World Journal of Stem Cells

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.4252/wjsc.v7.i2.490

World J Stem Cells 2015 March 26; 7(2): 490-494
ISSN 1948-0210 (online)

MINIREVIEWS

Adult stem-like cells in kidney

Keiichi Hishikawa, Osamu Takase, Masahiro Yoshikawa, Taro Tsujimura, Masaomi Nangaku, Tsuyoshi Takato

Keiichi Hishikawa, Osamu Takase, Masahiro Yoshikawa, Taro Tsujimura, Masaomi Nangaku, Tsuyoshi Takato, Department of Advanced Nephrology and Regenerative Medicine, the University of Tokyo, Tokyo 113-8655, Japan
Tsuyoshi Takato, Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, University of Tokyo, Tokyo 113-8655, Japan
Author contributions: All authors contributed to this paper.
Conflict-of-interest: All authors certify that there is no conflict of interest (including but not limited to commercial, personal, political, intellectual, or religious) regarding the material discussed in the manuscript.

Correspondence to: Keiichi Hishikawa, MD, PhD, Department of Advanced Nephrology and Regenerative Medicine, The University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113-8655, Japan. hishikawa-tky@umin.ac.jp
Telephone: +81-3-3155411
Received: July 29, 2014
Peer-review started: July 30, 2014
First decision: October 16, 2014
Revised: November 20, 2014
Accepted: December 3, 2014
Article in press: December 10, 2014
Published online: March 26, 2015

Abstract

Human pluripotent cells are promising for treatment for kidney diseases, but the protocols for derivation of kidney cell types are still controversial. Kidney tissue regeneration is well confirmed in several lower vertebrates such as fish, and the repair of nephrons after tubular damages is commonly observed after renal injury. Even in adult mammal kidney, renal progenitor cell or system is reportedly presents suggesting that adult stem-like cells in kidney can be practical clinical targets for kidney diseases. However, it is still unclear if kidney stem cells or stem-like cells exist or not. In general, stemness is defined by several factors such as self-renewal capacity, multi-lineage potency and characteristic gene expression profiles. The definite use of stemness may be obstacle to understand kidney regeneration, and here we describe the recent broad findings of kidney regeneration and the cells that contribute regeneration.

Key words: Stem cell; Label-retaining cells; rKS56; SP cells; CD24; CD133; Sca-1; Induced pluripotent stem; ES cell

Core tip: Controversies still persist whether kidney stem cells exist or not, but renal progenitor cell or system is reportedly presents suggesting that adult stem-like cells in kidney can be practical clinical targets for kidney diseases. In this mini-review, we describe the recent broad findings of kidney regeneration and the cells that contribute regeneration.

Hishikawa K, Takase O, Yoshikawa M, Tsujimura T, Nangaku M, Takato T. Adult stem-like cells in kidney. *World J Stem Cells* 2015; 7(2): 490-494 Available from: URL: http://www.wjgnet.com/1948-0210/full/v7/i2/490.htm DOI: http://dx.doi.org/10.4252/wjsc.v7.i2.490

INTRODUCTION

Recent developments in human pluripotent cells including both embryonic stem cells and induced pluripotent stem (iPS) cells[1] are promising for clinical development of cell therapies and tissue

engineering[2-4]. There is an urgent need for stem cell and regenerative medicine approaches to kidney diseases, because patients with end-stage kidney disease require lifelong dialysis treatment or transplantation that incurs a significant cost. Several established protocols for derivation of cardiomyocytes and neurons were already reported, but that for kidney cell types are still controversial. Recently human iPS cells were successfully differentiated into kidney lineage *via* OSR1 (+) cells[5,6]. However metanephric progenitors were not induced from OSR1(+) cells[7], and efficient differentiation of human pluripotent cells into intermediate mesoderm was reported by treatment the cells with glycogen synthase kinase-3beta inhibitor[8]. Different from mammals, the capacity to regenerate kidney tissue is well confirmed in several lower vertebrates such as fish[9]. Kidney regeneration, such as the repair of nephrons after tubular damages, is commonly observed after renal injury even in humans[10,11]. Concerning adult mammal kidney, there are lots of evidences that suggest existence of renal progenitor system[12-19]. Collectively, these results suggest the potential role of adult stem-like cells in kidney for practical clinical treatment of kidney diseases. In this review, we describe the localization and recent functional findings of kidney regeneration and the cells that contribute regeneration.

