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## Elevated serum xanthine oxidase activity is associated with the development of type 2 diabetes: A prospective cohort study

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We aimed to evaluate whether xanthine oxidase (XO), a key enzyme in uric acid (UA) metabolism and a major source of reactive oxygen species, plays a causal and important role in the development of type 2 diabetes mellitus (T2DM) in a large prospective cohort study. A total of 4,412 diabetes-free adults (2,071 women and 2,341 men) aged 30-65 years at baseline in 2008 were involved. Participants were followed for incident change of glucose metabolism during an average of 4.7 years. At baseline serum XO and UA, serum lipids and glucose homeostasis indexes including fasting blood glucose (FBG), 2-h blood glucose (PBG), glycosylated hemoglobin A1c (HbA1c) and fasting insulin were tested for analysis. During an average follow-up period of 4.7 years, 249 women and 360 men developed new-onset T2DM. Serum XO activity was positively associated with UA concentration (all P-values 0.001). When XO activity and UA concentration were considered in the same model of the sex-specific analysis, only XO activity was significantly associated with the incidence of T2DM, with the hazard ratios (95% confidence intervals) from the bottom to the top quartile of XO activity being 1.00, 1.67 (1.00-2.79), 1.86 (1.11-3.13) and 2.36 (1.43-3.90) in women and 1.00, 1.01 (0.68-1.52), 1.41 (0.98-2.03), 1.90 (1.30-2.78) in men. In summary, elevated serum XO activity, but not UA concentration, was associated with an increased risk of developing T2DM in women and men with mutual adjustment for XO and UA. Further studies are needed to examine the underlying mechanisms.