RENAL CELL CARCINOMA PROGRESSION IS ENHANCED BY LYMPH NODE STROMAL CELL REGULATION OF CANCER CELL PROTEIN EXPRESSION

G GOBE[1], Q-H NGUYEN[2], R MORET[2], C MORAIS[1], X ZHANG[2], G MARESH[2], L HELMERS[2], S TALWAR[3], M LATSIS[3], M VARIANO[3], D CANTER[3], S BARDOT[3], L LI[1]
[1]*University Of Queensland, Brisbane, Australia,* [2]*Institute of Translational Cancer Research, Ochsner Health System, New Orleans, USA,* [3]*Department of Urology, Ochsner Health System, New Orleans, USA*

Aim: To determine the molecular mechanisms by which lymph node (LN) stromal cells stimulate growth and progression of renal cell carcinomas (RCC).
Introduction: RCC are the most common solid tumour of the adult kidney, with a cancer specific mortality of 30–40%. LN metastases are strongly negative for RCC prognosis. RCC metastases are incurable and affect up to 25% of patients. In our previous experiments using orthotopic xenograft models, LN stromal cells (HK cells) enhanced RCC tumor progression, with growth of the RCC cell line ACHN dependent on HK cells, and SN12K1 RCC cells relatively independent of HK cells in tumour formation, tumour growth and distant organ metastasis.
Methods: To investigate alterations in protein expression, RCC cells lines (ACHN and SN12K1) were cultured with or without HK cell supernatant and cell lysates were subjected to proteomic mass spectroscopy analysis (TRI Proteomics Facility, Australia). Significantly-altered protein markers were selected using data and bioinformatics analysis and information from the web-based proteinatlas database.
Results: 1540 proteins were detected by proteomic analysis. 128 proteins were present in both cell lines. In response to HK cell supernatant treatment, the following 10 novel cancer progression-related proteins were significantly differentially expressed: CTSD, SAMHD1, FAM114A1, RFC5, NAPA, SRP68, SNX6, AIMP1, PSMD6, and YWHAE. Quantitative analysis by Western blotting validated the differential expression of these proteins in response to the conditioned medium from stromal cells.
Conclusions: The presence of conditioned media from HK LN stromal cells altered expression of specific cancer proteins in RCC. Further studies into the pathways affected by these proteins and, subsequently, blocking those pathways may lead to novel treatments for RCC patients.

DIETARY RESISTANT STARCH PROTECTS AGAINST DIABETIC NEPHROPATHY BY INHIBITION OF COMPLEMENT

M SNELSON[1], S TAN[1], D DELIYANTI[1], J WILKINSON-BERKA[1], M COUGHLAN[1]
[1]*Department of Diabetes, Monash University, Melbourne, Australia*

Aim: To investigate immune mechanisms by which resistant starch (RS) supplementation may be protective against diabetic nephropathy.
Background: Activation of complement occurs in diabetic nephropathy. C5a is a downstream complement component that activates the innate immune system contributing to inflammation. Dietary RS may be nephro-protective, however the effects of dietary RS on complement activation and the innate immune system have not been explored.
Methods: Six week old non-diabetic mice (db/h), diabetic mice (db/db) and db/db mice on a regular chow diet supplemented with 25% RS (dbdb+RS) were maintained for ten weeks. 24-hour urine was collected for albumin and C5a measurement by ELISA. Kidneys were digested and enriched for leukocytes using Percoll gradient. Cells were stained with BV786-CD45, AF700-CD11b, PE-Cy7-CD11c, BV711-Siglec F, BV605-Ly6C, PE-CD86, FITC-C5aR antibodies and flow cytometry was performed.
Results: Diabetes was associated with an increase in albuminuria (28.0±6.5 vs 411.3±275.8μg/24h, P<0.001, dbh vs dbdb), which was reduced in diabetic mice receiving RS supplementation (411.3±275.8 vs 125.6±37.3μg/24h, P<0.01, dbdb vs dbdb+RS). Urinary C5a excretion was increased by diabetes (92.6±17.6 vs 1324.0±429.7pg/24h, P<0.001, dbh vs dbdb) and decreased by RS (1324.0±429.7 vs 577.7±123.1pg/24h, P<0.05, dbdb vs dbdb+RS). In diabetes there was an increase in CD86 MFI (a marker of activation) on infiltrating macrophages (CD45+ CD11b+ CD11c- Siglec F- Ly6C hi), which was attenuated with RS (3.7±1.8 vs 1.5±1.0 fold change to dbh, P<0.05, dbdb vs dbdb+RS). Furthermore, infiltrating macrophages were more likely to be positive for C5aR with diabetes (4.8±3.9 vs 54.0±27.8%, P<0.001, dbh vs dbdb), which RS supplementation reduced (54.0±27.8 vs 11.7±4.2%, P<0.01, dbdb vs dbdb+RS).
Conclusions: These studies support the notion that dietary RS is protective against renal disease via inhibition of complement.

