Adrenergic influences on the development and distribution of renin cells in nephrogenesis

Edward J. Johns

Department of Physiology, University College Cork, Cork, Republic of Ireland

RENIN-CONTAINING CELLS have generated a great deal of interest, from understanding their characteristic phenotype to following their location during nephrogenesis and evaluating the regulation of their renin-secreting activity by cAMP and β-adrenoceptors. It is now evident that the renin-containing cells arise from a distinct genetic lineage (7) and can express not only cell markers for renin but also for vascular smooth muscle cells such as actin, which is unlike the situation with either endothelial or vascular smooth muscle cells that only express lineage markers for their own cell phenotype. As fetal development progresses, excess renin cells become reassigned as vascular smooth muscle cells but in the adult these cells can be mobilized when extra renin is required as occurs during exposure to a low dietary sodium intake. In the adult, it is cAMP that has been found to be a key factor in determining the levels of renin secretion (1). This occurs both by an action at the gene level by binding of cAMP to a responsive element on the gene as well as by depressing the rate of renin gene mRNA degradation (2). CAMP is also a primary factor in the cell-signaling mechanisms within the renin-containing cells that regulate granule exocytosis in the adult (6). Indeed, both renin gene expression and secretion can be modulated by the renal sympathetic nerves in the adult (3). Understanding of these interactions between β-adrenergic control of renin via the renal sympathetic nerves is particularly important as in the spontaneously hypertensive rat, where sympathetic control of renin secretion is much more intense (4) even at the earliest time of measurement, some 4–5 wk of age, then this may become an important mechanism potentially contributing to the genesis of hypertension. What is difficult to assess is how these interactions become important at the fetal stages of development and how they impact on renin secretion in the adult.

It is the issue of the interaction between β-adrenoceptors and their modulation of cAMP-mediated processes determining renin expression during nephrogenesis that is the focus of the paper by Wagner and co-workers (5). The approach taken by this group has been to use gene-deleted mice and to apply an adrenoceptor gene deletion. Moreover, the ability of the renin-containing cells to secrete renin in response to a combined challenge of a low-sodium diet and angiotensin-converting enzyme inhibition was comparable to that found in the wild-type mice. The findings of this manuscript reinforce their view arising from the earlier report (5) of cAMP being a key element necessary for the appropriate development and distribution of the renin-containing cells. What is particularly fascinating about the present study (5) is the inference that cAMP must be signaled via a number of sources during development, of which the β1/β2-adrenoceptors represent one significant input. It also highlights the importance of the renal innervation in determining the level of renin cell development and may be involved in the generation of pathophysiological states such as hypertensive disease in the adult.

DISCLOSURES

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REFERENCES