TUBULAR CELLS (LRC, RKS56, NFATC-1$^+$, ALDH^{HIGH}, CD24$^+$/CD133$^+$, MRPC)

To identify the stem cells, BrdU-DNA labeling is commonly used to find slow-cycling cells because stem cells have a slow cell cycle. Slow cycling cells were also called label-retaining cells (LRC), and LRC in tubules were confirmed by several groups[20-22] (Table 1). In rat kidneys, LRC were distributed among renal epithelial tubular cells[20]. In 3 dimensional culture system, LRC formed tubule-like structure. Moreover, injected LRC into cultured metanephros formed nephrons and collecting ducts[23]. rKS56 cells were established form proximal tubules (S3) by using microdiseection of a single nephron[24]. rKS56 cells expressed markers of an immature progenitor state such as c-Kit and Sca-1. When rKS56 cells were transplanted into acute kidney disease models, the cells differentiated into epithelium. A resident progenitor cells in proximal tubular (PTC) cell was identified by Nfatc1-P2-Cre reporter system[25]. Nfatc-1-labeled PTC cells were apoptosis-resistant and proliferated to repair the damaged proximal tubule segment. ALDH activity was used to isolate cells with progenitor-like characteristics from the tubular fraction of the renal cortex[26-29]. ALDH^{high} cells displayed typical stem cell properties such as sphere formation and anchorage-independent growth. CD24/CD133 double-positive cells were localized in the tubular epithelium, and demonstrated clonogenic multipotency and self-renewal ability[28]. Bombelli *et al*[30] recently proposed existence of CD133$^+$/CD24$^-$ renal stem cells but Romagnani reported that CD133$^+$ renal stem definitely co-express CD24 in human kidney[31]. Gupta *et al*[32] reported localization of stem-like cells around the tubules. They named the cells multi-potent renal progenitor cells (MRPC). By using similar culture condition used for culture of bone marrow-derived mult-ipotent adult progenitor cells, MRPS were isolated from rat kidney. The plasticity of MRPC was confirmed by expression of endothelial, hepatocyte, and neural markers by RT-PCR and protein expression. When MRPC were injected under the capsule of an uninjured kidney or arterially into acute kidney injury model, the cells differentiated into renal tubules. However, differentiation/induction of matured kidney cells from MRPC *in vitro* was not confirmed yet.

RENAL PAPILLA (LRC, CD133$^+$)

To identify the stem-like cells in kidney, Oliver *et al*[33,34] performed pulse label of rat and mouse pups by BrdU, and confirmed the existence of LRC cells in the kidney. LRC cells was very sparse in the kidney, but they found numerous LRC cells in renal papilla[33]. In 3 dimensional culture, LRC cells in renal papilla spontaneously formed spheroids, and clones from single cell of LRC cells expressed both mesencymal and epithelial markers. The papillary cells also differentiated to myofibroblasts and neuronal cells. In acute kidney injury model such as ischemic injury, LRC cells in papilla migrated to the upper papilla and formed a compartment of rapidly proliferating cells suggesting that the cells contributed to repair of kidney tissue[34]. Papillary cells that expressed CD133 were also expressed nestin and embryonic cell markers (Oct3/4, Nanog, SOX2 and SSEA-4)[35].

INTERSTITIAL SPACE (SCA-1$^+$CD45$^-$, SP, CD133$^+$)

Several groups have found adult stem-like cells in murine kidney interstitial space using different approaches. Stem cell angiten-1 (Sca-1)-positive and CD45-negative cells were isolated from whole kidney tissue by magnetic assisted cell sorting and fluorescence activated cell sorting (FACS) sorting[36]. The cells were negative for hematopoietic stem cell and lineage markers and located in the renal interstitial spaces. The differentiation of the cells into multi-lineage (myogenic, osteogenic, adipogenic and neural) was also confirmed. In acute kidney injury model, injected Sca-1$^+$CD45$^-$ cells contributed