SURGEON VERSUS NEPHROLOGIST-INSERTED PERITONEAL DIALYSIS CATHETERS: EXPERIENCES FROM A METROPOLITAN CENTRE IN SYDNEY

N SHAH[1], A GOSWELL[2], C CUESTA[3], I KATZ[3]
[1]*St George-Sutherland Basic Physician Training Network, Kogarah, Australia,* [2]*St George Hospital, Kogarah, Australia,* [3]*Department of Renal Medicine, St George Hospital, Kogarah, Australia*

Background: Peritoneal dialysis (PD) is an effective home-based form of renal replacement therapy. Delays in insertion, higher costs, primary catheter failure, and patient choices are contributors to its under-use and lower rates of penetration
Aim: To describe and compare outcomes of percutaneous PD catheter insertion (PDCI) by a nephrologist compared with surgical insertion.
Methods: A retrospective study at St. George Tertiary Hospital, Sydney, using a prospectively-collected database over 8-years. The data analysed included195 PD catheters inserted using two techniques (72 percutaneous (PCDI), 123 surgical). Analysis included patient demographics, date of catheter insertion, and complications.
Results: Patients were well matched for age, and primary cause of renal failure. Those receiving PDCI had lower BMIs versus surgically inserted lines (p = 0.027). Time-to-insertion was significantly shorter with the PDCI (p = 0.0014). The over-all complication rate was similar (44% vs. 36%, p =0.24). Significant differences in the type of adverse outcomes were seen. Patients with surgically-inserted catheters experienced more exit site leaks (p = 0.026), and peritonitis (p =0.028). Nephrologist-inserted catheters had more technical complications. These included bowel puncture (p = 0.0085) or procedure cancelation due to inadequate preparation (p=0.0008). There were no differences in primary failure between the techniques (p = 0.436), and increasing BMI did not confer an increased risk of primary failure in either cohort (p= 0.601).
Conclusions: The study confirms the complementary roles of nephrologist and surgical insertion. With fewer delays to catheter insertion and similar absolute complication rates, a nephrologist-inserted PD catheter, using the percutaneous technique, is a good option to consider in the right patient in metropolitan areas. Especially in Australia where higher uptake of home based therapies is so important.

AN AUDIT OF POST-RENAL BIOPSY COMPLICATION RATE AND DIAGNOSTIC YIELD OF ALLOGRAFT AND NATIVE KIDNEYS

A KHAN[1], B NANKIVELL[1], A KHAN[2], J CHAPMAN[1]
[1]*Renal Medicine Department Westmead Hospital, Westmead, Australia,* [2]*Storr Liver Center, Westmead Institute of Medical Research, University of Sydney, Westmead , Australia*

Background/Aims: Real time ultrasound guided percutaneous kidney biopsy (PCKB) is considered a standard procedure worldwide, for the pathological diagnosis of native and transplant kidneys. Monitoring the adequacy of sample and post biopsy complications is important as quality indicators. We thus monitor safety and adequacy of the real time ultrasound guided biopsy technique to correlate with the level of experience of the operator.
Method: A total of 449 (398 transplant and 51 native) elective day case biopsies performed at Westmead Hospital Sydney over one year were retrospectively reviewed to determine the overall complication and adequacy rates.
Results: A total of 355 biopsies (group 1) were performed by a consultant by either ultrasound guidance or assistance and 94 biopsies (group 2) were performed by supervised trainees using ultrasound guidance. The overall tissue specimen adequacy was 97.1 %, however, it differed significantly, between group 1 (97.7% adequacy) and 2 (94.7% adequacy, p< 0.03). The overall biopsy complications rate was 3.3%, with a statistically significant difference between group 1 (1.1%) and group 2 (11.7%, p<0.001). Overall, post biopsy transient haematuria was detected in 3.1% patients (p<0.001), 1.6% cases had a diagnosed haematoma, 1.6% cases had gross haematuria and 0.4% patient developed an AV fistula. A total of 97.6% patients were discharged after 4 hours observation and 2.4% required admission.
Conclusion: Complication rates following PCKB are low and are reduced when performed by experienced nephrologists. It remains important to provide rigorious education and supervision programs to train nephrologists to perform safe and effective native and transplant renal biopsies.