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Research project summary

Endothelial Progenitor Cell Exosomes and MicroRNA Transfer as Therapy for Acute Kidney Injury

- Principal Investigator: Kevin Burns
- Co-Investigators: Dylan Burger, Dean Fergusson, David Allan
- Awarded $742,050 from the Canadian Institutes of Health Research (CIHR) in January 2018

Acute kidney injury (AKI) is a serious condition in which kidney function falls rapidly (often over minutes to hours), commonly because of loss of blood flow. AKI is frequent, affecting about one out of every twenty people in hospital. In severe cases treatment includes dialysis, but kidney function recovers in only about one half of patients, and mortality is high. Unfortunately, there are no treatments to improve kidney repair after AKI. Use of stem cells may help kidneys recover from AKI. Recently, we isolated "progenitor" cells from human umbilical cord blood and infused them into mice with AKI caused by temporary blockage of blood flow to the kidneys. While the cells reduced kidney damage, they did not incorporate into the kidneys, but rather appeared to release factors that stimulated recovery. In fact, the cells shed tiny membrane particles ("exosomes") that contain a substance called "miR-486-5p". Injection of mice with the exosomes strongly protects them from kidney injury, and the benefits may relate to transfer of miR-486-5p. Use of exosomes may be preferable to cell treatments, since exosomes have a low risk of immune "rejection", and are not likely to cause abnormal cell growth. However, several questions must be answered before exosomes can be given to humans with AKI. Do infused exosomes target specific kidney cells to promote repair, and does miR-486-5p transfer to these cells? How does transfer of miR-486-5p from exosomes reduce kidney injury, and what other effects may occur in the kidney with this treatment? Do exosomes protect against other causes of AKI, such as due to kidney toxins? In this grant, we will conduct animal studies to address these key questions. Detailed animal studies will also be performed to determine the effects of exosome dose, timing of administration, and differences in response according to sex. Our proposal represents the critical next step in developing exosome treatments that could help humans with AKI.

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