Acteoside-induced PKM2 secretion from skeletal muscle is associated with functional recovery of chronic spinal cord injury

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Spinal cord injury (SCI) causes serious locomotor dysfunction due to the disruption of descending motor tracts at the lesion site. There is no successful medication showing enough effect on chronic SCI. To discover the new approach for medication, we focused on skeletal muscle atrophy as a detrimental condition in chronic SCI. Therefore, we aim to find a drug that improves skeletal muscle atrophy and promotes the releases of axonal growth factors from skeletal muscle because skeletal muscle constitutively secretes myokine to maintain skeletal muscle function and possibly neuronal function. We screened herbal extracts to look for myokine release activity. Primary cultured myocytes from newborn mice hindlimb skeletal muscle were treated by herbal extracts, and conditioned medium (CM) was prepared. CM was treated to primary cultured cortical neurons to evaluate axonal growth activity. CM from Cistanchis herba extract treated-myocytes induced axonal growth. Acteoside was identified as an active compound in Cistanchis herba. Acteoside enhanced also proliferation of primary cultured myocytes. Acteoside was administered (3 times/week) intramuscularly to SCI mice (T12 contusion injury) from 30 days after injury. During observation period (for 62 days after the injection start), locomotor function was significantly improved by acteoside. At the end point of the observation, wet weights of skeletal muscle were significantly increased compared with vehicle-treated group. Released factors from myocytes by acteoside stimulation were investigated, and pyruvate kinase M2 (PKM2) was identified. Recombinant PKM2 enhanced axonal growth in primary cultured cortical neurons. In the present study, we discovered new medication acting skeletal muscle, that improves locomotor dysfunction and skeletal muscle atrophy in chronic SCI, and new myokine PKM2 may play a role in the recovery phenomena.