Our results show that although class X drugs improve organ preservation, the combination of mannitol class X drugs is even more efficacious. Our results underscore the utility of our model system and suggest that addition of class X drugs to organ preservation solutions containing mannitol may improve organ transplant outcomes. Provisional Patent Application Filed

Institution

University of Pittsburgh

Inventors

Travis Jackson
Zaichuan Mi
Edwin Jackson

联系我们

叶先生

电 话：021-65679356
手 机：13414935137
邮 箱：yeyingsheng@zf-ym.com