Table 1 Localization and characteristics of adult stem-like cells in kidney

Localization	Characteristics	Species	Ref.
Tubular cells	LRC	Rat	[20-23]
	rKS56	Rat	[24]
	Nfactc-1$^+$	Mice	[25]
	ALDH^{high}/CD24$^+$/CD133$^+$	Human	[26-29]
	MRPC	Rat	[32]
Renal papilla	LRC	Rat, mice	[31,32]
	CD133$^+$	Human	[33]
Interstitial space	Sca-1$^+$/CD45$^-$	Mice	[34]
	SP cell	Rat, mice, human	[38-41]
	CD133$^+$	Human	[27]
Bowman's capsule	CD24$^+$/CD133$^+$/PDX$^+$	Human	[44-48]
	CD24$^+$/CD133$^+$/PDX$^-$	Human	[44-48]

LRC: Label-retaining cells; MRPC: Multi-potent renal progenitor cell; PDX: Podocyte marker.

kidney repair. To isolate hematopoietic stem cell-rich population in a single step, Goodell *et al*[37] stained cells with Hoechst 33342 dye and isolated the cells by FACS. The cells isolated by this method were nemaed side population (SP) cells. This method was also used to purify a stem cell-rich population in various kinds of tissue. SP cells isolated from adult kidney demonstrated ability of self-renewal and differentiation into multiple lineages[38]. SP cells isolated from adult kidney located in interstitial spaces, and secreted reno-regenerative/protective factors (HGF, VEGF, and BMP-7)[39-42]. The injection of SP cells isolated from adult kidney cells into a model of acute kidney injury demonstrated the recovery of renal function[39,40]. Interestingly, Inowa *et al*[43] confirmed the existence of kidney SP cells in human. Concerning CD133 positive cells, Bussolati *et al*[27] reported that the cells were localized to the interstitium, but not in glomeruli Kidney CD133 positive cells lacked expression of hematopoietic markers and expressed Pax-2, an embryonic renal marker. Intravenous injection of kidney CD133 positive cells in SCID mice with glycerol-induced tubulonecrosis, the cells homed into the injured kidney and integrated in tubules.

BOWMAN'S CAPSULE (CD24$^+$CD133$^+$PDX$^+$, CD24$^+$CD133$^+$PDX$^-$)

Some parietal epithelial cells (PEC) are reported to be adult stem-like cells[44-47]. Sagrinati *et al*[45] confirmed the existence of PEC that expressed CD24, CD133 Oct-4 and Bml-1 in the Bowman's capsule CD24$^+$CD133$^+$ PEC were isolated by culture of capsulated glomeruli plated on fibronectin-coated dishes. CD24$^+$CD133$^+$ PEC showed potential of self-renewal and a high cloning efficiency. Transplantation of CD24$^+$CD133$^+$ PEC into acute kidney injury model significantly improved not only morphologic but functional kidney damage. Further characterization using podocyte marker (PDX) of CD24$^+$CD133$^+$ PEC revealed a hierarchial population of the cells in a precise sequence with Bowman's capsule and exhibited heterogenous potential such as differentiation and regeneration[48]. CD24$^+$CD133$^+$PDX$^-$ cells localized to the urinary pole could differentiate into both tubular cells and podocytes, but CD24$^+$CD133$^+$PDX$^+$ cells localized between the urinary pole and vascular pole could differentiate into only podocytes. Transplantation of CD24$^+$CD133$^+$PDX$^-$ cells reduced proteinuria and improved chronic glomerular damage in adriamycin-induced nephropathy models.

FUNCTIONAL REGULATION OF ADULT STEM-LIKE CELLS IN KIDNEY

As mentioned above, different kinds of adult stem-like cells in kidney have been reported, but their functional regulations were poorly understood. If it is possible to regulate multi-potent adult stem like-cell *in situ*, this can be a good regenerative treatment. Recently MyoR was reported to regulate regenerative function of kidney SP cells[49], and such a molecule can be a good target for pharmacological treatment for kidney disease.

CONCLUSION

Several adult stem-like cells in kidney reportedly demonstrated multi-potency. However, it is impossible to get enough cells for cell therapy from the patient. The adult stem-like cell in kidney is expected to play key role to preserve kidney function, and the cells may be the good targets for pharmacological treatment. For cell therapy, iPS or ES cells might be the applicable as in the case with neural and cardiac regeneration.

