*Nature Reviews Nephrology* published online 12 August 2014; doi:10.1038/nrneph.2012.290-c1

# The *Drosophila* nephrocyte has a glomerular filtration system

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We read with interest the Review by Paola Romagnani and colleagues (Renal progenitors: an evolutionary conserved strategy for kidney regeneration. *Nat Rev Nephrol.* **9**, 137–146; 2013),[1] which discusses the importance of the evolutionarily conserved nephron structure in kidney regeneration. Nephrology students who read this paper will get the incorrect impression that insects have renal tubular structures but do not have a glomerular filtration system. This oversight is reasonable because the filtration system has only recently been discovered in *Drosophila melanogaster* and its existence has not yet been fully accepted in nephrology research.[2,3]

The nephron is the basic functional and structural unit of the kidney; the glomerulus controls ultrafiltration and the renal tubule is responsible for reabsorption and secretion.[4,5] The *Drosophila* excretory system is composed of Malpighian tubules and nephrocytes.[6] The Malpighian tubules are responsible for urine modification and secretion, and have been extensively studied in the past two decades.[7,8] However, the first evidence that insects have podocyte-like cells was obtained fairly recently. In 2009, Weavers *et al*. showed that the *Drosophila* nephrocyte has a highly specialized filtration structure—the nephrocyte diaphragm—with remarkable similarities to the slit diaphragm of mammalian glomerular podocytes.[2] In the *Drosophila* nephrocyte, foot processes created by infolding of the plasma membrane generate 30 nm slit pores that are comparable to those created by podocyte foot processes in the mammalian glomerulus. The nephrocyte diaphragms, together with a basement membrane that covers the entire nephrocyte, form a size-selective and charge-selective filtration barrier that filters haemolymph. In *Drosophila*, two different types of nephrocyte are present: pericardial nephrocytes flank the heart tube and garland nephrocytes wrap around the oesophagus. At the embryonic stage the garland nephrocytes are the only functional filtration cells; pericardial nephrocytes are the primary filtration cells at the larval and adult stages.[2,3]

Our research group has developed a reliable functional readout for *Drosophila* nephrocytes *in vivo* and established an RNA interference system to identify genes that are required for nephrocyte function.[9] Using this system, we performed large-scale screens and showed that *Drosophila* nephrocytes share remarkable functional, structural and molecular similarities with mammalian renal proximal tubule cells.[10] Both *Drosophila* nephrocytes and renal proximal tubule cells have high endocytosis activity, and nephrocytes use orthologues of mammalian cubilin and amnionless—the two major receptors for protein reabsorption in the renal proximal tubule—to take up proteins from haemolymph. Similar to renal proximal tubules, numerous endocytic-related organelles, such as endosomes, lysosomes and large vacuoles, are present in *Drosophila* nephrocytes. The lacuna structures of the nephrocytes resemble the brush border structures of renal proximal tubules, which provide a large membrane surface for protein reabsorption. Taken together, these findings suggest that the *Drosophila* nephrocyte not only has glomerular filtration function but is able to reabsorb protein in a similar way to the renal proximal tubule.

The availability of powerful genetic tools and the tremendous genetic resources of *Drosophila* make it an ideal model for large-scale screens to identify and study genes that are involved in normal physiological functions or diseases of various organs. Our understanding of the genetic network required for renal function has been hindered by the relative intractability of characteristics of mammalian nephron structure and function *in vivo*. With the emergence of *Drosophila* nephrocytes as an ideal model system to study renal biology, we expect that novel genes will be identified with unprecedented speed and studied in great detail, facilitating our understanding of genetic kidney diseases.

To date, whether mammalian glomerular podocytes and renal proximal tubular cells are derived from the same progenitor cells during embryonic kidney development remains unknown.[1] The ability of a murine kidney-derived stem cell line to differentiate into either podocytes or renal proximal tubule cells has been reported, suggesting that these cells are developmentally related.[11] The fact that the *Drosophila* nephrocyte shares remarkable similarities with both mammalian glomerular podocytes and renal proximal tubules suggests that these cell types have the same evolutionary origin. Whether nephrocyte-like progenitor cells exist in *Drosophila*, and whether such cells could perform a role in the regeneration of nephrocytes after injury, is not clear.[12,13] In the future, it would be very interesting to examine whether a cellular regeneration or nephron neogenesis process occurs in *Drosophila* nephrocytes after injury, and explore whether nephrocyte-like progenitor cells exist in this organism.

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**Acknowledgements**
X.C.'s work is supported by the National Basic Research Program of China (973 Program, No. 2013CB530800).

**Competing interests**
The authors declare no competing interests.

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