Control of glycogen metabolism.

Diabetes is a major cause of blindness and renal disease, and is known to significantly increase the risk of cardiovascular disease, leading to heart attack, stroke and amputation of the lower extremity(ies). Almost 90% of all diabetics are type 2 (T2D) and cannot be treated with exogenous insulin. T2D (non insulin-dependent diabetes mellitus) afflicts 23 million people in Europe and will soon be one of the world's commonest diseases. The global incidence of T2D is projected to afflict more than 300 million people worldwide by the year 2005, and many of those affected will be young adults. The costs of T2D medication exceed 4% of the annual health care budget in EU countries. Current preventative and therapeutic strategies are inadequate, and there is a need for the research community (both academic and industrial) to develop novel healthcare interventions to address this substantial biomedical challenge.

T2D is characterized by excessive glucose production from the liver. A molecular approach, aimed at reducing excessive glucose production from the liver involves the identification and optimization of novel, potent and selective inhibitors of human liver glycogen phosphorylase (hGP), a rate controlling enzyme of the glycogenolytic pathway. In fact, inhibitors of GP have been proposed as a therapeutic strategy for improving glycaemic control in T2D mellitus and various studies have shown the efficacy of such compounds at lowering blood glucose or inhibiting liver glycogenolysis in vitro or in vivo. In our group the design of hGP inhibitors is the focus of much effort to find new compounds to treat T2D.

(Collaborations: Dr. S.E. Zographos, Inst. of Organic & Pharmaceutical Chemistry, National Hellenic Research Foundation, Assoc. Prof. W.A. Loughlin, Dept of Biological Sciences, Griffith University, Brisbane, QLD, Australia, Assoc. Prof. D. Komiotis, Dept. Biochemistry and Biotechnology, University of Thessaly).