We identified 70 recipients (51% male; 49% female). Median age at HTX was 46±15 years. Median time from cancer to HTX was 12±10 years. The types of cancer were haematologic (26%), breast (14%), genitourinary (18%) and soft tissues (10%). The types of cardiomyopathy leading to HTX were toxic (53%), ischemic (17%) and idiopathic (11%). Survival at 5, 10, 15 and 20 years of study population compared to overall Belgian HTX population was respectively 80% vs 72%, 76% vs 56%, 60% vs, 39% and 54% vs 22% ($p<0.05$). Twenty-seven% developed post-transplant malignancy during follow-up (78±87 months). Patients transplanted <5years following cancer were more likely to have recurrence (4 />16; 25%), while patients transplanted >5 years following cancer had more new cancers (11/56; 20%) ($p<0.05$). Cancer recurrence and new cancers were the cause of respectively 2% 3% mortality.
In our series, baseline characteristics study population vary from general htx recipients (more female, more toxic cardiomyopathies). A history prior to is not associated with an increased incidence or increase post-transplant (cfr. lund et al. j heart lung transplant. 2016).

VILLIN-1 IS A NOVEL SEROLOGICAL MARKER FOR INTESTINAL ISCHEMIA AND REPERFUSION INJURY IN RATS AND HUMANS.

Ceulemans L, De Hertogh G, Farré R, Decuypere J-P, Verbeke L, Jochmans I, Monbaliu D, Lenaerts K[1], Pirenne J.
Leuven, Belgium, [1]Maastricht, The Netherlands

The aim was to analyse villin-1 -a protein anchoring the actin filaments of the enterocytes at the epithelial brush border- as a serological marker in a rodent and human model of intestinal ischemia reperfusion injury (IRI).
In a rat model of intestinal IRI (temporary mesenteric artery clamping), 4 conditions were included: (i) laparotomy only (sham); (ii) 30min ischemia + 5 reperfusion periods (0min/30min/60min/120min/24hours); (iii) 45min ischemia + 5 reperfusion periods; (iv) 60min ischemia + 5 reperfusion periods; (n=6/group). For survival analysis, 7-day reperfusion was included in each condition (n=10/group). Other end-points that were analysed: histology (Park-Chiu/villus length); intestinal permeability (Ussing chamber); villin-1 (Western-Blot). In a human model of intestinal IRI (6cm jejunal-clamping during pancreaticoduodenectomy; 45min ischemia + 0min/30min/120min reperfusion) villin-1 was analysed by immunoprecipitation (n=6).
In rat, increasing ischemia resulted in decreased survival (30min: 90%; 45min: 50%; 60min: 10%) and loss of intestinal integrity (histology/permeability). From 45min ischemia, villin-1 appeared in the plasma at 0min reperfusion and remained detectable until 120min reperfusion. At 0min reperfusion, villin-1 could differentiate between 45min or 60min ischemia corresponding to the different survival. Overall, villin-1 had a strong correlation with Park-Chiu score ($r=0.7954;p<0.0001$); villus length ($r=-0.6127;p=0.0019$). and permeability in human, villin-1 was released with ischemia remained detectable until 120min reperfusion.
For the first time, we showed that is a serological marker of intestinal iri rat human. These findings open perspectives further clinical investigations.

ADMINISTRATION OF THIRD-PARTY MESENCHYMAL STROMAL CELLS AT THE TIME OF KIDNEY TRANSPLANTATION: INTERIM SAFETY ANALYSIS AT ONE YEAR FOLLOW-UP.

Weekers L, Erpicum P, Detry O, Bonvoisin C, Delbouille M-H, Lechanteur Ch, Briquet A, Baudoux E, Jouret F, Beguin Y.
Liège, Belgium

Mesenchymal stromal cells (MSC)-based therapy has been proposed in kidney transplantation (KTx). We report on the 1-year follow-up of an open-label phase I trial using MSC in KTx.
On postoperative day 3, third-party MSC (~$2.0x10^6$/kg) were administered to 7 non-immunized first-transplant recipients from deceased donors, under standard immunosuppression (Basiliximab, Tacrolimus, MMF and steroids). No HLA matching was required for MSC donors. Seven comparable KTx recipients were included as controls. Informed consent was obtained.
No side-effect was noted at the time of MSC injection. Still, 1 patient with a history of ischemic heart disease had a NSTEMI ~3h after MSC infusion. Ten months after KTx, 1 MSC patient had type B aortic dissection and STEMI. Four MSC patients had at least 1 opportunistic infection, whereas 3 controls had polyoma-BK viremia. At day 14, eGFR in MSC and control groups was 47.1 ± 6.8 and 39.7 ± 5.9 ml/min, respectively (*p, 0.05*). At 1 year, eGFR in MSC and control groups was 46.5 ± 18.6 and 54.2 ± 16.3 ml/min, respectively (*p, 0.42*). Per-cause biopsies evidenced 1 borderline and 1 acute rejections in MSC group, whereas no AR was biopsy-proven in controls. Three patients developed anti-HLA antibodies against MSC (n=1) or shared kidney/MSC (n=2) mismatches.

