Doxycycline protects the transplant kidney during cold perfusion- proteomic analysis

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Abstract

Since dialysis is accompanied by low quality of life and life expectancy, kidney transplantation is the option of choice for many patients [1]. However, the transplantation of a kidney is necessarily accompanied by injury [2,3]. The consequences include delayed allograft function, acute tubular necrosis, and acute kidney injury [4].

A pharmaco-proteomics approach was used to identify potential molecular targets associated with kidney preservation injury. The main aim was to better describe the nephroprotective activity of doxycycline (Doxy) during ex vivo kidney cold perfusion in a rat model.

Rat kidneys were cold perfused with or without Doxy for 22 hours. Perfusates were analyzed for the presence of injury markers. Proteins extracted from kidneys were analyzed by 2-dimensional gel electrophoresis. Proteins of interest were identified by MS.

A two-fold increases in LDH activity and 10-fold in NGAL was seen in perfusates from ischemic kidneys compared to the controls ($p<0.05$). Levels of all analyzed markers were normalized by 100 µM Doxy. Perfusion with 100 µM Doxy protected mitochondria and inhibited formation of dense bodies, observed by the electron microscopy.

Mass spectrometry analysis identified that N(G),N(G)-dimethylarginine dimethylaminohydrolase and phosphoglycerate kinase 1 were decreased after cold perfusion, and perfusion with Doxy led to an increase in their levels.

Machine cold perfusion led to significant kidney injury, however doxycycline, an inhibitor of MMPs, decreased kidney injury, may be as a result of mitochondrial protection and hence the maintenance of mitochondrial structure.

Biography:

Iwona Bil-Lula is serving at an esteemed position in Wroclaw Medical University, Canada. She is the recipient of numerous awards for his expert research works in related fields. Her research interests reflect in her wide range of publications in various national and international journals.