S-C25

성체신장줄기세포는 피질수질경계부에 존재한다

울산대학교 의과대학 서울아산병원 병리과

김경은 · 이경미 · 한덕종 · 유은실 · 조영미

Adult Renal Stem Cells Reside in the Corticomedullary Junction of the Kidney

Kyungeun Kim, Kyoung Mee Lee, Duck Jong Han, Eunsil Yu, Yong Mee Cho

Department of Pathology University of Ulsan College of Medicine Asan Medical Center

Background : Embryonic stem cells generate intermediate mesoderm, which eventually develops into adult kidneys and is finally organized into the cortex and medulla. The medulla is further divided into the outer and inner stripes of the outer medulla, the inner medulla, and the renal papilla. Although the adult kidney is composed of mitotically quiescent cells, it is capable of rapid cell division in response to regenerative stimuli, as in acute tubular necrosis (ATN). It suggests the presence of adult renal stem cells. However, the location, or niche, of adult renal stem cells has not been clearly defined yet.

Methods : To identify the niche of adult renal stem cells, we studied regional slow cycling property, proliferating activity, clonogenic capacity, and multipotency. To test the slow cycling property and proliferating activity, we administered a pulse of the thymidine analogue BrdU into mouse embryos at multiple time points to label the DNA of proliferating stem cells of the embryonic kidneys. We then assessed the spatial and temporal distribution patterns of BrdU label-retaining cells (LRC) and Ki-67-positive proliferating cells in early postnatal and developed mouse kidneys. Unilateral transient ATN was induced by clamping of the left renal vessels of adult mice. We then investigated the spatial distribution patterns of proliferating cells and LRC to determine regional contribution to renal regeneration. To determine the regional clonogenic capacity and multipotency, mouse and human kidneys were dissected into the cortex, corticomedullary junction (CMJ), medulla, and renal papilla. We cultured the regional tubular cells and examined the clonogenic capacity and multilineage differentiation as well.

Results : In early postnatal kidneys, the CMJ was constantly positive for both BrdU and the proliferation marker Ki-67. In developed kidneys, the LRC were concentrated constantly in the outer stripe of the CMJ, especially in the area adjacent to the arcuate vessels. Following the induction of unilateral ATN, Ki-67 positive cells were concentrated in the outer stripe of the CMJ, both in the ATN and contralateral non-ATN kidneys, suggesting high proliferating potential of the CMJ. Culture of regional tubular cells of adult mouse and human kidneys revealed high colony-forming capacity of the CMJ with multilineage differentiation, including epithelial, distal tubular, glomerular podocyte, neuronal, and mesenchymal differentiation.

Conclusion : These results demonstrate that the CMJ contains LRCs and multipotent clonogenic cells, suggesting that the CMJ is the niche of adult renal stem cells.