Title: IL-3 maintains the post-stroke hematopoietic response in the chronic phase of recovery

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Introduction: Inflammation plays a critical role in recovery after stroke. We have shown that ischemic stroke activates bone marrow hematopoiesis, and that IL-3 governs hematopoiesis in other chronic neurological diseases..

Objective: We sought to explore IL-3's role in the regulation of chronic-phase post-stroke inflammation.

Methods: Transient middle cerebral artery occlusion(MCAO) for 45 minutes in wild-type(WT) and IL-3 knockout(KO) mice was performed. Cerebral perfusion changes were measured using Laser Doppler Flowmetry. Flow cytometry was performed to examine cell populations in the brain, bone marrow, and blood 2 weeks post-stroke.

Results: MCAO led to a significant increase in CD45+ leukocytes infiltrating the ipsilateral (I) hemisphere vs. contralateral (C) hemisphere in both WT (I: $6.1*10^4 \pm 2.1*10^4$ cells, C: $1.0*10^4 \pm 1.9*10^3$ cells) and IL3-KO (I: $5.6*10^4 \pm 3.1*10^4$ cells, C: $4.8*10^3 \pm 3.0*10^3$ cells,) ($p<0.05$ I vs. C). There was a decrease in the number of microglia cells in the IL3-KO group compared to WT in the ipsilateral hemisphere (WT: $2.5*10^4 \pm 5.5*10^3$ cells, IL3-KO: $1.4*10^4 \pm 3.0*10^3$ cells,) however this trend was nonsignificant ($p>0.05$). There was an increase in Ly6-high monocytes in both the WT and IL3-KO ipsilateral hemispheres without a significant difference between genotypes (WT: $1.7*10^3 \pm 8.7*10^2$ cells, IL3-KO: $2.2*10^2 \pm 2.1*10^3$ cells,). There was however a significant decrease in the number of infiltrating Ly6-C low monocytes in the IL3-KO vs. WT in the ipsilateral hemisphere (WT: $1.6*10^3 \pm 3.3*10^2$ cells, IL3-KO: $3.3*10^2 \pm 1.6*10^2$ cells)($p<0.05$).

In the bone marrow, there were significant decreases in overall cell populations between WT and IL3-KO mice consistent with exhaustion of hematopoiesis. There were significant decreases in neutrophils (WT:$8.8*10^6 \pm 1.4*10^6$ cells, IL3-KO: $3.2*10^6 \pm 3.9*10^6$ cells), common lymphoid progenitors (WT:$9.9*10^3 \pm 4.3*10^3$ cells, IL3-KO: $1.2*10^3 \pm 1.5*10^3$ cells), and common myeloid progenitors (WT:$1.2*10^5 \pm 2.3*10^5$ cells, IL3-KO: $4.1*10^4 \pm 9.5*10^4$ cells)

Conclusion: IL3 is involved in the maintenance of post-stroke hematopoiesis in the chronic phase of recovery. Deficiency of IL3 leads to decreased myeloid cells in the ipsilateral hemisphere post-stroke.