

Diet influences the development of nephropathy in a mouse model of glycogen storage disease type Ia

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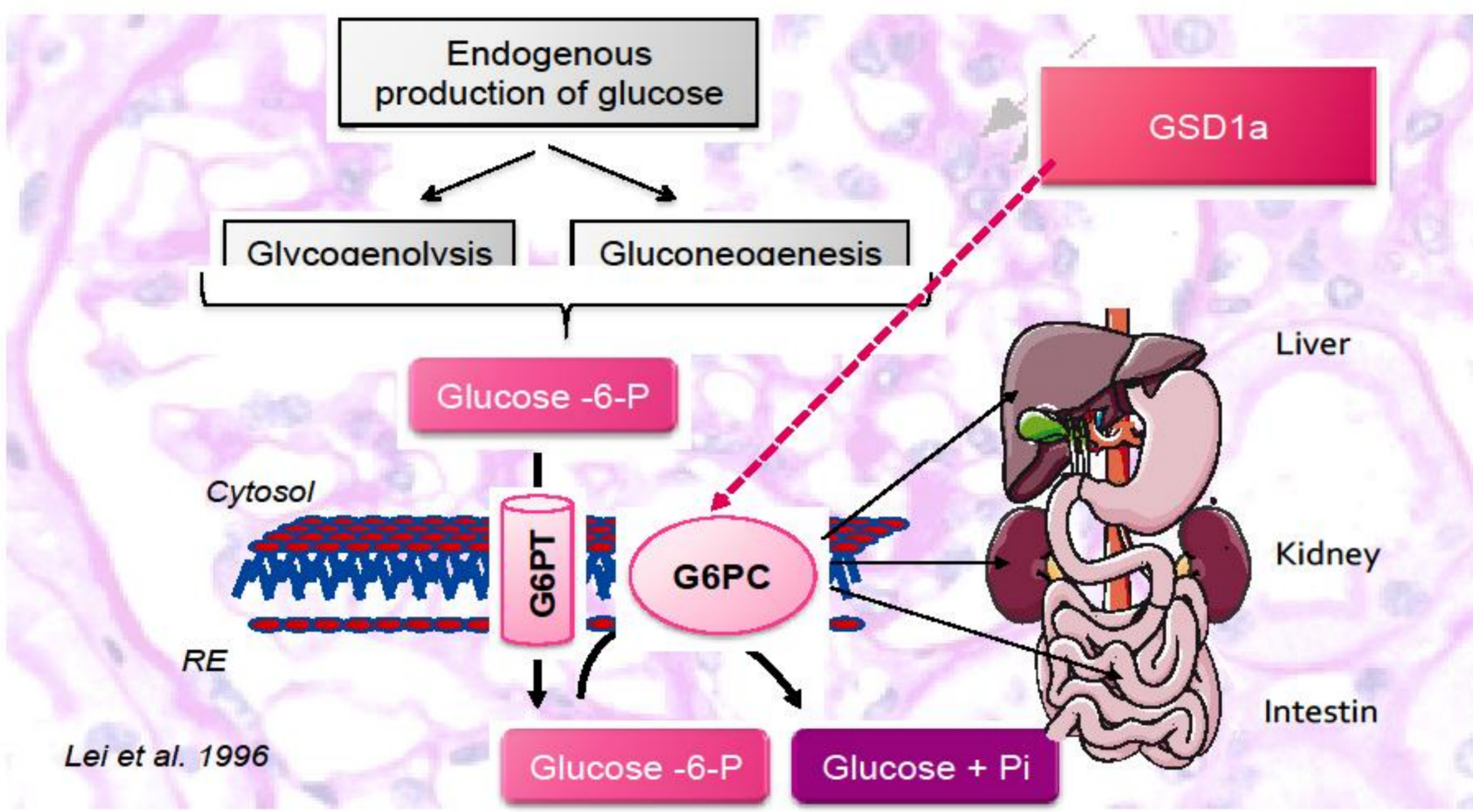
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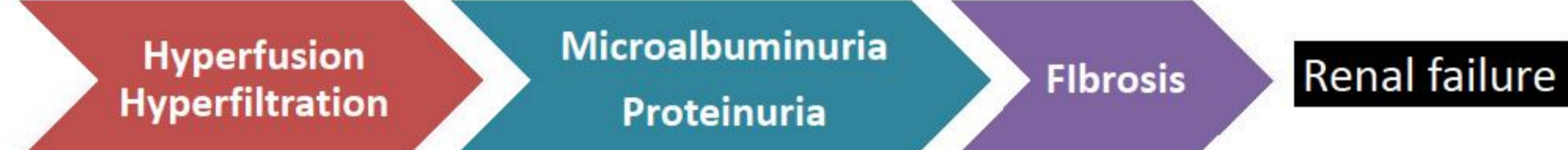
INTRODUCTION

Glycogen storage disease type Ia (GSD1a)

- Glucose-6 phosphatase catalytic subunit (G6PC) deficiency
- Absence of endogenous glucose production
- Severe hypoglycemia, hypertriglyceridemia, hypercholesterolemia, hyperuricemia as well as liver, kidney & intestine pathologies



