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Remodeling of Connecting Tubule and Collecting Duct in *Hoxb7-cre;Mib1$^{f/f}$* Mice

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The intercalated cells (ICs) in kidney actively regulate the acid-base homeostasis by existing transporters and these cells localize at the connecting tubule (CNT) and the collecting duct (CD). Recently, Foxi1 mediate the differentiation of ICs from epithelial precursor cells,however,the molecular mechanisms are certainly unknown. The Notch signaling pathway is involved in cell fate determination and has been implicated in proximal-distal patterning in the mammalian kidney.This study was examined to identify the change of ICs number in the adult mice (more than 12 weeks) which Mind bomb-1 (*Mib1*),an E3 ubiquitin ligase required for the initiation of Notch signaling,was specifically inactivated in the ureteric bud (Hoxb7-cre). The *Hoxb7-cre;Mib1$^{f/f}$* mice at postnatal day 17 showed progressive unilateral or bilateral hydronephrosis of distended kidneys, so we examined the single kidney per animal, which did not show hydronephrosis. We tried multiple immunohistochemistry using the antibodies for H^+-ATPase, pendrin,anion-exchanger 1 to identify ICs and the antibodies for aquaporin 2 or calbindin D28K to identify tubular segment. In CNT and CD, apical H^+-ATPase-positive, basolateral anion-exchanger 1-positive type A ICs were significantly increased in the *Hoxb7-cre;Mib1$^{f/f}$* compared with *Mib1$^{f/f}$*. Diffuse H^+-ATPase-positive, apical pendrin-positive type B and apical H^+-ATPase -positive, apical pendrin-positive non A-non B ICs, however, respond differently in the *Hoxb7-cre;Mib1$^{f/f}$*. Pendrin-positive ICs were significantly increased in CD and significantly decreased in CNT in the *Hoxb7-cre;Mib1$^{f/f}$*. In CD, diffuse H^+-ATPase-positive type B ICs were increased and apical H^+-ATPase-positive non A-non B ICs were decreased in CNT. The origin of kidney was two places, metanephrogenic blastema and ureteric bud. Glomerulus and proximal and distal tubules originate in metanephrogenic blastema and collecting duct in ureteric bud.In other study performed by our colleague, pendrin-positive ICs develop from separate foci, one in the CNT and one in the CD and these cells may arise from proliferation of undifferentiated precursor cells in the differentiating CNT and CD rather than via selective proliferation of pendrin-positive cells. Taken together, these results suggest that the origin of ICs in CNT is undifferentiated precursor cells and these precursor cells arise from ureteric bud or metanephrogenic blastema, therefore, even though Notch signal is specifically inactivated in ureteric bud, the compositional change of CNT is different to the change of CD.

Key Words: Origin of intercalated Cell, Metanephrogenic blastema