

## Effects of a Ketogenic Diet on Murine Models of Cystinosis

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Ketogenic diet, known for its high-fat, low-carbohydrate composition, has been studied for its potential therapeutic effects in several diseases. Originally developed to treat refractory epilepsy, it has since been studied for its effects on conditions such as obesity, type 2 diabetes, many neurological disorders, and more recently, ketogenic interventions have been explored in animal models of kidney diseases.

In our study in cystinotic mice and rats, published in 2024, this diet was shown to significantly protect kidney function. It almost completely prevented the symptoms of Fanconi syndrome, such as low molecular weight proteinuria, glycosuria, and polyuria, helping the kidneys work better. Mice on a ketogenic diet did not have the elevated blood urea nitrogen (BUN) levels seen in cystinotic mice on a standard diet. Their kidneys appeared similar to those of wild-type animals and had significantly less inflammation and scarring. Even when the diet was introduced after the onset of proximal tubular dysfunction, beneficial effects were observed. Similar, but less pronounced, benefits were observed in *Ctns*<sup>-/-</sup> rats.

In addition, we observed that this intervention was also beneficial for muscles. Specifically, we observed that ketogenic diet increased the levels of important proteins needed for muscle repair and regeneration.

Although a dietary regimen based on the ketogenic diet is probably not suitable for lifelong therapy in humans, these results suggest that targeted nutritional interventions may be helpful in the management of cystinosis. It will be important to understand which components of this regimen mediate the beneficial effects we observed in mice and rats. These studies are underway.