REFERENCES

1 **Takahashi K**, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell* 2006; **126**: 663-676 [PMID: 16904174 DOI: 10.1016/j.cell.2006.07.024]

2 **Song JJ**, Guyette JP, Gilpin SE, Gonzalez G, Vacanti JP, Ott HC. Regeneration and experimental orthotopic transplantation of a bioengineered kidney. *Nat Med* 2013; **19**: 646-651 [PMID: 23584091 DOI: 10.1038/nm.3154]

3 **Humes HD**, Weitzel WF, Bartlett RH, Swaniker FC, Paganini EP, Luderer JR, Sobota J. Initial clinical results of the bioartificial kidney containing human cells in ICU patients with acute renal failure. *Kidney Int* 2004; **66**: 1578-1588 [PMID: 15458454 DOI: 10.1111/j.1523-1755.2004.00923]

4 **Tumlin J**, Wali R, Williams W, Murray P, Tolwani AJ, Vinnikova AK, Szerlip HM, Ye J, Paganini EP, Dworkin L, Finkel KW, Kraus MA, Humes HD. Efficacy and safety of renal tubule cell therapy for acute renal failure. *J Am Soc Nephrol* 2008; **19**: 1034-1040 [PMID: 18272842 DOI: 10.1681/ASN.2007080895]

5 **Mae S**, Shono A, Shiota F, Yasuno T, Kajiwara M, Gotoda-Nishimura N, Arai S, Sato-Otubo A, Toyoda T, Takahashi K, Nakayama N, Cowan CA, Aoi T, Ogawa S, McMahon AP, Yamanaka S, Osafune K. Monitoring and robust induction of

nephrogenic intermediate mesoderm from human pluripotent stem cells. *Nat Commun* 2013; **4**: 1367 [PMID: 23340407 DOI: 10.1038/ncomms2378]

6 **Araoka T**, Mae S, Kurose Y, Uesugi M, Ohta A, Yamanaka S, Osafune K. Efficient and rapid induction of human iPSCs/ESCs into nephrogenic intermediate mesoderm using small molecule-based differentiation methods. *PLoS One* 2014; **9**: e84881 [PMID: 24454758 DOI: 10.1371/journal.pone.0084881]

7 **Taguchi A**, Kaku Y, Ohmori T, Sharmin S, Ogawa M, Sasaki H, Nishinakamura R. Redefining the in vivo origin of metanephric nephron progenitors enables generation of complex kidney structures from pluripotent stem cells. *Cell Stem Cell* 2014; **14**: 53-67 [PMID: 24332837 DOI: 10.1016/j.stem.2013.11.010]

8 **Lam AQ**, Freedman BS, Morizane R, Lerou PH, Valerius MT, Bonventre JV. Rapid and efficient differentiation of human pluripotent stem cells into intermediate mesoderm that forms tubules expressing kidney proximal tubular markers. *J Am Soc Nephrol* 2014; **25**: 1211-1225 [PMID: 24357672 DOI: 10.1681/ASN.2013080831]

9 **Diep CQ**, Ma D, Deo RC, Holm TM, Naylor RW, Arora N, Wingert RA, Bollig F, Djordjevic G, Lichman B, Zhu H, Ikenaga T, Ono F, Englert C, Cowan CA, Hukriede NA, Handin RI, Davidson AJ. Identification of adult nephron progenitors capable of kidney regeneration in zebrafish. *Nature* 2011; **470**: 95-100 [PMID: 21270795 DOI: 10.1038/nature09669]

10 **Remuzzi G**, Benigni A, Remuzzi A. Mechanisms of progression and regression of renal lesions of chronic nephropathies and diabetes. *J Clin Invest* 2006; **116**: 288-296 [PMID: 16453013 DOI: 10.1172/JCI27699]

11 **Ma LJ**, Nakamura S, Aldigier JC, Rossini M, Yang H, Liang X, Nakamura I, Marcantoni C, Fogo AB. Regression of glomerulosclerosis with high-dose angiotensin inhibition is linked to decreased plasminogen activator inhibitor-1. *J Am Soc Nephrol* 2005; **16**: 966-976 [PMID: 15728787 DOI: 10.1681/ASN.2004060492]

12 **Blanpain C**, Horsley V, Fuchs E. Epithelial stem cells: turning over new leaves. *Cell* 2007; **128**: 445-458 [PMID: 17289566 DOI: 10.1016/j.cell.2007.01.014]

13 **Romagnani P**. Toward the identification of a "renopoietic system"? *Stem Cells* 2009; **27**: 2247-2253 [PMID: 19739254 DOI: 10.1002/stem.140]

