Muscle Wasting in Children with Cystinosis

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Muscle wasting is prevalent in children with cystinosis and is associated with significant morbidity and mortality. It is associated with the syndrome of cachexia, which is defined by significant body weight loss (or lack of weight gain in children), with fat and muscle mass reduction. Anorexia (reduced appetite) and increased metabolic rate result in energy deficit which in turn causes the changes in body composition.

We have used a mice model of cystinosis to study cachexia and muscle wasting. We found that these abnormalities happen early, before the onset of chronic kidney disease and that vitamin D deficiency and inflammation are important factors. Correction of vitamin D deficiency is obviously important but suppressing inflammation holds the key to preventing and correcting muscle wasting and cachexia associated with cystinosis. We have shown that activation of the NLRP3 inflammasome is central to the inflammation associated with cystinosis. By inhibiting the overactivity of this pathway, we are able to suppress inflammation and reverse muscle wasting. There are several therapies targeting the NLRP3 pathway, some of which are already approved by the FDA, and others which are now undergoing clinical trials for safety and efficacy.

In conclusion several novel treatments could be available to children with cystinosis, in the very near future, to combat the devasting complications of cachexia and muscle wasting.