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### **Increased susceptibility of aging kidney to toxic injury**

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#### **Objectives:**

Elderly people are prone to progress to chronic kidney disease following acute kidney injury than young people. With this notion, we conducted an experiment to evaluate how aging kidney respond to injury in mouse model of adenine-induced chronic kidney disease.

**Methods:** Mice used for experimentation were either 2-month-old or 20 to 22-month-old male C57BL/6 mice. They were fed with either adenine-free normal chow or 0.2% adenine-enriched diet for 4 weeks and sacrificed. Kidneys were harvested and flash frozen in liquid nitrogen for mRNA and protein analysis or fixed in 4% paraformaldehyde for paraffin section. In addition, we performed RNA-Seq on kidney samples from 2-month (n=3), 12-month (n=3), 24-month (n=3)-old male C57BL/6 and 2-month-old C57BL/6 fed with normal chow or adenine-enriched diet.

**Results:** The kidney in old mice showed more extensive tubular injury and interstitial fibrosis than one in young mice with more increased level of BUN and creatinine. Old mice expressed more senescence markers (p16, p21, and p53) than young mice at baseline. In addition, perivascular immune cell clusterings were spontaneously developed in old mice without overt insult and their areas were boosted up after 4 weeks of adenine-enriched diet, which were considered as tertiary lymphoid organ. RNAseq analysis, which compared between control young mice and adenine-fed young mice and between young mice and old mice, revealed that inflammaging is a key feature that explains increased susceptibility of aging kidney to injury.

#### **Conclusions:**

Our results suggest that an inflammation and cellular senescence predispose aging kidney to tubular injury and interstitial fibrosis following insult, progressing to chronic kidney disease.