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Oral treatment with herbal formula B307 alleviates skeletal muscle atrophy from hind-limb unloading

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Introduction: Muscle atrophy can result from physical inactivity, chronic bedrest, and ageing. Traditional Chinese herbal formula B307 is a health supplement with multiple potential protective functions of organs. We investigated the effects of herbal formula B307 on muscle atrophy using the hind-limb unloading (HU) model in mice.

Methods: Eight-week-old ICR mice were randomly divided into four groups: Sham, B307, HU, and HU+B307 groups. HU model was established in the HU and HU+B307 groups for 14 days. Mice in the B307 and HU+B307 groups were given oral B307, while the Sham and HU groups were treated with the vehicle for 14 days. Phenotypes and biomarkers of muscle atrophy were examined using laser Doppler, luminol chemiluminescence, immunohistochemistry, and western blotting.

Results: The muscle mass of mice in the HU and HU+B307 groups was significantly lower than the Sham group ($P<0.05$). Muscle mass was significantly higher in the HU+B307 group versus HU group ($P<0.05$), but no significant difference was found between the Sham and B307 groups. Reactive oxygen species (ROS) of blood, expressions of tumour necrosis factor alpha (TNF-α), vascular endothelial growth factor (VEGF), and caspase-3 in the skeletal muscle was significantly higher in the HU versus Sham and B307 groups ($P<0.01$), while alleviated after B307 treatment in the HU+B307 group ($P<0.05$). Blood flow in the hind-limb and whole body increased after B307 treatments ($P<0.05$). However, no significant differences in muscle strength, B-cell lymphoma 2 (Bcl-2), Bcl-2-associated X protein (Bax), caspase-9, and endothelial NOS (eNOS) expression in the skeletal muscle of mice were found between the four groups.

Conclusion: Oral B307 treatment may alleviate skeletal muscle atrophy from HU. Potential underlying mechanisms include improvement in blood flow and downregulation of oxidative stress, inflammation, and apoptosis.

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Whole-exome sequencing identified novel genetic mutations in a pedigree of familial myeloproliferative neoplasm

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Introduction: Myeloproliferative neoplasm (MPN) encompasses a group of diseases characterised by increased proliferation of erythroid, megakaryocytic, or granulocytic cells in the bone marrow. Clinically, MPN includes chronic myeloid leukaemia (CML) carrying Philadelphia-chromosome (BCR/ABL translocation) as well as polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF) that carry gene mutations such as janus kinase 2 (JAK2), calreticulin (CALR), and thrombopoietin receptor (MPL). Approximately 10% of MPNs showed familial occurrence, suggesting inheritance of genes that make them susceptible to MPN.

Methods: A family with three members affected by ET, PV and CML across two generations were identified; another three members were shown to have consistent elevated platelet count. DNA were extracted and subjected to whole-exome sequencing (WES), co-segregated variants were filtered and validated by Sanger sequencing. Intronic JAK2 haplotypes were also tested in these family members.

Results: All family members being tested in this study were shown to carry homozygous JAK2 haplotypes, previously shown to predispose to MPN. WES result has identified several candidate genes co-segregated in affected family members. Truncating mutation in *ZNF467* was of particular interest because of its role in transactivating *STAT3*, a gene shown to induce MPN upon deletion.

Conclusion: We conclude that WES was able to identify candidate gene potentially responsible for the pathogenesis of MPN.