In the GSD1a kidneys: Nephromegaly due to glycogen accumulation



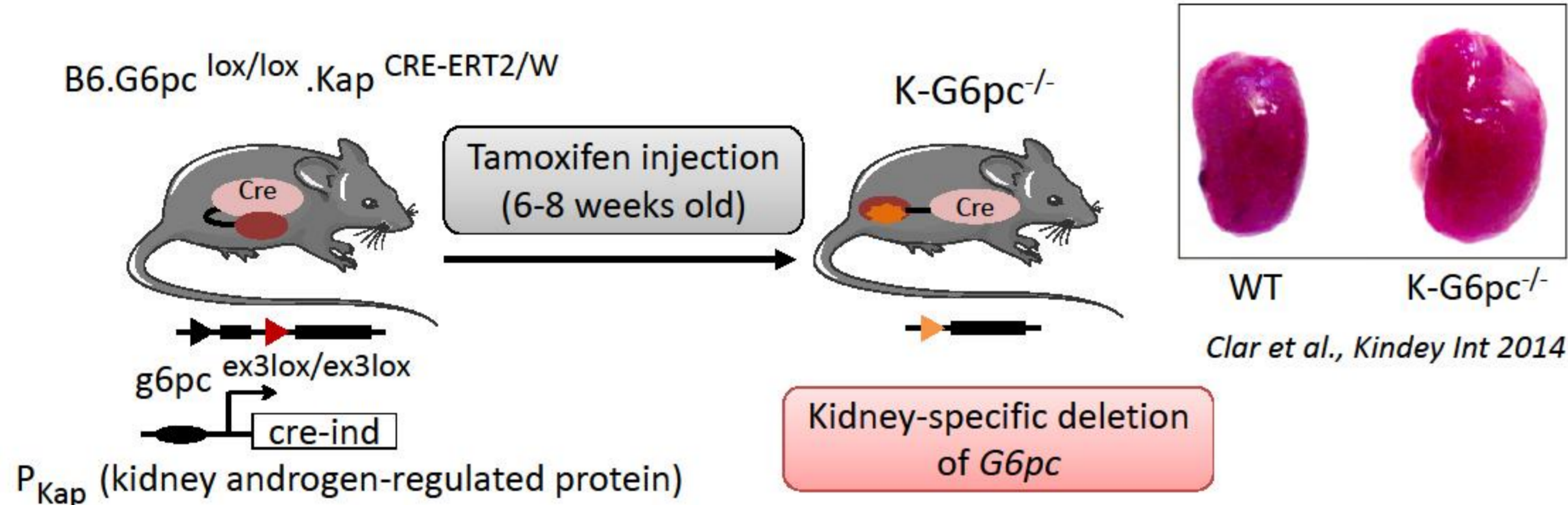
Treatment:

- Nutritional care to avoid hypoglycemia and glycogen accumulation
- Frequent slow-release carbohydrate meals (uncooked starch), continuous nocturnal nasogastric drip-feeding
- Restricted or prohibited intake of sweets, fruits (containing fructose) and dairy products (containing galactose)

QUESTION

Does junk food accelerate GSD1a nephropathy?

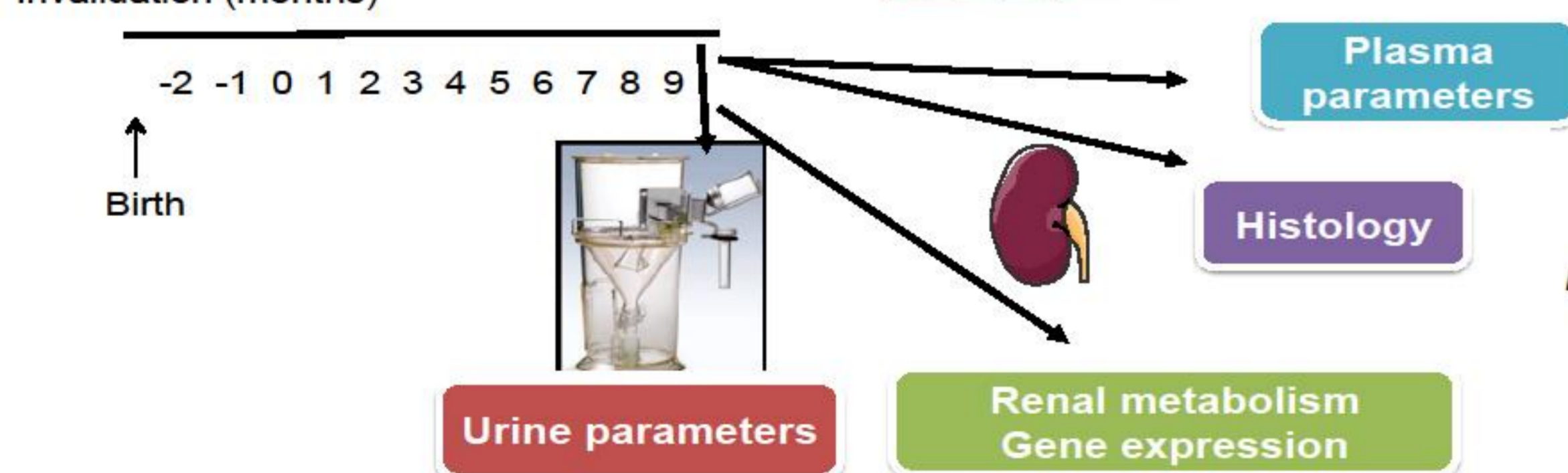
METHODS



Standard diet: (3,1% lipids, 60% glucides (starch), 20% proteins)

