The vitamin E binding protein Afamin is associated with the metabolic syndrome and infertility

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The metabolic syndrome is characterised by metabolic risk factors including abdominal obesity, atherogenic dyslipidemia, elevated blood pressure or insulin resistance. Patients with the metabolic syndrome are at increased risk of coronary heart disease, other atherosclerotic conditions and type 2 diabetes. The pathogenesis of the metabolic syndrome is multifactorial and polygenic; a long list of lifestyle and genetic factors has been attributed to ultimately lead to the metabolic disorders described above. Several heritability studies indicated a major
role of genetic susceptibility to the metabolic sndrome.

We have identified by comparative proteomics strategy the human vitamin E binding protein afamin (a member of the albumin gene family) that is associated with several key parameters of the metabolic syndrome. By measuring its plasma concentration in the prospective population-based Bruneck study (n=826) we found significant associations with waist-to-hip ratio, body mass index, obesity, systolic and diastolic blood pressure, diabetes, and plasma concentrations of LDL- and HDL-cholesterol, triglycerides, free fatty acids, glucose and Hba1c. In addition, afamin concentrations were also positively correlated with increasing numbers of these parameters in a 10 years follow-up prospective observation.

These results (in particular those from the prospective observation) indicate not only an association between afamin and the metabolic syndrome but suggest causality and a high predictive potential of afamin for developing this modern epidemic disease.

In contrast, genetically modified mice in which the afamin gene was deleted were infertile already at the chimeric (heterozygous) level. Male animals exhibited a grossly altered testis histology showing severely degenerated testis tissue and almost absent spermiogenesis. Application of exogenous recombinant mouse afamin (via implanted diffusion pump) could completely restore testes tissue histology and fertility.

In summary, afamin seems to play major roles in the development of cardiovascular and infertility disorders.