Are there good and bad kidneys? A transcriptional approach

Prior to organ donation both the donor and organ are assessed for suitability for transplantation. Some organs, including kidneys, have biopsies taken to assess the health of the tissue. Through histological scoring clinical decision can be made which affect the outcome for the recipient for example carrying out a single or a duel kidney transplant.

We hypothesised that by studying the RNA profile of donor tissue and correlating this with patient outcome we could develop a test using a “Molecular Microscope” to identify suitable kidneys for transplant and predict outcome.

Initially we analysed the transcriptome of kidneys which were rejected for transplantation and found over 5,000 genes differently expressed between the cortex and medulla. As clinical biopsies for transplant are core biopsies there are differing ratios of cortex and medulla which would confound analysis. We developed a novel method for correcting for this using marker genes which we defined. Subsequently we performed RNASeq on 40 core biopsies from QUOD. These were taken at time of retrieval so giving an insight into the transcriptional state of the organ before any effect of cold ischemia.

After correction for tissue composition we correlated gene expression with incidence of delayed graft function (DGF) and 3 and 12 month glomerular filtration rate (GFR). We found there were 240 genes which were significantly associated with DGF and a smaller number with long term GFR.

These data imply that the transcriptional state of the organ at retrieval has a huge effect on outcome. Further we have discovered suitable marker genes that could be used in a rapid test to assess potential organ suitability which we are currently validating. These data give us insight into transcriptional pathways which effect the outcome of transplantation and highlight targets for therapeutic intervention to ensure success and potentially increase the number of organs available for transplantation.