High fat/High sucrose diet (36,1% lipids, 35% glucides (50% sucrose), 20% proteins)

Standard K.G6PC^{-/-} HF/HS K.G6PC^{-/-}

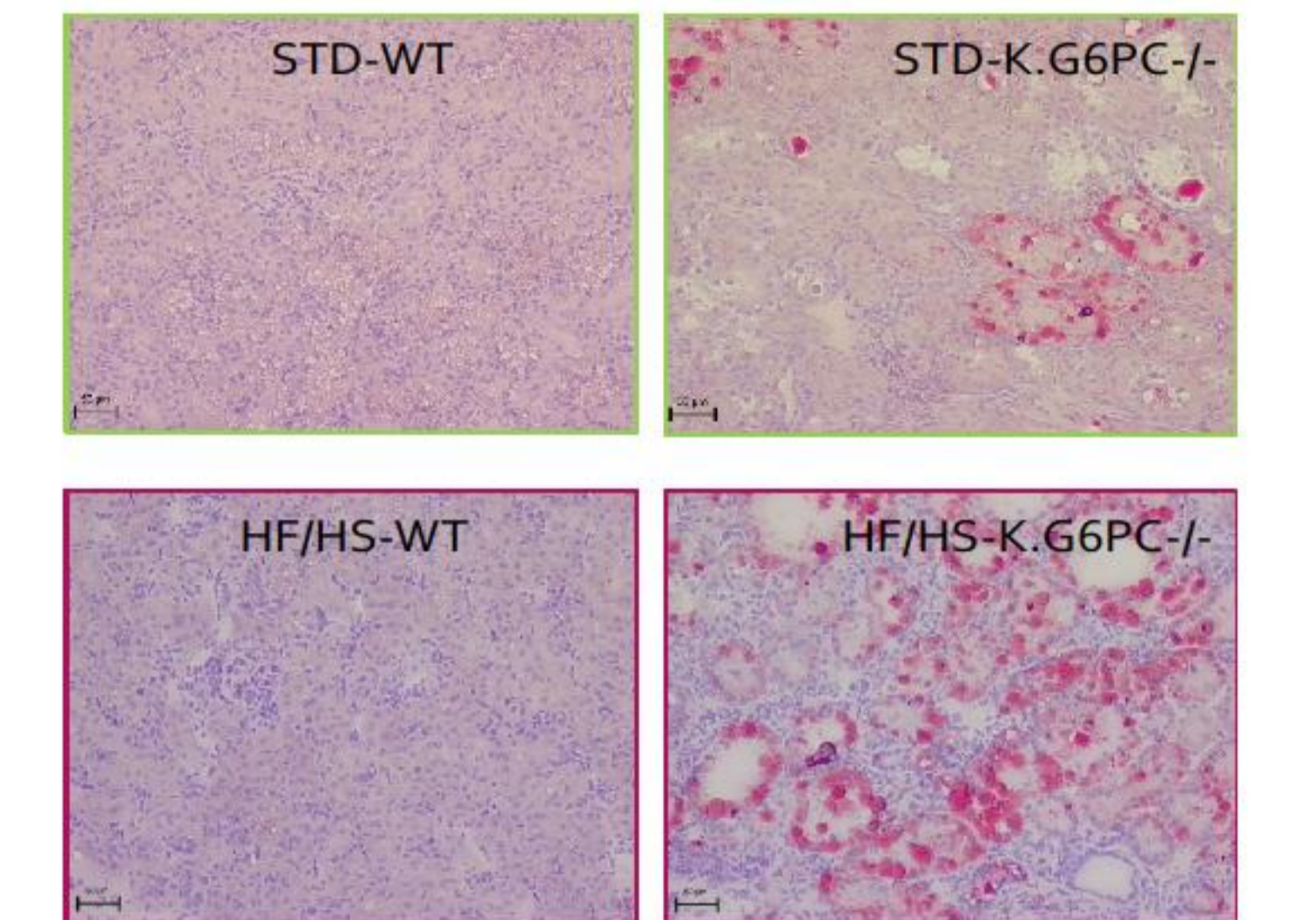
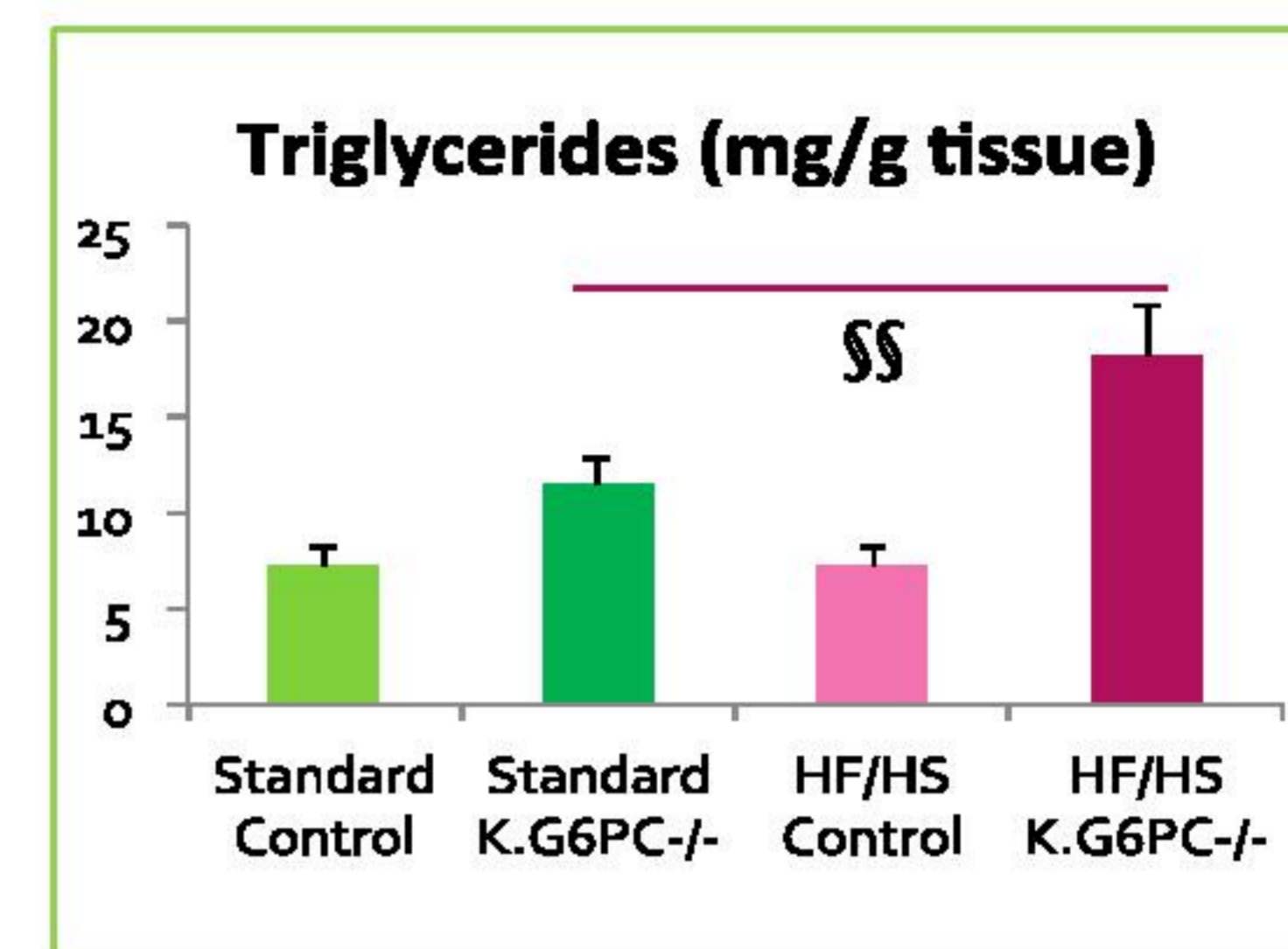
