

correcting defective genes in future organ banking applications.

Poster Presentation 23

PERFUSION SYSTEM FOR TISSUES AND ORGANS

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Recent advances in regenerative and transplantation medicine offer exciting possibilities for new therapies and treatment of injuries; however, many surgical and treatment outcomes are still affected by the limited amount of time available for organ or tissue preservation following a trauma induced injury. Surgical outcomes could be improved if tissue salvage and conservation could be achieved over longer time periods without seriously injuring the tissue. TDA Research, Inc., with our collaborators, is developing a novel perfusion system for the salvage and repair of trauma injured tissue. TDA's perfusion system is designed to be rugged and portable so that it can be used under a wider array of scenarios than currently available technology for both civilian and military applications. It is highly insulated, temperature controlled, battery operated, and automated via a suite of sensors so that the clinician is automatically warned about any deviations from normal behavior. Furthermore, it is lightweight, small, and man-portable. In conjunction with the development of the perfusion system, our collaborator, Southwest Research Institute, is developing a novel perfusate which can oxygenate the tissue without relying on a high concentration oxygen tank (which is an explosion risk) or blood, which is in limited supply. This system will increase the preservation time for tissue, enabling advanced treatments or transplant capabilities.

Poster Presentation 24

NOVEL BIONANOTECHNOLOGICAL SOLUTIONS BASED ON METAL OXIDE AND METAL TO PRESERVE AND ASSESS ORGANS FOR TRANSPLANTATION

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Our research has focused on nanomaterials for the diagnosis and treatment of cardiovascular disease (CVD) such as thrombosis. These materials can be adapted for preserving and assessing organs for transplantation. Magnetic resonance imaging (MRI) has been used as a powerful and indispensable tool in medical research and clinical diagnosis. We have developed both targeted negative contrast agents and targeted dual positive/negative contrast agents for molecular imaging of thrombosis. The simultaneous use of positive and negative MRI imaging that employs the same contrast agents will significantly improve detection accuracy. Using the dual contrast agent, both T₁- and T₂-weighted MRI of thrombosis can be simultaneously recorded which enables self-confirmation of images and leads to a greater diagnostic accuracy¹. To prepare these targeted agents, we employed a single-chain antibody that targets activated platelets, a major player in thrombus formation. Our contrast agents can be adapted for assessing organs during and after transplantation. It has been reported that platelets are activated early during reperfusion after an ischaemia/reperfusion injury (IRI). Therefore, by targeting activated platelets and platelet accumulation, it is possible to noninvasively detect and assess IRI early, maximizing medical interventions.

We have also developed smart MRI nanosensors based on iron oxide and gadolinium that can not only detect, but also sense and report the stage or progression of CVD such as thrombosis. The early detection and accurate characterization of life-threatening diseases such as CVD are critical to the design of treatment. Knowing whether a thrombus in a blood vessel is new/fresh or old/constituted is very important for physicians to decide on

a treatment protocol. These nanosensors can be adapted, modified and applied for detecting and grading other diseases such as cancer, and also for sensitive detection of inflammatory reactions during organ preservation, perfusion and transplantation processes. It can be a useful technique to potentially allow other researchers to access information previously difficult to obtain. It can also be a new tool for clinicians to assess organs before and after transplantation, maximizing opportunities for medical intervention. Since our nanosensors are iron oxide and gadolinium based materials, they can also be used for preservation of organs/tissues. Recently researchers have reported a way to safely thaw frozen tissues with the aid of iron oxide nanoparticles². By suffusing the nanosensors over organs/tissues before freezing, they may help in the thawing process and may directly provide information on inflammatory reactions within the organs/tissues after thawing and reperfusion.

References:

1. Molecular Imaging of Activated Platelets via Antibody-Targeted Ultra-small Iron Oxide Nanoparticles Displaying Uniqued Dual MRI Contrast. Hang T. Ta* et al. *Biomaterials*. 2017. 134, 31–42.
2. Improved tissue cryopreservation using inductive heating of magnetic nanoparticles. Manuchehrabadi N., et al. *Sci Transl Med*. 2017, 9, 379.

Poster Presentation 25

LEVERAGING MACHINE PERFUSION FOR WHOLE ORGAN PRESERVATION USING PARTIAL FREEZING

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The United States is facing an organ donor shortage, with over 117,000 people awaiting an organ transplant in the US alone. By optimizing organ preservation, we stand to increase the geographical range of available organs. This would promote international patient-donor matching and improve outcome by superior HLA matching, thereby contributing to the reduction of the organ shortage. Our approach, termed partial freezing, promotes extracellular ice nucleation, while intracellular ice formation is prevented. In this capacity, partial freezing yields the advantage of reducing metabolism by passive temperature effects as well as cellular dehydration due to extracellular ice formation. One critical tool is the application of machine perfusion systems. We use multi-step sub-normothermic machine perfusion (SNMP), followed by hypothermic machine perfusion (HMP) to load the organ with cryoprotectants. This is carefully controlled to reduce damage to endothelial cells and the vasculature. Following a static frozen storage phase, our protocol also includes a thawing and recovery phase during which we leverage SNMP to revive the organ and assess organ viability. We present encouraging preliminary results that whole organs can survive in the presence of ice, with a focus on how machine perfusion technology is an essential counterpart to static storage approaches.

Poster Presentation 26

SUPERCOOLED RENAL GRAFT PRESERVATION USING HYPERACTIVE ICE-BINDING PROTEINS

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Traditional hypothermic kidney preservation involves graft perfusion with a cold intracellular-like solution, followed by static storage at 4 °C for ~24 h. Due to increasing demands for transplantable organs, the ability to significantly prolong the storage time would be highly beneficial; however, extension of hypothermic preservation often results in the accumulation of irreparable ischemic injury. Our hypothesis is that this constraint might be overcome by preserving the kidneys below 0 °C in an ice-free state, decreasing the progression of ischemic damage by reducing the tissue's