# NITRIC OXIDE AND REGULATION OF INFLAMMATION IN THE THERAPY OF MUSCULAR DYSTROPHIES

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Duchenne muscular dystrophy is a relatively common disease that affects skeletal muscle leading to progressive paralysis and death. There is currently no resolutive therapy, although recent studies with systemic delivery of a specific stem cell, the mesoangioblast, have opened promising perspectives. We have developed a novel treatment, in which we combined the known beneficial effects of nitric oxide (NO) in muscle repair with non steroidal anti-inflammatory activity using HCT 1026, a NO-releasing derivative of flurbiprofen. Here we report the results of long term (one-year) oral treatment with HCT 1026 of two murine models for limb girdle and Duchenne muscular dystrophies (α-sarcoglycan null and mdx mice). In both models, HCT 1026 significantly ameliorated the morphological, biochemical and functional phenotype in the absence of secondary effects, efficiently slowing down disease progression. HCT 1026 acted by reducing inflammation, preventing muscle damage and preserving the number and function of satellite cells. HCT 1026 was significantly more effective than the corticosteroid prednisolone analyzed in parallel. As an additional striking beneficial effect, HCT 1026 increased fourfold the ability of mesoangioblasts to migrate into dystrophic muscles, to resist their apoptogenic environment and engraft into them, enhancing significantly their therapeutic efficacy.
The new therapeutic strategy we propose is not selective for a subset of mutations, provides ground for immediate clinical experimentation with HCT 1026 alone, which is approved for use in humans, and may set the stage for combined therapies using donor or autologous, genetically-corrected stem cells.