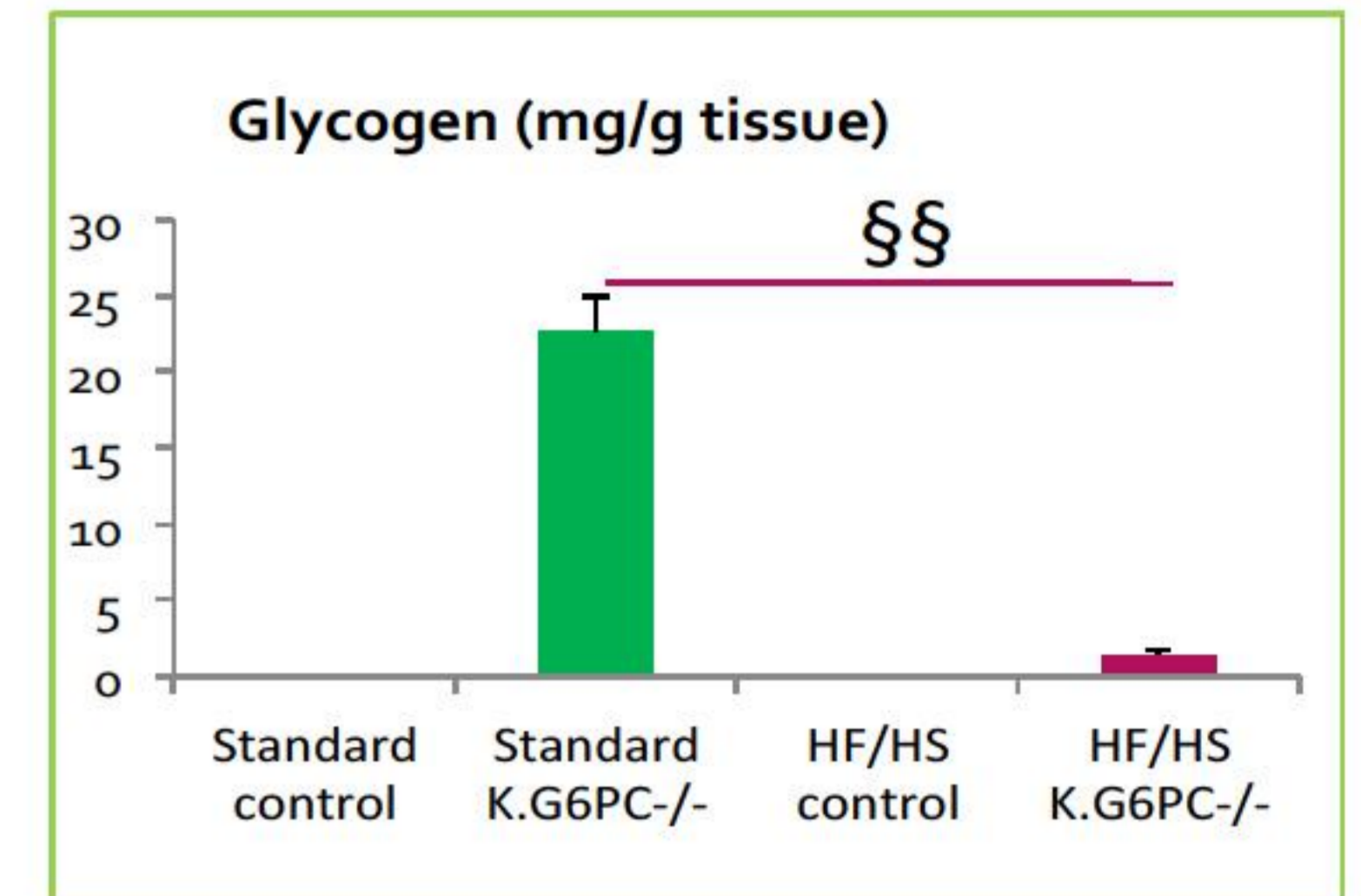
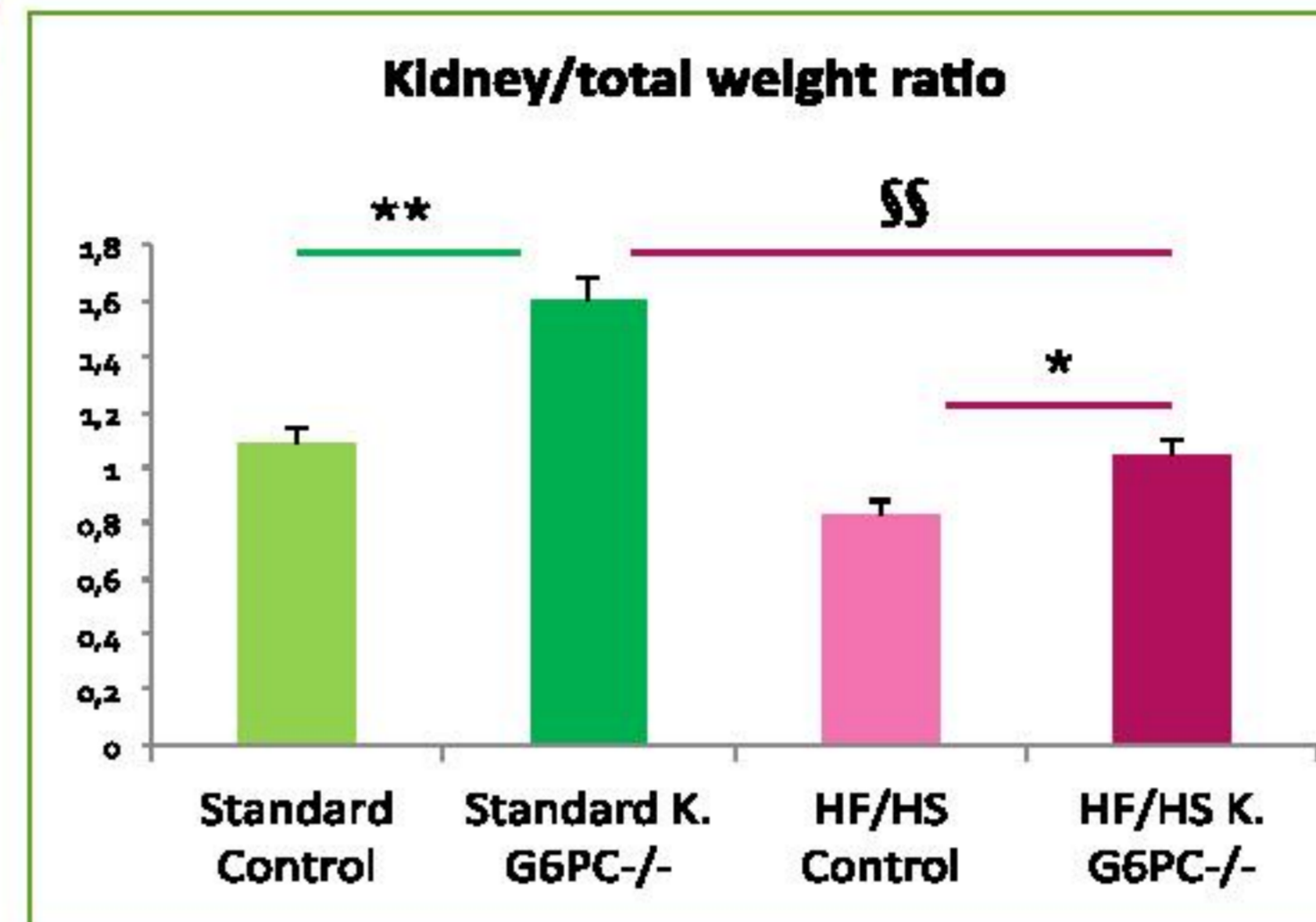


