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Stem cell and novel neurotropic factors to promote functional recovery in limb transplantation - Shashikumar K Salgar, Madigan Army Medical Center, USA

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Recently, transplantation of hand and face has become a new clinical specialty. However, functional recovery of the graft is sub-optimal and it is a significant problem. The objective of this study was to determine whether adult Mesenchymal Stem Cells (MSCs), Granulocyte-Colony Stimulating Factor (G-CSF) and/or Dihexa [N-hexanoic-tyrosine-isoleucine-(6) aminohexanoic amide] can promote limb transplant function. Methods: We used rat sciatic nerve transection-repair model (Figure 1). There were 10 experimental groups (n=6/group). Bone marrow derived syngeneic MSCs (2 million), G-CSF (50-100µg/kg), (Dihexa 2-4mg/kg) and/or Vehicle were administered locally via hydrogel at the site of nerve repair, i.v./i.p., and to gastrocnemius muscle.

Results: Total sensory function was ~1.4, 1.7, 2.7 and 2.9 at 2, 4, 8 and 16 weeks post-nerve repair, respectively, on a scale of Grade 0-3 (0=No function; 3= Normal function) in all groups combined; peroneal nerve function recovered quickly by one week (~2.0) and sural nerve function recovered rather slowly, by four weeks it was ~1.0. Motor function at 16 weeks post-nerve repair as determined by walking foot print grades 0-4 (0=no print; 4=heel plus 4-5 toe prints) was 3.0±0.9, 3.0±0.8, and 2.0±0.6 in MSC+G-CSF, MSC+Dihexa and MSC+vehicle groups with gastrocnemius injections, respectively; however, without gastrocnemius injection it was ~1.6. G-CSF or Dihexa injections to gastrocnemius significantly ($P<0.05$) improved motor function (Figure 1), mitigated muscle atrophy and reduced flexion contractures. MSCs expanded ex vivo were CD29+, CD90+, CD34-, CD31-, MHC Class I+, Class II- and multipotent. In a parallel study with tibial nerve repair we observed significant nerve regeneration/myelination with MSC therapy (n≥6). Also, in a limb transplantation model, MSCs improved sensory and motor functions, marginally. Conclusion: It appears, MSC, G-CSF and Dihexa are promising candidates for adjunct therapies to promote limb transplant functional recovery.

Our examination included four test gatherings (n = 9–12/gathering). Gathering A. Sciatic Nerve Repair (SNR) model, gotten saline (vehicle); Group B. SNR model, gotten MSC; Group C. Singular Nerve Repair (INR) model, gotten saline (vehicle); and Group D. INR model, gotten MSC. The SNR included crosscut and fix of the primary sciatic nerve branch (proximal nerve harm), while INR included crosscut of the distal parts of the sciatic nerve (tibial, sural, and peroneal) and fix (distal nerve harm). Nerve crosscut and fix was done on the correct rear appendage, and the contralateral appendage filled in as a non-cut across (guileless) nerve control. Beginning ≥1 week post-SNR or INR, creatures got manual physiotherapy for the correct rear appendage (≤5 min, 1–2 times each week) as depicted already [40]. Essential result measures were appendage tactile and engine capacities, and optional result measures were gastrocnemius mass, flexion contractures, and nerve histology.

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