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PPARs and their role in diabetic dyslipidaemia

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Type 2 diabetes (T2D) is often associated with metabolic syndrome that is characterised by a peculiar dyslipidaemia comprising of elevated serum triglyceride levels in association with low HDL-Cholesterol levels (HDL-C). This disordered metabolic state leads to a build up of fatty acids in the liver and skeletal muscles, making these tissues resistant to the effects of insulin. The initial response of the body to insulin resistance is to increase insulin production that is effected by the beta cells of pancreas. Eventually, the beta cells are overwhelmed and can no longer produce enough insulin to maintain normoglycaemia, leading to the development of T2D.

Peroxisome proliferator activated receptors (PPARs) are nuclear receptors that act as transcription regulators of various genes involved in energy metabolism. PPAR α and γ are the most studied and their agonists have been in use to treat both, T2D and dyslipidaemia. These agents have shown positive effects on multiple surrogate markers of cardiovascular disease. Furthermore, more recently, these agents have also demonstrated beneficial effects on hard clinical end points such as retinopathy as in the FIELD study.

Although these metabolic benefits of PPAR agonists are mainly mediated through their genomic effects, our work has shown that some effects are potentially mediated through non-genomic effects as well. This is particularly well demonstrated in the enucleate platelet. We not only demonstrated the prescence of PPAR receptors in human platelets, but also that activating them has the potential to alter platelet aggregation and activation.

Biography

Dr Manish Khanolkar has completed his specialist training in Diabetes and Endocrinology from the UK in 2009. He was awarded MD from Cardiff University for his work on 'Effects of insulin sensitizing therapy on platelet, vascular function and blood pressure in type 2 diabetes'. He is currently employed as a Consultant Physician and Diabetologist at Auckland Diabetes Centre, NZ.

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