Statistical analyses: -T-test; (*p<0.05; **p<0.01; ***p<0.001)

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RESULTS

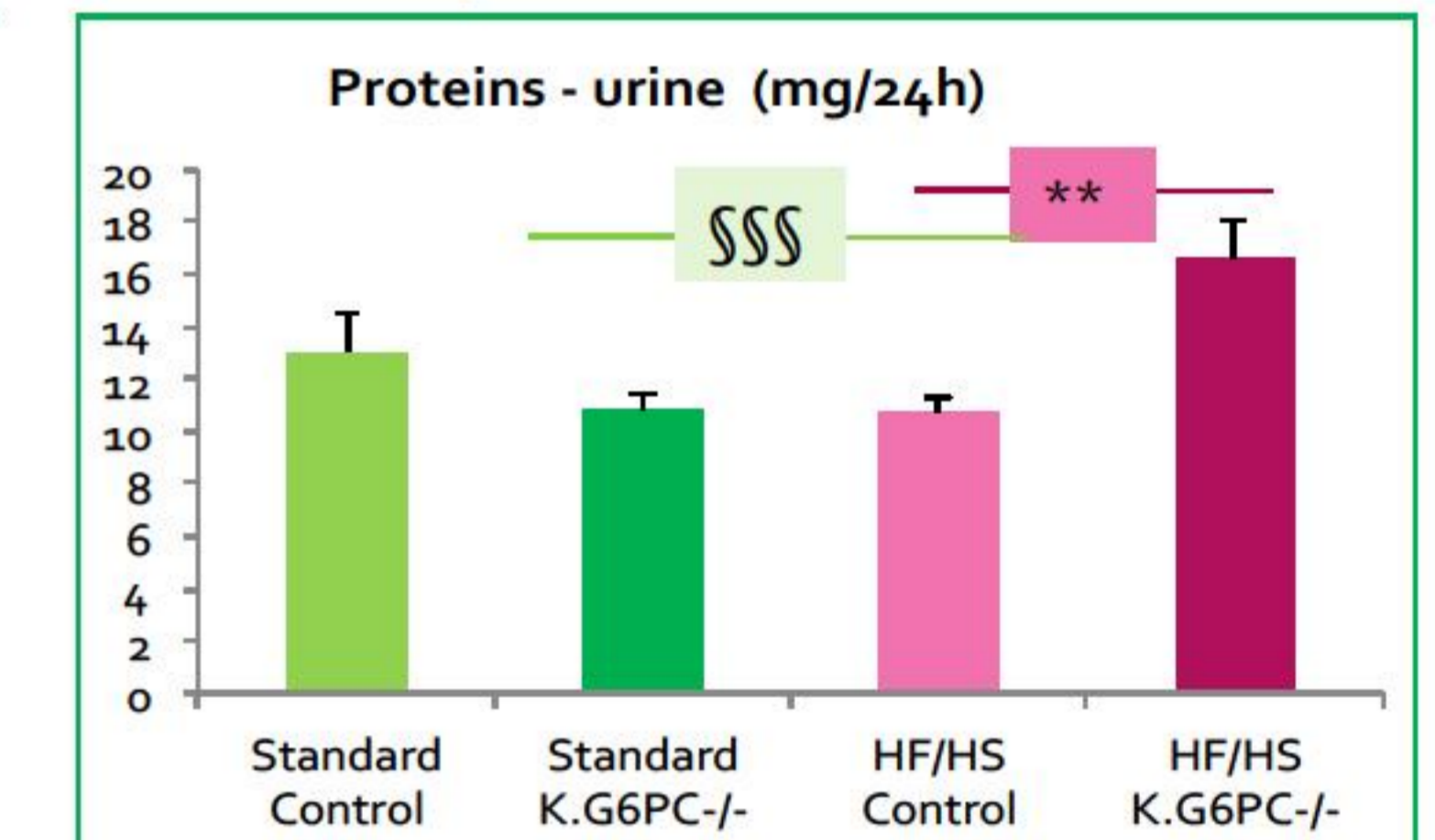
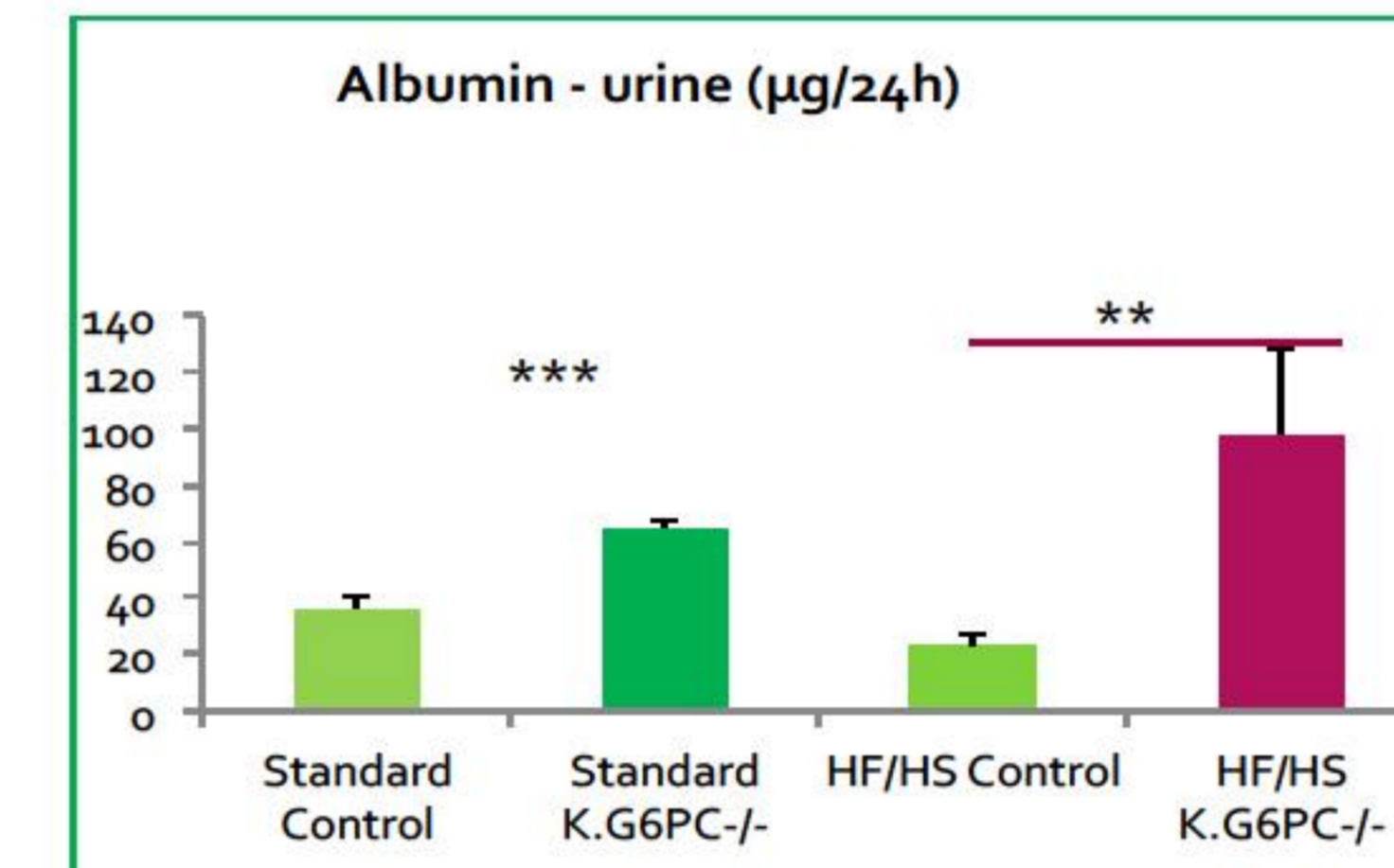
Effect of nutrition on nephromegaly in K-G6pc^{-/-} mice



