A Chronic Model of Experimental IBD Reveals Sarcopenia and Long-Term Motor Dysfunction

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Background and aims:

Sarcopenia represents a relevant systemic complication of inflammatory bowel disease (IBD), emerging from complex interactions between chronic intestinal inflammation and microbial dysbiosis [1,2]. While acute models of DSS-induced colitis have provided preliminary insights into the early effects of inflammation on skeletal muscle—highlighting perturbations in inflammatory pathways and the gut microbiota—such models remain limited in their ability to replicate the prolonged and relapsing nature of intestinal disease [3]. A refined preclinical model is therefore needed to investigate the long-term impact of intestinal inflammation on muscle function. In this context, we developed and functionally characterized a chronic murine model of colitis to explore sarcopenia-related features, with particular attention to sustained inflammation and motor performance decline.

Methods:

To induce chronic colitis, C57BL/6 mice received three cycles of 2,5% dextran sulfate sodium (DSS) in drinking water for 7 days, each followed by a 14-day recovery period. Disease Activity Index (DAI) was monitored longitudinally across the 9-week experimental timeline. Motor function was assessed using the rotarod test, performed every other day to evaluate changes in coordination and endurance over time. Statistical analysis was performed using two-way ANOVA with repeated measures to assess differences in DAI and rotarod performance between groups over time. A p-value < 0.05 was considered statistically significant.

Results:

DSS-treated mice exhibited progressive alterations in Disease Activity Index (DAI) parameters—including weight loss, changes in stool consistency, and presence of occult blood—consistent with a clinical profile suggestive of ongoing intestinal involvement over time ($p < 0.0001$, two-way ANOVA).

Notably, DSS-treated animals exhibited a significant reduction in latency to fall in the rotarod test compared to untreated controls ($p < 0.01$), indicating a progressive impairment in motor performance

likely reflecting compromised muscle function. These findings extend previous observations obtained in acute models and support the hypothesis that prolonged intestinal inflammation contributes to functional decline *in vivo*.

Conclusion:
The present chronic murine model successfully reproduces key features of IBD-associated sarcopenia, including persistent intestinal inflammation and measurable motor deficits. This platform enables the investigation of longitudinal changes in the gut–muscle axis and provides a robust tool for the future evaluation of targeted therapeutic strategies aimed at mitigating muscle wasting in chronic inflammatory conditions.

Bibliography.

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