

## THE CONTROL OF MESENCHYMAL STEM CELL DELIVERY BY AORTIC INJECTION AND ANTIBODY COATING

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The delivery of stem cells to a target organ remains a major challenge for cellular therapy. The optimal method to introduce cells into the body is still unclear, although systemic administration is preferred. Most current methods rely on the cells' own innate ability to direct itself to a specific organ or anatomic location. We hypothesized that arterial cell injection is superior to tail vein injection because the cells can bypass the lungs. Furthermore, we hypothesized that cells coated with an antibody to the endothelial cell surface of our target organ would promote docking to that organ. We evaluated our proposed method by targeting E-selectin, which is upregulated in irradiated endothelium.

**Methods:** BMC-9 cells, a mouse MSC cell line (Dennis et al. J Bone Miner Res, 1999), were transduced with a triple reporter gene containing luciferase and purified by flow cytometry. Antibody coating of the MSCs was achieved by incubating the cell with palmitated protein-G followed by incubation with antibody (Dennis et al. J Orthop Res, 2004). In this study, we used anti-E-selectin antibody. Uncoated MSCs served as controls. Nude mice were irradiated on one leg and  $1 \times 10^6$  coated or uncoated MSCs were injected either through the tail vein or through a catheter inserted into the carotid artery and down to the aortic arch (Hoit et al. Am J Physiol, 1997). The mice were then imaged for bioluminescence.

**Results:** Both coated and uncoated cells injected via the tail vein were located primarily in the lungs (Fig. A). In contrast, MSCs injected into the aortic arch circulated throughout the entire body (Fig. B&C). However, only cells coated with anti-E-selectin antibody and injected into the aortic arch showed preferential localization at the site of irradiation (Fig. C). The ratio of bioluminescence from the irradiated leg compared to the non-irradiated leg was 0.98 (n=3) for the tail vein injection with antibody-coated MSCs, 1.01 (n=2) for the aortic arch injection with uncoated MSCs, and 2.06 (n=3) for the aortic arch injection with coated MSCs.

**Conclusion:** Cells coated with anti-E-selectin antibody showed greater accumulation in the irradiated leg when given the opportunity to encounter the targeted site via arterial injection. Thus, arterial injection and antibody coating gives us the ability to control the delivery of MSCs to a specific site.

**Figure. E-selectin antibody coated MSCs injected into the aorta circulated throughout the body and preferentially accumulated at the site of irradiation.** Representative images showing MSCs that were either uncoated (B), or coated with e-selectin antibody (A & C) and injected into mice via the tail vein (A) or into the aortic arch via a catheter inserted into the carotid artery (B & C). The white arrow points to the irradiated leg.