Sudan Red staining

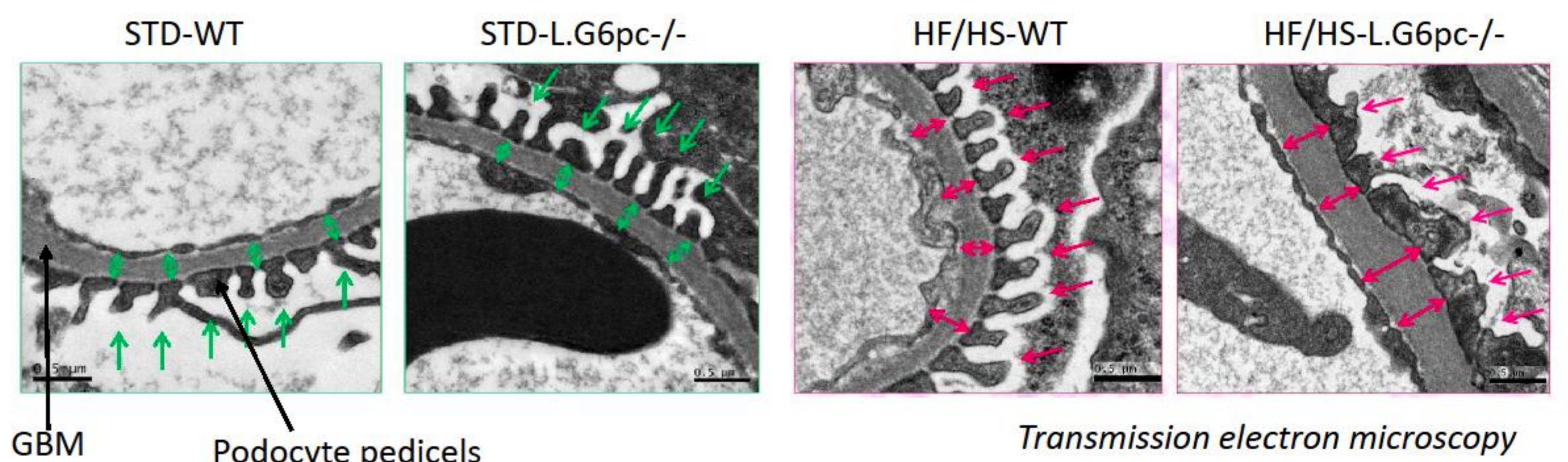
- Nephromegaly was lower in K.G6pc^{-/-} mice fed a HF/HS diet compared to STD diet
- Renal lipid deposits in K.G6pc^{-/-} mice due to *de novo* lipogenesis
- STD diet: strong glycogen accumulation in L.G6pc^{-/-} kidneys
- HF/HS diet: light glycogen accumulation and strong accumulation of triglycerides in L.G6pc^{-/-} kidneys

