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Mackenzie Fleischer

Michael Newton

Samantha Hartner

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Anthony Arveschoug

See next page for additional authors

Authors

Mackenzie Fleischer, Michael Newton, Samantha Hartner, John A. Driscoll, Anthony Arveschoug, Chritopher C. Vasileff, and Kevin Baker

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Paper 23

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Mackenzie Fleischer, Ph.D. / Royal Oak, MI
Michael Newton, Ph.D. / Royal Oak, MI
Samantha Hartner / Royal Oak, MI
John A. Driscoll, M.D. / Royal Oak, MI
Anthony Arveschoug, M.D. / Royal Oak, MI
*Christopher C. Vasileff, M.D. / Royal Oak, MI
Kevin Baker, Ph.D. / Royal Oak, MI

PURPOSE: Augmentation of MSC immunomodulation is an unexplored, potentially useful therapeutic to combat PTOA following ACLR. Lower kynurenine-to-tryptophan ratios observed in synovial fluid of ACL rupture (ACLR) rats suggests decreased activity of tryptophan metabolizing enzyme, Ido, known to be secreted by MSCs to promote T-reg expansion and Th17 suppression. This study aims to characterize the immunomodulatory capacity of pharmacologically mobilized MSCs in conjunction with exogenously delivered Ido.

METHODS: Rats (N = 48) underwent ACLR to evaluate the effects of mobilized MCSs on Ido1 and inflammatory cytokine expression profiles in the synovial fluid. Additionally, rats (N = 160) underwent ACLR to assess the immunomodulatory influence of therapeutic Ido in vivo via gait analysis parameters known to correlate to pain and inflammation. Gait data was collected longitudinally prior to injury and at 3, 7, 10, and 14 days post-injury.

RESULTS: ACLR induced an increase in inflammatory markers including TNF-α and Fractalkine. Treatment with AMD3100, which induces MSCs recruitment, increased Ido within the injured joint while decreasing inflammatory markers. Gait analysis following ACLR demonstrates that AMD3100 and exogenous Ido exhibited normalizing effects on several gait parameters compared to control.

CONCLUSION: Increased MSC recruitment and exogenous Ido delivery following ACLR may be effective at modulating joint pain and inflammation associated with PTOA.