**Molecular pathogenesis and novel therapeutic strategies of Fabry disease, a lysosomal storage disease**

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Fabry disease (FD) is a lysosomal storage disorder caused by deficiency of alpha-galactosidase A (α-gal A), which results in the deposition of globotriaosylceramide (Gb3) in the vascular endothelium. Globotriaosylsphingosine (lyso-Gb3), a deacylated Gb3, is also increased in the plasma of patients with Fabry disease. Patients develop painful neuropathy and vascular occlusions that progressively lead to cardiovascular, cerebrovascular, and renal dysfunction and early death. Renal fibrosis is a key feature of advanced Fabry disease patients. Enzyme replacement therapy (ERT) directed at the underlying metabolic defect became available in 2001-2003. Knowledge of the pathophysiology and clinical features of FD is vital for assessing the rationale and evidence of efficacy of therapies for FD and their limitations. Whilst ERT improves many of the symptoms of FD, its effect on the natural history of the disorder has yet to be fully demonstrated. Plasma lyso-Gb3 levels in FD patients might be more reliable to monitoring disease progress and ERT effectiveness rather than plasm Gb3 levels. Improved understanding of the appropriate use of adjunctive therapies and the development of new treatment strategies, including pharmacologic chaperone therapy and gene therapy, coupled with long term clinical outcome data on the effects of ERT are all key components of optimising treatment for FD. Adeno-associated virus vector and lentivirus vector mediated gene therapy have been investigated and could be strong successful options for the treatment of FD.