High-throughput microfluidic platform for generating, culturing and conditioning cell microaggregates

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First stages of embryonic limb development - namely cell condensation, expansion of an undifferentiated mesenchymal cell pool and chondrogenesis - are tightly regulated by specific signaling pathways (Wnt, FGF, TGF/BMP)[1]. A microfluidic platform for generation and culture of cell microaggregates was developed, consisting of two functional elements: (i) a serial dilution generator and (ii) a cell culture area. Dilutions of chemicals could be generated and delivered to 6 downstream culture units, each comprised of 30 cubic chambers (side 0.15 mm). The microfluidic platform was used to assess the spontaneous condensation of hBM-MSC. Their 3D proliferation potential was evaluated and compared to that obtained through standard macroscale models[2]. Finally, the onset of chondrogenesis was assessed at the microscale. Interestingly, the platform allowed hBM-MSCs to undergo spontaneous condensation in micro chambers within 3 hours upon seeding. By activating key signaling pathways, much higher proliferation rates were observed within the microaggregates compared to the standard macroscale model (EDU+ cells about 30% vs 1%). Immunofluorescence analyses revealed an increase in collagen II expression within the microaggregates from day 3 to day 7, ultimately demonstrating chondrogenic differentiation within the microfluidic system. In conclusion, limb bud models obtained through the proposed microfluidic platform provided a more uniform response to external cues in terms of cell proliferation and pre-chondrogenic differentiation compared to traditional 3D approaches.

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