Stem Cells from Umbilical Cord Blood Differentiate into Myotubes and Express Dystrophin *in vitro* only after Exposure to *in vivo* Muscle Environment

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Duchenne muscular dystrophy is a disease characterized by progressive and irreversible muscle degeneration for which there is no therapy. Human umbilical cord blood has been considered as an important source of hematopoietic and mesenchymal stem cells, each having been shown to differentiate into distinct cell types. However, it remains unclear if these cells are able to differentiate into muscle cells. We have shown that stem cells from human cord blood did not differentiate into myotubes or express dystrophin when cultured in muscle-conditioned medium or with human muscle cells. However, delivery of GFP-transduced mononucleated cells from cord blood, which comprises both hematopoietic and mesenchymal populations, into quadriceps muscle of *mdx* mice resulted in the expression of human myogenic markers such as Human M-cadherin, MRF4 and PAX-7. After recovery of these cells from *mdx* muscle and *in vitro* cultivation, they were able to fuse and form GFP-positive myotubes that expressed dystrophin as well as the myogenic markers M-cadherin, myogenin and PAX-7. These results indicate that chemical factors and cell-to-cell contact provided by *in vitro* conditions were not enough to trigger the differentiation of stem cells into muscle cells. Nevertheless, we showed that the HUCB-derived stem cells were capable of acquiring a muscle phenotype after exposure to *in vivo* muscle environment, which was required to activate the differentiation program.