Development of cure for sarcopenia focusing on glycolytic enzymes

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In Japan, which has been a super-aged society, to maintain the function of skeletal muscle is regarded as a primary concern that is directly related to the extension of healthy life expectancy. Therefore, the discovery of new genes involved in skeletal muscle regulation and the elucidation of the molecular mechanisms of muscle regeneration and degradation are important research subjects based on contemporary social needs.

In this study, we focus on pyruvate kinase M (PKM), a glycolytic enzyme. PKM has two splicing isoforms, PKM1 and PKM2, generated by alternative splicing, and PKM1 predominantly is expressed in skeletal muscle. Thus, we hypothesized that regulation of PKM1/PKM2 balance through modulating splicing could be one of the essential mechanisms in skeletal muscle, and then carried out a screening for identification of compounds inducing M1-type splicing with our original splicing reporter. Consequently, we obtained several approved drugs as candidates of PKM1 inducer.