

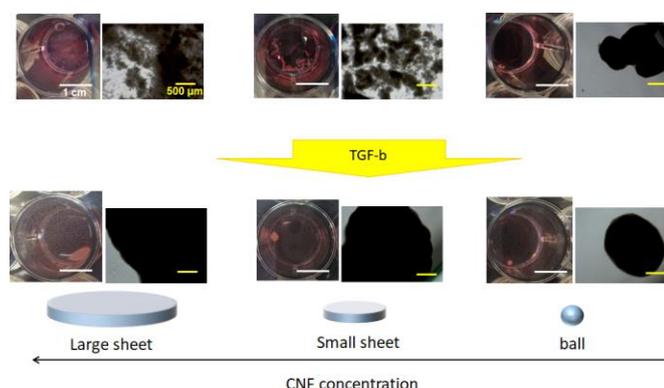
# Cellular flocculation using concentrated polymer brush-modified cellulose nanofibers

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Our body is formed through self-assembly. Sophisticated and hierarchical structures of our tissues and organs are built from individual smaller components such as DNA, peptides, collagens and cells. Inspired by nature's design principles, we have developed a cellular flocculation system using cellulose nanofibers modified with concentrated polymer brushes (CNF-CPBs) as artificial ECMs.<sup>1-5</sup> First, we demonstrated that human hepatocyte cells (HepG2) spontaneously formed flocs (self-



**Figure 1.** Structure changes by chondrocyte differentiation (with or without TGF- $\beta$ ).

assembled) with negatively charged CNF-CPBs, affording to able to control their sizes and shapes, and it enhanced the cell functions.<sup>1</sup> Next, by varying the charge of polymers (zeta-potential = -23, -19, 17, 11 mV), we revealed that appropriate electrostatic interactions are essential for floc formation and the regulation of cell functions.<sup>2</sup> Importantly, the results indicate that colloidal flocculation theory is the driving mechanism behind this unique phenomenon. Furthermore, CNF-CPBs with different fiber lengths (0.16 ~ 1.8  $\mu\text{m}$ ) were used for the cellular flocculation (HepG2, L929 and hTERT).<sup>3</sup> We confirmed that the size of the flocs is greatly affected by the concentration and length of CNF-CPB. Finally, considering the potential of CNF-CPBs as a new 3d cell culture tool, particularly as a novel cellular self-assemble system, we examined cartilage regeneration of human mesenchymal stem cells (hMSCs) using CNF-CPBs.<sup>4</sup> Interestingly, hMSCs were self-assembled with CNF-CPBs and formed ball- or sheet-type giant cellular structures, depending on the CNF-CPB concentration (0.1, 0.05, 0.005 wt%) in the presence of chondrogenic induction medium (Fig. 1). The highest concentration of CNF-CPB remarkably enhanced chondrogenic differentiation, in comparison to lower concentrations and a cell pellet. The details will be discussed.

## References

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