Results: The molecular analysis of KGN- and TGF-β3-chondrogenic induced 3a6 pellets is depicted in figure 1A. For zonal markers expression, both conditions showed a significant downregulation in PRG4 with time, concomitant with an upregulation of CILP, for TGF-β3 but not for KGN-induced cells. However, PRG4 and CILP were found on the protein level (Figure 1B) for both conditions. The studied zonal markers were found heterogeneously distributed for KGN-induced pellets (Figure 1C). This difference is also supported by proteoglycans SO staining, with an earlier formation of a more mature tissue for KGN- than TGF-β3-induced pellets. No expression was found for the main hyaline-like cartilage collagen (COL2A1). RUNX1 was practically unaltered in both conditions. For hypertrophic markers, RUNX2 was upregulated at 14 days in TGF-β3 whilst in KGN-induced cells expression was non-significant.

Conclusion: This is the first study to report the chondrogenic effect of kartogenin on 3a6 immortalized human bone marrow MSCs line. On the molecular level, no significant differences were found between KGN- and TGF-β3 chondroinduction, although transition into a hypertrophic phenotype seems to be delayed. On the protein level, zonal markers and proteoglycan synthesis were found improved by kartogenin after 14 days.

REFERENCE:

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Results: Participants had a mean age 47±9 yrs and 6 out 7 (86%) were female. All had KL grade ≥2 with substantial knee pain at baseline. Enough SF (>500 μL) could be obtained from n=7 at baseline, n=4 at midpoint, and n=3 at endpoint of distraction. For the first time in this same group, we show how MSC number initially decline upon KJD (figure 1A-B) as seen previously in our animal study [4]. Also, MSCs present in the SF showed changes in their gene expression profile upon KJD, most clearly observed during the treatment (3 weeks; figure 1C). GDF5 and Grem1 presented with a statistically significant increased expression (p<0.05) during KJD treatment while IFABP expression was decreased. ACAN, PTH1R, and DDR expression had the tendency to increase over time. ADAMTS4, SOX9 and PTHLH expression showed a trend to decrease over time.

Conclusion: This explorative study provides for the first-time data on changes in SF MSC number and their gene expression profiles upon knee joint distraction. As such, first clues are provided for the involvement of MSCs in the regenerative process induced by joint distraction for knee joint distraction. Bar indicates statistically significant changes (p<0.05).

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Figure 1. Changes in synovial fluid MSCs numbers and gene expressing profiles upon knee joint distraction. Bar indicates statistically significant changes (p<0.05).