14 **Davidson AJ**. Uncharted waters: nephrogenesis and renal regeneration in fish and mammals. *Pediatr Nephrol* 2011; **26**: 1435-1443 [PMID: 21336813 DOI: 10.1007/s00467-011-1795-z]

15 **Lazzeri E**, Mazzinghi B, Romagnani P. Regeneration and the kidney. *Curr Opin Nephrol Hypertens* 2010; **19**: 248-253 [PMID: 20061947 DOI: 10.1097/MNH.0b013e32833680dc]

16 **Biancone L**, Camussi G. Stem cells in 2013: Potential use of stem or progenitor cells for kidney regeneration. *Nat Rev Nephrol* 2014; **10**: 67-68 [PMID: 24296627 DOI: 10.1038/nrneph.2013.257]

17 **Dziedzic K**, Pleniceanu O, Dekel B. Kidney stem cells in development, regeneration and cancer. *Semin Cell Dev Biol* 2014; **36**: 57-65 [PMID: 25128731 DOI: 10.1016/j.semcdb.2014.08.003]

18 **Aggarwal S**, Moggio A, Bussolati B. Concise review: stem/progenitor cells for renal tissue repair: current knowledge and perspectives. *Stem Cells Transl Med* 2013; **2**: 1011-1019 [PMID: 24167320 DOI: 10.5966/sctm.2013-0097]

19 **Zhu XY**, Lerman A, Lerman LO. Concise review: mesenchymal stem cell treatment for ischemic kidney disease. *Stem Cells* 2013; **31**: 1731-1736 [PMID: 23766020 DOI: 10.1002/stem.1449]

20 **Maeshima A**, Yamashita S, Nojima Y. Identification of renal progenitor-like tubular cells that participate in the regeneration processes of the kidney. *J Am Soc Nephrol* 2003; **14**: 3138-3146 [PMID: 14638912]

21 **Vogetseder A**, Karadeniz A, Kaissling B, Le Hir M. Tubular cell proliferation in the healthy rat kidney. *Histochem Cell Biol* 2005; **124**: 97-104 [PMID: 16133123 DOI: 10.1007/s00418-005-0023-y]

22 **Fujigaki Y**, Goto T, Sakakima M, Fukasawa H, Miyaji T, Yamamoto T, Hishida A. Kinetics and characterization of initially regenerating proximal tubules in S3 segment in response to various degrees of acute tubular injury. *Nephrol Dial Transplant* 2006; **21**: 41-50 [PMID: 16077144 DOI: 10.1093/ndt/gfi035]

23 **Maeshima A**, Sakurai H, Nigam SK. Adult kidney tubular cell population showing phenotypic plasticity, tubulogenic capacity, and integration capability into developing kidney. *J Am Soc Nephrol* 2006; **17**: 188-198 [PMID: 16338966 DOI: 10.1681/ASN.2005040370]

24 **Kitamura S**, Yamasaki Y, Kinomura M, Sugaya T, Sugiyama H, Maeshima Y, Makino H. Establishment and characterization of renal progenitor like cells from S3 segment of nephron in rat adult kidney. *FASEB J* 2005; **19**: 1789-1797 [PMID: 16260649 DOI: 10.1096/fj.05-3942com]

25 **Langworthy M**, Zhou B, de Caestecker M, Moeckel G, Baldwin HS. NFATc1 identifies a population of proximal tubule cell progenitors. *J Am Soc Nephrol* 2009; **20**: 311-321 [PMID: 19118153 DOI: 10.1681/ASN.2008010094]

26 **Ma I**, Allan AL. The role of human aldehyde dehydrogenase in normal and cancer stem cells. *Stem Cell Rev* 2011; **7**: 292-306 [PMID: 21103958 DOI: 10.1007/s12015-010-9208-4]

27 **Bussolati B**, Bruno S, Grange C, Buttiglieri S, Deregibus MC, Cantino D, Camussi G. Isolation of renal progenitor cells from adult human kidney. *Am J Pathol* 2005; **166**: 545-555 [PMID: 15681837 DOI: 10.1016/S0002-9440(10)62276-6]

