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The physiological roles of urea transporters

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Urea is the main breakdown product of mammalian protein catabolism and was historically viewed simply as a waste product excreted in the urine. The discovery of facilitative urea transporters has revealed that urea actually plays a key role in a number of important physiological processes – including osmoregulation and nutrition. Urea transporters have a long evolutionary history and facilitate bi-directional urea transport across membranes, down a concentration gradient and in a phloretin-sensitive manner. In mammals, they can be derived from two distinct genes (UT-A and UT-B) and a number of different isoforms are present in various tissues. Research utilising mouse knockout models has shown that renal UT-A transporters are crucial in producing concentrated urine (Fenton *et al.* 2004). The expression, cellular localization and function of these UT-A proteins is controlled by the anti-diuretic hormone vasopressin (Stewart *et al.* 2009). In contrast to the kidney, the urea transporters expressed within the mammalian gastrointestinal tract are predominantly UT-B proteins. Evidence is now emerging that these transporters function to allow urea from the blood to enter into the gastrointestinal tract as part of the urea nitrogen salvaging process, particularly in ruminants such as cattle (Stewart *et al.* 2005). Recent work on dietary regulation of UT-B transporter expression (Stewart *et al.* 2008) and function (Tickle *et al.* 2009) suggest a key role in regulating the symbiotic relationship between mammals and their gut bacteria and hence in mammalian nitrogen balance. Finally, a role for UT-B within the human colon is also now being investigated and these transporters may play a crucial role in our own health and well-being. It is therefore apparent that urea can no longer be viewed as just another waste product.

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