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## Long-Term Treatment of Tamoxifen and Raloxifene Alleviates Dystrophic Phenotype and Enhances Muscle Functions of FKRP Dystroglycanopathy.

Wu B<sup>1</sup>, Shah SN<sup>2</sup>, Lu P<sup>2</sup>, Bollinger LE<sup>2</sup>, Blaeser A<sup>2</sup>, Sparks S<sup>3</sup>, Harper AD<sup>3</sup>, Lu QL<sup>4</sup>.

### Author information

### Abstract

The third most common form of limb-girdle muscular dystrophies is caused by mutations of the Fukutin-related protein (FKRP) gene, with no effective therapy available. Selective estrogen receptor modulators, tamoxifen and raloxifene, have been widely used for human conditions for their anti-inflammatory, antifibrosis, prevention of bone loss, and muscle building effects (essential features for muscular dystrophy therapies). We evaluated therapeutic values of tamoxifen and raloxifene in FKRP448L mutant mouse with severe dystrophic phenotype. The mice were treated with the drugs for 1 year through daily gavage. We demonstrate that tamoxifen and raloxifene significantly ameliorated the disease progression. The improvement includes increase in grip force production, extended running time and distance in treadmill test, and enhancement in cardiac and respiratory functions. Significant reduction in muscle pathology includes diminished fibrosis and fiber degeneration. Tamoxifen and raloxifene also significantly mitigated bone loss. Tamoxifen, but not raloxifene, caused severe adverse effects on male reproductive organs. The results demonstrate that tamoxifen and raloxifene hold significant potential for treating FKRP-related muscular dystrophy and probably other muscular dystrophies. Sex-related differential effects of the drugs call for a careful consideration for the drug and dosage selection in male and female patient populations.

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