MSC infusion was safe in all patients except one. Incidence of opportunist infections was similar in both groups. No difference in eGFR was found at 1-year *post* KTx. Putative immunization against MSC was observed in 3 patients.

PRETRANSPLANT GLYCOMIC ANALYSIS OF PERFUSATE IS PREDICTIVE OF PRIMARY NON FUNCTION AFTER LIVER TRANSPLANTATION: A PROOF OF CONCEPT.

Verhelst X, Geerts A, Rogiers X, Vanlander A, Berrevoet F, Callewaert N, Troisi R, Van Vlierberghe H.
Gent, Belgium

Primary non function (PNF) is a rare but major complication after liver transplantation requiring urgent retransplantation. It is associated with the use of extended-criteria donors. The donor risk index is a clinical score that can guide the estimation of graft quality but lacks the power to predict PNF risk in individual patients. Perfusate analysis is an attractive tool for assessment of donor liver function before implantation. Glycomic assessment of serum has proven useful in the diagnosis of liver disease. Here, we performed a comprehensive glycomic analysis of perfusate in relation to the appearance of PNF.
In this prospective monocentric study 66 consecutive liver transplantations between October 2011 and July 2013 were included. Perfusate samples were collected after flushing of the hepatic veins before implantation of the liver graft. All donor grafts were transported using cold static storage. Based on an optimized DNA sequencer technology we performed glycomic analysis of these perfusate samples and searched for glycomic alterations in PNF patients.
One single glycan, an agalacto core-alpha-1,6-fucosylated biantennary glycan (NGA2F) was significantly increased in the perfusate of the 3 patients that developed PNF after liver transplantation. It could identify PNF patients with 100% accuracy. This glycomarker was the only predictor of PNF in a multivariate analysis including donor risk index and perfusate AST/ALT levels ($p<0.0001$).
In this proof-of-concept study, patients who developed pnf after liver transplantation showed a specific glycomic signature perfusate (before transplantation) that could distinguish them from non-pnf with 100% accuracy. Approach guides the removal of donor grafts at risk for pool, especially when use high-risk organs are considered.

THE EFFECT OF IN VITRO TACROLIMUS EXPOSURE AND PHARMACOGENETIC VARIATION ON MULTILEVEL CYP3A5, ABCB1 EXPRESSION AND CTGF PRODUCTION IN HUMAN PROXIMAL TUBULE CELLS.

Knops N, Ramazani Y, Levtchenko E, Van den Heuvel B, Kuypers D.
Leuven, Belgium

Our aim was to study the functional implications of Tacrolimus exposure in a human proximal tubule cells (PTC) with variation in CYP3A5 and ABCB1(Pgp) on the expression of these genes and CTGF. Methods: We selected conditional immortalized PTC (ciPTC) with different combinations of CYP3A5(rs776746) and ABCB1(rs1045642) genotypes. Cells were incubated with medium supplemented with vehicle or Tac for 24 and 72hrs. Quantitative RT-PCR, WB and was performed for CYP3A5, ABCB1 and CTGF. Functional CYP3A5 expression was assessed by midazolam (MDZ) hydroxylation and P-gp by calcein efflux. Results: Baseline mRNA, protein and functional CYP3A5 expression was higher in ciPTC with the *1 versus *3/*3 allele. Increasing Tac conc. resulted in decreasing 1'OH MDZ ($p=0.01$). Increasing Tac resulted in a progressive decrease in calcein efflux (50ng/ml: 79.1%; 300ng/ml: 68.8%; $p<0.001$). prolonged incubation resulted in decreased abcb1 mrna and protein expression ($p=0.01$) cc />CT's. In accordance, efflux decreased, but remained higher in TT's (29.90% vs. 41.26%; $p=0.016$). CTGF protein expression increased with Tac conc. (vehicle: 0.57; 50ng/ml: 0.71; 300 ng/ml 0.79; $p=0.04$). CTGF expression was similar for all, but decrease more after 72hrs. In *1 carriers (0.32 vs 0.52; $p=0.001$) and CC/CT's (0.79 vs. 0.41; $p<0.001$).
TAC exposure in ciPTC results a concentration-dependent increase CTGF expression. The initial is independent from genetic variation CYP3A5 or ABCD1, but concurs with concentration dependent decrease functional expression and pgp. After 72 hours observed, especially *1 carriers, abcb1 3435 cc />CT's.

DONOR AGE IS ASSOCIATED WITH EPIGENETIC CHANGES IN GENES INVOLVED IN FIBROSIS IN THE KIDNEY.

Heylen L, Sprangers B, Thienpont B, Moisse M, Kuypers D, Lambrechts D, Naesens M.
Leuven, Belgium

Advanced donor age is one of the key factors associated with allograft fibrosis and impaired outcome after kidney transplantation. Recently, it has become clear that DNA methylation changes hallmark aging. In this study, we investigated aging-associated changes in DNA methylation in kidney transplants.