P10 & FP - **Combined effects of nutrients and gut microbiota in the immunomodulation of DMD**

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Duchenne muscular dystrophy (DMD) patients present alteration of gastrointestinal motility and suffer from constipation, pseudo-obstruction, acute dilatation: although no attention was paid to investigate these processes, smooth muscle fibrosis was observed throughout the gastrointestinal tract [1]. Similarly, the mdx mice shared impairments in the intestinal contractility, linked to important abnormalities of the mucosal epithelial morphology normally associated to inflammatory state [2,3]. These evidences would suggest the contribution of alternative pathological pathways, other than the musculoskeletal one, in the disease pathogenesis. Skeletal muscle inflammation in mdx has a peak at 7 weeks and decreases at 12 weeks: cellular infiltrates involve both macrophage and pro-inflammatory CD4/CD8+ T-cells, whose amount remain elevated throughout the life of mice [4]. On the contrary, although it is known that mdx intestinal wall is inflamed, few is known regarding the contribution of different immune subpopulations: altered gut microbiota together with modified mucosal permeability could unbalance gut homeostasis favouring the expansion of inflammatory T-lymphocytes reactive against muscular proteins [5]. We suggest that dystrophic intestinal inflammation is dependent on the relationship between the intestine and its microbiota and that this axis is responsible for spreading the inflammatory cues throughout the muscles. For the first time, we have analysed the microbiota of mdx at 10-weeks and 9-months old (n=3 each) and we detected important differences among these mice. Thus, we demonstrated that following specific anti-inflammatory treatment mdx mice showed alteration of gut microbiota, especially in older ones. This way, we will unravel the role of microbiota in DMD aetiology and its contribution in determining immune system activation leading to muscle damage. If intestinal commensals promote the development of the disease, we will attempt to identify the microorganisms involved. As a result, we will employ different strategies to modulate the microbiota in mdx mice to counteract the development of intestinal inflammation and its effect on muscle degeneration. These proof-of-concept pre-clinical studies will lead to microbiota studies in DMD cohort and, if successful, will open to microbiota manipulation for therapeutic purpose in DMD patients.

References

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