

Role of arginase-II in kidney aging and renal effects by L-arginine supplementation

Diogo Bernardo Ladeiras

With advancing age kidney undergoes severe morphological changes that might affect renal function, and ultimately predispose the elderly to chronic kidney disease and renal failure. Understanding the molecular aging mechanisms will provide new insights into the development of novel therapies for the promotion of a healthier kidney. The type-II L-arginine:ureahydrolase, arginase-II (Arg-II), has been shown to play a role in the acceleration of aging. Arg-II is highly expressed in the kidney, but its physiological functions are still uncertain. In the first part, we aimed to investigate the role of Arg-II in age-associated renal structural and functional changes.

Young (8 months) and old (24 months) male and female wild type (WT) C57BL/6 and Arg-II knockout mice (Arg-II^{-/-}) were investigated. We found a clear gender difference with higher Arg-II protein in kidney of female mice, an increase in Arg-II levels with age, and a partial prevention of the age-associated induction of renal inflammation and fibrosis in female Arg-II^{-/-} mice. Our study reveals that Arg-II plays a role in kidney aging process, particularly in female mice. Arg-II represents a promising therapeutic target for the treatment of age-associated kidney diseases.

L-arginine, the substrate of Arg-II enzyme, has been used as a complementary supplement for health improvement. However, its effects remain controversial, as clinical studies reported both beneficial as well as harmful effects from L-arginine supplementation. Therefore, the second part of this work aims to clarify the long-term impact of dietary L-arginine in the kidney.

Young and old C57BL/6J mice of both genders were fed during 16 weeks with normal chow or chow supplemented with L-arginine (1,82% additional to 0.64% in NC). Results showed that prolonged L-arginine did not alter kidney function, inflammation nor fibrosis, however it induced mortality in aged supplemented mice. Therefore, L-arginine supplements should be used with caution.

Jury:

Prof. Zhihong Yang (thesis supervisor)

Prof. Dr. Eric Féraillé (external co-examiner)

PD. Dr. Xiu-Fen Ming (internal co-examiner)

Prof. Dr. David Hoogewijs (internal co-examiner)

Prof. Eric Rouiller (president of the jury)