Atherosclerosis – Exposing "the Elephant in the Room"

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Statins are the most commonly prescribed class of drug worldwide and therapy is highly effective in reducing low-density lipoprotein cholesterol levels and cardiovascular events. However, there is large variability in clinical response to statin treatment. Recent research provides evidence that genetic variation contributes to this variable response to statin treatment.

The important role of drug transporters in drug absorption and disposition has been well-documented. Statins are subjected to active transport of membrane proteins of the superfamilies ATP-binding cassette and solute carrier, and there is limited understanding of the mechanisms by which differences in transporter expression and activity contribute to variability of pharmacokinetics (PKs)/pharmacodynamics (PDs) of statins. *In vivo* and *in vitro* studies have shown that efflux and uptake transporters modulate the PKs/PDs of statins. Until now, organic anion transporting polypeptides (OATP) 1B1 variants have been considered major factors in limiting the uptake of statins and increasing statin exposure, and, consequently, increasing risk of myopathy. Further studies in pharmacogenetics and *in vitro* models to assess statin disposition and toxicity are required to understand the contribution of other transporters, such as multidrug resistance-associated protein (MRP)1, MRP2, breast cancer resistance protein, OATP2B1, OAT1B3 and OATP1A2, in inter-individual variability to efficacy and safety of statins.