The search for an ideal mesenchymal stromal cell donor in the horse

J. Lacy Kamm, Christopher B Riley, Natalie A Parlane, Erica K Gee and C. Wayne McIlwraith

The search allogeneic (cells from one unrelated horse put into another) mesenchymal stromal cell (MSC; also called "stem cells") that do not stimulate and immune reaction is a motivation for many human biomedical researchers. This is also true for equine medicine and surgery, where MSCs are used for research and clinical cases for the treatment of musculoskeletal diseases like osteoarthritis and bone infections. An ideal allogeneic MSC suppresses the immune system of the recipient horse, leading to decreased inflammation in the face of disease. The ideal MSC also expresses the markers of a multipotent cell, retains a high level of viability and is able to stimulate anabolic activities to enhance repair.

Our research aimed to define the expression of MSC markers (molecules that identify and define the immune reactions of these cells) harvested from different equine MSC donors. Bone marrow-derived MSCs from Thoroughbreds, Standardbreds, and a subset of universal blood donor-type Standardbreds were compared. Standardbred MSCs showed significantly less MHC class II expression (a common cell surface marker) at early cell culture passages compared with Thoroughbreds. When universal blood donor Standardbreds were compared to non-blood donor Standardbreds, the only significant variation was that one cell surface marker, CD90, was expressed more highly on universal blood donor MSCs. The conclusion from this experiment was that universal blood donor-type Standardbred horses are less likely to cause an immune reaction and had the highest levels of bone marrow-derived MSC markers expressed at cell culture passage 2-4.

Next, we compared the MSC donor cells in an in vitro trial exploring the immune system so as to understand the effects of the MSCs without prior activation of the immune cells, as has been done previously. We found that MSCs of allogeneic origin cause very little to no activation of the immune system as compared to autologous MSCs. B cell and activated T lymphocyte populations were similar between the autologous (cells collected from a horse and administered to itself) and allogeneic MSCs. Those allogeneic MSCs that expressed little MHC II prior to interaction with the immune cells (MHC II-low MSCs) had reduced activation of recipient lymphocytes and neutrophils as compared to those expressing high levels of MHC II prior to interaction with immune cells (MHC II-high MSCs).

MHC II-low MSCs, both of universal blood donor and non-blood donor origin, had higher expression of the genes we studied when placed in an allogeneic environment. These include anabolic molecules known to assist in healing and some catabolic molecules. This knowledge, combined with published information that 'activated' MSCs can be more beneficial to healing than inactivated MSCs, support the use of the more metabolically active MHC II-low MSCs as compared to MHC II-high MSCs.

Based upon a wide array of testing, allogeneic MHC II-low MSCs created a low level of immune activation and an increased level of gene anabolic gene expression compared with autologous MSCs. In conclusion, MHC II-low MSCs are preferred for use in allogeneic therapy.

In summary, this research improved our understanding of the immune responses that occur when MSCs from one horse are injected into another horse for treatment. It also identified MSCs that are less likely to stimulate an immune response when transferred from one horse to another.

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