a.) Adipose-derived mesenchymal stem cells (ADMSC) are an attractive source for cartilage repair because of their self-regeneration potential, accessibility and abundance. Because transplanted MSCs produce structurally inferior fibrocartilage, maintenance of a high chondrogenic differentiation potential with resistance to hypertrophy and terminal differentiation, becomes a great challenge. A previous report has demonstrated that FGF-2 treatment of bone marrow-derived MSCs (BMSCs) in monolayer upregulates the expression of the chondrocyte marker alpha10 integrin and enhances BMSC chondrogenic differentiation. In this study we developed a similar pre-conditioning strategy which primes ADMSC towards chondrogenesis. b.) Human ADMSCs and BMSCs were cultured in monolayer for 5 days with or without FGF-2 (10 ng/ml) under normoxia or hypoxia. Afterwards, MSCs were subjected to chondrogenic differentiation in pellet culture for 28 days in the presence or absence of TGFβ1 and BMP2 (T/B). Differences in integrin and chondrogenic gene expression patterns were investigated by RT-PCR. Protein expression levels were determined for integrin α10 by immunoblotting. Safranin-O (SO) staining for proteoglycans and immunohistochemistry (IHC) for collagen II and aggregcan were performed on sections to demonstrate chondrogenesis in pellets. Biomechanical properties and structure of cartilaginous matrix were examined by atomic force microscopy (AFM). c.) FGF-2 supplementation of ADMSC and BMSC monolayers increased the expression of Itga10 and Sox9, while decreased Itga11 and Agc1, independently of the oxygen tension. Additionally, Itga10 protein levels were elevated in FGF-2 treated MSCs. SO staining and IHC demonstrated superior chondrogenic differentiation of BMSCs with T/B administration in pellet cultures compared to ADMSCs. ADMSCs showed patches proteoglycan deposition and increased Col2a1 mRNA expression in T/B-treated pellets only upon FGF-2 and hypoxic preconditioning. AFM topography and indentation measurements confirmed collagen fibers development in peripherally differentiated ADMSC pellets and entirely differentiated BMSC controls. d.) These results demonstrate that FGF-2 pretreatment of ADMSCs strongly increases the expression of the chondrogenic markers Itga10 and Sox9 in monolayer. Furthermore, high level of Itga10 mRNA enhances the chondrogenic differentiation potential of ADMSCs in pellet culture. We suggest that modulation of Itga10 expression on ADMSCs may help to develop better cell-based therapeutic strategies to treat osteoarthritis.