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Assessment of the Composition and Biologic Activity of Platelet Rich Plasma and its Relationship to Clinical Outcomes in Patients with Knee Osteoarthritis

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Assessment of the Composition and Biologic Activity of Platelet Rich Plasma and its Relationship to Clinical Outcomes in Patients with Knee Osteoarthritis

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Recent studies suggest positive clinical outcomes associated with platelet-rich-plasma (PRP) administration to treat knee osteoarthritis (OA). However, the results remain inconclusive in part because of the high variability in PRP preparations and the limited information regarding the relevant biologically active components of PRP. We hypothesize that the variability in clinical response is driven by the heterogeneous composition of PRP. In this study we evaluated the composition and biological activity of PRP and further correlated our findings to clinical outcomes in patients receiving intra-articular injections for knee OA. After IRB approval and patient consent, we enrolled 51 patients (mean age: 57.9 ± 10.1 ; mean BMI: 26.0 ± 4.1) with mild-moderate knee OA (Kellgren Lawrence grades 1-3), eligible for intra-articular PRP injection. We obtained MRI at baseline and outcome measures (KOOS JR and PNS) at baseline, 6 weeks, 6 months, and 12 months after PRP injection. Patients were categorized as “good” and “poor” responders based on the outcome measures, corrected using published Minimally Clinically Important Difference (MCID) values. Aliquots of PRP and whole blood from the same patients were used to evaluate composition (CBC with differential and multiplex ELISA) and biologic activity, using a co-culture system of macrophages and fibroblast incubated with TNF α with and without PRP (10% v:v) for 24 hours. Total RNA from cells was used for RNAseq, Nanostring, and RTqPCR analysis. On average, we collected 4.07 ± 0.105 mL of PRP, and 3.24 ± 0.85 mL of PRP were injected intra-articularly. PRP preparations yielded mean fold-changes of 1.60 ± 0.37 platelets and 0.19 ± 0.08 v leukocytes, relative to whole-blood from the same patients (set as 1). On average, all patients that reached the 6-month time-point (N = 32) reported improved outcomes at 6-weeks and 6-months after PRP administration (KOOS and PNS $p < 0.05$ vs. baseline). After MCID corrections, we identified “good” (N=17, positive response using both measures) and “poor” responders (N=15, poor response in one or both measures). RNAseq analyses showed PRP-dependent changes in the TNF α -induced modulation of a number of genes, including CXCL7 and CCL5. NanoString and RTqPCR analyses confirmed the RNAseq results. Comparisons of PRP from good and poor responders identified changes in the composition and biologic activity between these groups. This pilot study integrated clinical data with genomic approaches to evaluate variability in the composition and activity of PRP, and how this may influence outcomes in patients with knee OA. We uncovered subsets of genes differentially modulated by co-treatment of PRP with TNF α , in agreement with the concept that the reduced knee OA pain in patients treated with PRP is driven by the ability of PRP to modulate inflammation. Furthermore, we identified changes in the composition and biologic activity of PRP between “good” and “poor” responders.