28 **Sallustio F**, De Benedictis L, Castellano G, Zaza G, Loverre A, Costantino V, Grandaliano G, Schena FP. TLR2 plays a role in the activation of human resident renal stem/progenitor cells. *FASEB J* 2010; **24**: 514-525 [PMID: 19843711 DOI: 10.1096/fj.09-136481]

29 **Lindgren D**, Boström AK, Nilsson K, Hansson J, Sjölund J, Möller C, Jirström K, Nilsson E, Landberg G, Axelson H, Johansson ME. Isolation and characterization of progenitor-like cells from human renal proximal tubules. *Am J Pathol* 2011; **178**: 828-837 [PMID: 21281815 DOI: 10.1016/j.ajpath.2010.10.026]

30 **Bombelli S**, Zipeto MA, Torsello B, Bovo G, Di Stefano V, Bugarin C, Zordan P, Viganò P, Cattoretti G, Strada G, Bianchi C, Perego RA. PKH(high) cells within clonal human nephrospheres provide a purified adult renal stem cell population. *Stem Cell Res* 2013; **11**: 1163-1177 [PMID: 24012544 DOI: 10.1016/j.scr.2013.08.004]

31 **Romagnani P**, Remuzzi G. CD133+ renal stem cells always co-express CD24 in adult human kidney tissue. *Stem Cell Res* 2014; **12**: 828-829 [PMID: 24467938 DOI: 10.1016/j.scr.2013.12.011]

32 **Gupta S**, Verfaillie C, Chmielewski D, Kren S, Eidman K, Connaire J, Heremans Y, Lund T, Blackstad M, Jiang Y, Luttun A, Rosenberg ME. Isolation and characterization of kidney-derived stem cells. *J Am Soc Nephrol* 2006; **17**: 3028-3040 [PMID: 16988061 DOI: 10.1681/ASN.2006030275]

33 **Oliver JA**, Maarouf O, Cheema FH, Martens TP, Al-Awqati Q. The renal papilla is a niche for adult kidney stem cells. *J Clin Invest* 2004; **114**: 795-804 [PMID: 15372103 DOI: 10.1172/JCI20921]

34 **Oliver JA**, Klinakis A, Cheema FH, Friedlander J, Sampogna RV, Martens TP, Liu C, Efstratiadis A, Al-Awqati Q. Proliferation and migration of label-retaining cells of the kidney papilla. *J Am Soc Nephrol* 2009; **20**: 2315-2327 [PMID: 19762493 DOI: 10.1681/ASN.2008111203]

35 **Ward HH**, Romero E, Welford A, Pickett G, Bacallao R, Gattone VH, Ness SA, Wandinger-Ness A, Roitbak T. Adult human CD133/1(+) kidney cells isolated from papilla integrate into developing kidney tubules. *Biochim Biophys Acta* 2011; **1812**: 1344-1357 [PMID: 21255643 DOI: 10.1016/j.bbadis.2011.01.010]

36 **Dekel B**, Zangi L, Shezen E, Reich-Zeliger S, Eventov-Friedman S, Katchman H, Jacob-Hirsch J, Amariglio N, Rechavi G, Margalit R, Reisner Y. Isolation and characterization of nontubular sca-1+lin- multipotent stem/progenitor cells from adult mouse kidney. *J Am Soc Nephrol* 2006; **17**: 3300-3314 [PMID: 17093069 DOI: 10.1681/ASN.2005020195]

37 **Goodell MA**, Brose K, Paradis G, Conner AS, Mulligan RC. Isolation and functional properties of murine hematopoietic stem cells that are replicating in vivo. *J Exp Med* 1996; **183**: 1797-1806 [PMID: 8666936]

38 **Hishikawa K**, Marumo T, Miura S, Nakanishi A, Matsuzaki Y, Shibata K, Kohike H, Komori T, Hayashi M, Nakaki T, Nakauchi

H, Okano H, Fujita T. Leukemia inhibitory factor induces multilineage differentiation of adult stem-like cells in kidney *via* kidney-specific cadherin 16. *Biochem Biophys Res Commun* 2005; **328**: 288-291 [PMID: 15670782 DOI: 10.1016/j.bbrc.2004.12.167]

39 **Hishikawa K**, Marumo T, Miura S, Nakanishi A, Matsuzaki Y, Shibata K, Ichiyanagi T, Kohike H, Komori T, Takahashi I, Takase O, Imai N, Yoshikawa M, Inowa T, Hayashi M, Nakaki T, Nakauchi H, Okano H, Fujita T. Musculin/MyoR is expressed in kidney side population cells and can regulate their function. *J Cell Biol* 2005; **169**: 921-928 [PMID: 15967813 DOI: 10.1083/jcb.200412167]

