目的　探讨经大鼠左侧肾动脉移植脂肪干细胞（ASCs）对急性缺血性肾损伤（iAKI）的治疗作用，同时观察ASCs的体内分布情况。 方法　采用胶原酶消化法分离培养ASCs并鉴定。夹闭SD大鼠双侧肾蒂45 min建立iAKI模型。按随机数字表法分成两组：对照组（再灌注后即刻经左肾动脉注射500 μl PBS，n=30）和ASCs治疗组（再灌注后即刻经肾动脉移植5×105 ASCs，n=30）。术后12、24、48、72 h和1周时处死大鼠，测定血清肌酐值（Scr），光学显微镜观察肾脏病理损伤及细胞凋亡、炎性反应及细胞增生情况，荧光显微镜观察ASCs在肾、肺、肝、脾、心脏的停留时间及分布情况。 结果　培养的第3代ASCs具有成脂、成骨等多向分化潜能，流式细胞仪检测高表达CD29（99.35%）和CD90（92.88%），低表达CD34（0.48%）和CD45（3.51%）。ASCs治疗组Scr水平各时间点均显著低于对照组（均P＜0.05）。与对照组相比，治疗组左侧肾小管间质损伤评分在再灌注12、24、48 h时显著降低（均P＜0.05）；肾组织TUNEL染色和巨噬细胞浸润染色积分在再灌注12、24、48、72 h和1周时显著降低（均P＜0.05）；核增殖抗原在再灌注48 h时显著增加（P＜0.05），72 h和1周时显著减少（均P＜0.05）。与治疗组右肾相比，治疗组左侧肾小管间质损伤评分在再灌注24 h时显著降低（P＜0.05）；肾组织TUNEL染色阳性细胞数在再灌注1周时减少（P＜0.05）；巨噬细胞浸润染色积分在再灌注12、48、72 h和1周时减少（均P＜0.05）；核增殖抗原48 h时增加（P＜0.05），72 h和1周时减少（均P＜0.05）。荧光显微镜观察显示ASCs在肾脏内停留时间超过1周，但移植48 h后明显减少，肺、肝、脾、心脏仅观察到极少量的DiI阳性细胞。 结论　ASCs经肾动脉移植可显著改善iAKI大鼠肾功能、减轻肾脏病理损伤和细胞凋亡、减少炎性细胞浸润、促进损伤后修复，这可能与经肾动脉移植可提高ASCs进入损伤肾脏的数量，减少循环过程中的其他器官截留效应有关。

"/> Objective　To explore the therapeutic effect of adipose derived stem cells (ASCs) transplanted via left renal artery on rat acute ischemia reperfusion kidney injury（iAKI） and the distribution of ASCs in different organs.　Methods　ASCs were isolated from inguinal subcutaneous adipose tissue of male SD ras. iAKI model was set in male SD rats by clipping bilateral renal pedicles for 45 min (ischemia reperfusion model). The iAKI rats were randomized into two groups (n=30): control group (renal intra-arterial administration of 500 μl PBS) and ASCs transplantation group (renal intra-arterial administration of 5×105 ASCs). Rats were sacrificed at 12, 24, 48, 72 hours and 1 week after reperfusion to measure renal function by serum creatinine (Scr). Renal pathology, cell apoptosis, inflammation and cell proliferation were analyzed by optical microscope. Distributions of ASCs were measured by fluorescent microscopy.　Results　ASCs at its third passage had the capacities for adipogenic and osteogenic differentiation, postive for CD29, CD90, and negative for CD34, CD45. Compared with control group, Scr in ASCs transplantation group were significantly lower at all time points (P＜0.05); score of left renal tubular interstitial damage degree in ASCs transplantation group was markedly lower at 12 hours, 24 hours, 48 hours (P＜0.05); TUNEL and macrophage infiltration score in ASCs transplantation group were significantly lower (P＜0.05); proliferating antigen increased at 48 hours and decreased at 72 hours and 1 week (P＜0.05). Meanwhile, comparing with right kidneys in ASCs transplantation group, score of left renal tubular interstitial damage degree was markedly lower at 24 hours(P＜0.05); the number of TUNEL positive cells at 1 week was observably lower (P＜0.05); macrophage infiltration score were dramatically lower at 12 hours, 48 hours, 72 hours and 1 week; proliferating antigen increased at 48 hours and decreased at 72 hours and 1 week (P＜0.05). Fluorescence microscope observation showed that residence time of ASCs in kidney was more than 7 days, but the number of ASCs significantly reduced after 48 hours, few DiI positive cells could be observed in lung, liver, spleen and heart.　Conclusions　ASCs transplantation via renal artery can significantly improve renal function and ameliorate pathological damage, relieve apoptosis and macrophage infiltration, and enhance the repair process after iAKI. It may due to renal intra-arterial transplantation increasing the amounts of ASCs migrated into the kidney in iAKI and reducing ASCs distribution in other organs.
"/>

中华肾脏病杂志
Chinese Journal of Nephrology
主　管：中国科学技术协会
主　办：中华医学会
编　辑：《中华肾脏病杂志》

经肾动脉移植脂肪干细胞对大鼠急性缺血性肾损伤的治疗作用

刘少鹏　俞小芳　钟一红　方艺　刘红　许嵘　郭佳　蔡洁茹　刘同强　谢婷　丁小强

DOI：10.3760/cma.j.issn.1001-7097.2013.10.008
基金项目：国家自然科学基金（81000307）；上海市科委基础研究重大项目（12DJ1400200）；科技部国家科技支撑计划（201
作者单位：200032 上海，复旦大学附属中山医院肾内科（刘红，现在杭州市中医院肾内科；许嵘，现在江苏省中医院肾内科；刘同
通信作者：丁小强，Email：ding.xiaoqiang@zs-hospital.sh.cn

Transplantation of adipose-derived stem cells via renal artery protects against a

LIU Shao-peng, YU Xiao-fang, ZHONG Yi-hong, FANG Yi, LIU Hong, XU Rong, GUO Jia, CAI Jie-ru, l
qiang.
Department of Nephrology, Zhongshan Hospital, Fudan University, Shanghai 200032, China
Corresponding author: DING Xiao-qiang, Email: ding.xiaoqiang@zs-hospital.sh.cn