Alterations of blood filtration in K-G6pc^{-/-} mice



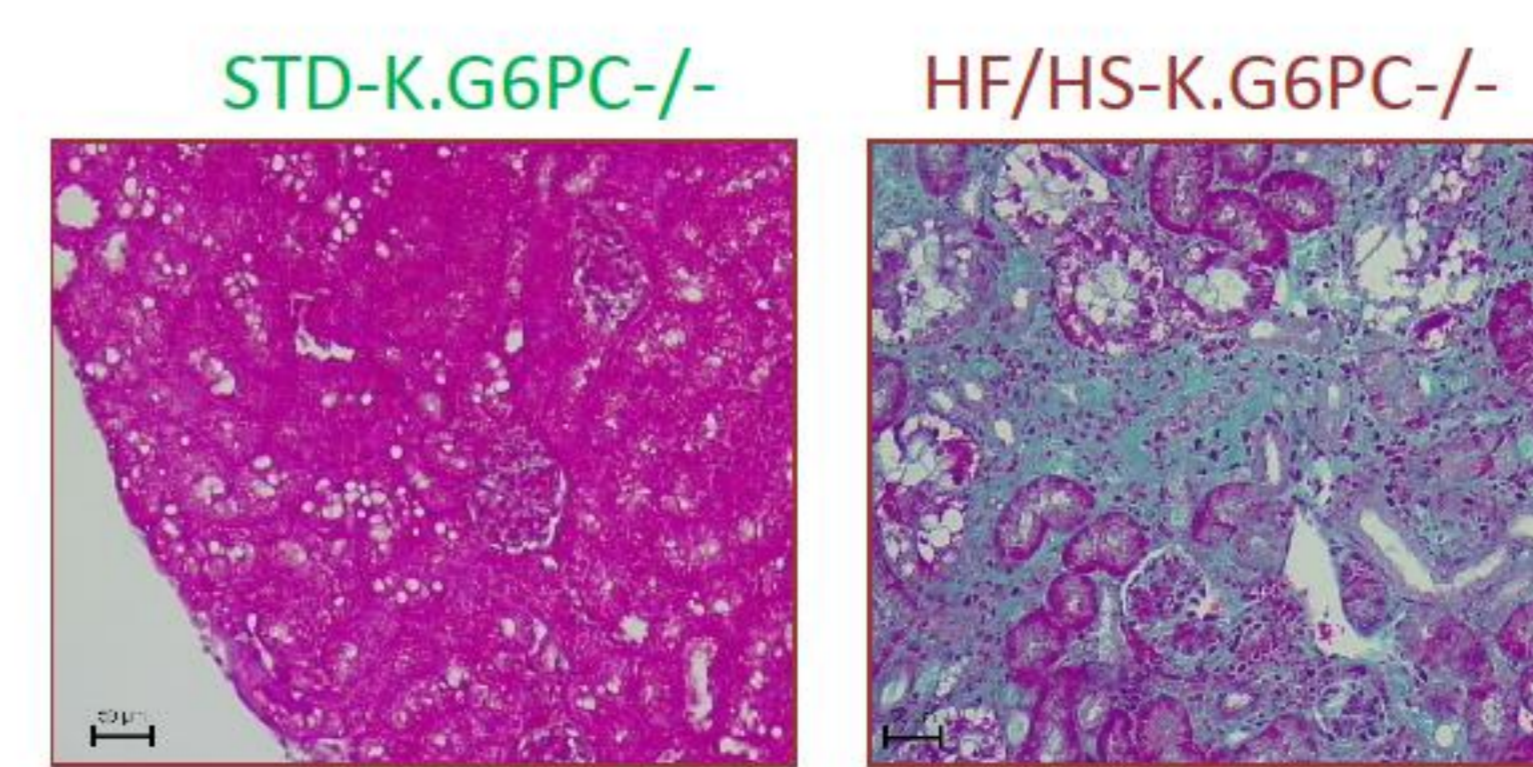
- In addition to microalbuminuria, proteinuria was also observed in HF/HS K.G6pc^{-/-} mice

Glomerular alterations in K-G6pc^{-/-} mice fed a HF/HS diet



- The podocyte pedicels were deformed and the glomerular basement membrane (GBM) was thicker in K.G6pc^{-/-} mice fed a HF/HS diet

Kidney fibrosis in K-G6pc^{-/-} mice fed a HF/HS diet



Masson's trichrome staining

- Development of fibrosis in K.G6pc^{-/-} mice fed a HF/HS diet

CONCLUSIONS

- High fat/high sucrose diet highly accelerates GSD1a nephropathy
- Avoid sucrose and fat consumption in excess to prevent nephropathy in patients with GSD1a

Management of patients with GSD1a



Pediatrician → ?