40 **Challen GA**, Bertoncello I, Deane JA, Ricardo SD, Little MH. Kidney side population reveals multilineage potential and renal functional capacity but also cellular heterogeneity. *J Am Soc Nephrol* 2006; **17**: 1896-1912 [PMID: 16707564 DOI: 10.1681/ASN.2005111228]

41 **Marumo T**, Hishikawa K, Matsuzaki Y, Imai N, Takase O, Shimosawa T, Okano H, Fujita T. Angiotensin II type 1 receptor blockade prevents decrease in adult stem-like cells in kidney after ureteral obstruction. *Eur J Pharmacol* 2007; **573**: 216-220 [PMID: 17692840 DOI: 10.1016/j.ejphar.2007.07.032]

42 **Nishinakamura R**, Sakaguchi M. BMP signaling and its modifiers in kidney development. *Pediatr Nephrol* 2014; **29**: 681-686 [PMID: 24217785 DOI: 10.1007/s00467-013-2671-9]

43 **Inowa T**, Hishikawa K, Takeuchi T, Kitamura T, Fujita T. Isolation and potential existence of side population cells in adult human kidney. *Int J Urol* 2008; **15**: 272-274 [PMID: 18304230 DOI: 10.1111/j.1442-2042.2007.01984.x]

44 **Lasagni L**, Romagnani P. Glomerular epithelial stem cells: the good, the bad, and the ugly. *J Am Soc Nephrol* 2010; **21**: 1612-1619 [PMID: 20829409 DOI: 10.1681/ASN.2010010048]

45 **Sagrinati C**, Netti GS, Mazzinghi B, Lazzeri E, Liotta F, Frosali F, Ronconi E, Meini C, Gacci M, Squecco R, Carini M, Gesualdo L, Francini F, Maggi E, Annunziato F, Lasagni L, Serio M, Romagnani S, Romagnani P. Isolation and characterization of multipotent progenitor cells from the Bowman's capsule of adult human kidneys. *J Am Soc Nephrol* 2006; **17**: 2443-2456 [PMID: 16885410 DOI: 10.1681/ASN.2006010089]

46 **Lazzeri E**, Crescioli C, Ronconi E, Mazzinghi B, Sagrinati C, Netti GS, Angelotti ML, Parente E, Ballerini L, Cosmi L, Maggi L, Gesualdo L, Rotondi M, Annunziato F, Maggi E, Lasagni L, Serio M, Romagnani S, Vannelli GB, Romagnani P. Regenerative potential of embryonic renal multipotent progenitors in acute renal failure. *J Am Soc Nephrol* 2007; **18**: 3128-3138 [PMID: 17978305 DOI: 10.1681/ASN.2007020210]

47 **Park HC**, Yasuda K, Kuo MC, Ni J, Ratliff B, Chander P, Goligorsky MS. Renal capsule as a stem cell niche. *Am J Physiol Renal Physiol* 2010; **298**: F1254-F1262 [PMID: 20200095 DOI: 10.1152/ajprenal.00406.2009]

48 **Ronconi E**, Sagrinati C, Angelotti ML, Lazzeri E, Mazzinghi B, Ballerini L, Parente E, Becherucci F, Gacci M, Carini M, Maggi E, Serio M, Vannelli GB, Lasagni L, Romagnani S, Romagnani P. Regeneration of glomerular podocytes by human renal progenitors. *J Am Soc Nephrol* 2009; **20**: 322-332 [PMID: 19092120 DOI: 10.1681/ASN.2008070709]

49 **Kamiura N**, Hirahashi J, Matsuzaki Y, Idei M, Takase O, Fujita T, Takato T, Hishikawa K. Basic helix-loop-helix transcriptional factor MyoR regulates BMP-7 in acute kidney injury. *Am J Physiol Renal Physiol* 2013; **304**: F1159-F1166 [PMID: 23515721 DOI: 10.1152/ajprenal.00510.2012]

P- Reviewer: Kita K, Yarema KJ **S- Editor**: Ji FF **L- Editor**: A
E- Editor: Lu YJ

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com