



## Research project summary

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

- Principal Investigator: Kevin Burns
- Awarded \$100,000 from the Canadian Institutes of Health Research (CIHR) in May 2017

Acute kidney injury (AKI) is a serious condition in which kidney function declines rapidly, often over minutes to hours. Therapy includes dialysis, and kidney function recovers in only about one half of patients. Unfortunately, there are no treatments to improve kidney repair after AKI. Use of stem cells has been proposed to 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 are loaded with 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. Exosomes offer distinct advantages over cell treatments, since they have a low risk of immune "rejection", and are not likely to cause abnormal cell growth. However, several questions remain to be answered before exosomes can be given to humans with AKI. How can we improve the delivery of exosomes to the injured kidneys? 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? In this grant, we will conduct animal studies to address each of these key questions. Detailed studies will also be performed to determine the effects of exosome dose, timing of administration, and differences in response according to sex in experimental animals with AKI. Our proposal represents the critical next step in developing exosome treatments that could help humans with AKI.

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