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COMMENTARY

How can juxtaglomerular renin-producing cells support the integrity of glomerular endothelial cells?

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Over the last years, findings have been accumulated to indicate that renin-producing cells and their "silent" precursors show a striking degree of plasticity not only to regulate renin. Renin-secreting cells of the kidney, which are typically located in a juxtaglomerular position at the entrance of afferent arterioles into their glomeruli, are the key regulators of the renin-angiotensin-aldosterone system. From their origin, they are pericyte-related cells [9] which descend from the FoxD1-positive stroma progenitor compartment of the kidney [2]. It is well established that the number of renin-secreting cells can increase by hyperplasia and also by reversible metaplastic transformation of "silent" renin-producing cells into active renin producers and vice versa [4]. The common genomic signature of "silent" and of active renin-producing cells has recently been unraveled [6]. A key step for renin expression is activation of the cyclic AMP signaling cascade [4].

Synthesis and secretion also serve other functions. Thus, it has been shown that genetic activation of the hypoxia signaling pathway in renin cells suppresses renin expression and induces erythropoietin expression [3]. Moreover, renin cells or their "silent" precursors have been found to serve glomerular function, for instance by repopulating the mesangium after mesangial cell injury [8]. Further evidence in this context has been reported that renin cells might also act as precursors for podocytes after podocyte damage [1]. Although renin cells cannot repopulate damaged glomerular endothelial cells [7], they appear to exert a protective effect on endothelial cells. The article by Steglich and coworkers entitled "Renin cells with defective Gsα/cAMP-signaling contribute to renal endothelial damage" as published in this issue of *Pflügers Archiv* now confirms and extends previous findings that renin cells have also influence on the integrity of the glomerular endothelium [5]. The authors report that continuous disruption of cAMP signaling by renin cell–specific deletion of the Gsα protein downregulated renin expression as expected, but in addition also led to endothelial damage of glomerular capillaries as indicated by the change of morphological and genetic markers. In reverse, this finding could indicate that intact cAMP signaling in juxtaglomerular cells is required for normal glomerular endothelial function. The authors present data that indicate that a loss of renin cells and the concomitant decrease in renin production induced by the expression of diphtheria toxin in renin cells per se exert no apparent detrimental effect on endothelial cells. They also found that deletion of Gsα protein in renin cells did not destroy the cells but instead caused a phenotype switch to a renin-negative and fibroblast-like cell. The authors suggest that the new profibrotic cell phenotype directly or indirectly causes endothelial damage. Notably, genetic induction of the hypoxia signaling pathway causes a similar profibrotic phenotype shift of renin cells as does deletion of Gsα protein [3]. It will be tempting to investigate therefore if phenotype changes of renin cells into fibroblast-like cells induced by maneuvers other than interruption of cAMP signaling will also cause endothelial damage or if the effect is causally related to insufficient cAMP signaling in the cells.

In summary, this paper provides new insights into a possible role of renin-producing cells beyond renin formation and thus adds a further piece of evidence to the existing knowledge about the functional plasticity of renin-producing cells.

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