

## **Diabetes and ACE2; light on the dark side of the renin angiotensin system**

*M.C. Thomas, Baker IDI Heart and Diabetes Institute, PO Box 6492, St Kilda Rd Central, Melbourne, VIC 8008, Australia. (Introduced by Stefan Bröer)*

Activation of the renin-angiotensin system (RAS) plays a key role in the development and progression of diabetic complications. Historically, these actions have been linked to reduced signalling through angiotensin II (Ang II)-dependent pathways, as drugs that inhibit Angiotensin Converting Enzyme (ACE) or block the activation of the type 1 angiotensin (AT1) receptor are effective in attenuating the impact of diabetes. However, some the systemic effects of RAS blockade may be mediated by Ang 1–7, a potent vasodilator, with actions that antagonize or compensate those of Ang II. In the kidney heart and vasculature, Ang 1–7 is largely derived from the degradation of Ang II by the zinc-dependent carboxypeptidase, ACE2. Consequently, ACE2 KO mice have increased tissue levels of Ang II and reduced levels of Ang 1-7. ACE2 expression is also significantly modified in both experimental and clinical diabetes, potentially contributing to local activation of the RAS as well as some of the haemodynamic manifestations of diabetes, including hyperfiltration and albuminuria. In addition, ACE2 appears to be important in the development and progression of diabetes associated cardiac injury. These studies point to ACE2 as a complex, and site-specific modulator of diabetic complications, and shed light on the usually dark side of the RAS.