142ax A Generalized Approach to Construction of Complex Tissues

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Tissue engineering aims at reconstructing tissues and organs that have complex architectures and are composed of multiple cells with functions. It is challenging to localize the cells at a specific site, regulate cell behavior, and guide formation and development of new tissues in a controllable manner. We present a simple, versatile approach of constructing complex tissues, based on low-temperature fusion of polymeric micro/nanostructures using subcritical carbon dioxide (CO_2). Different types of cells are first cultured in polymer scaffolds. These scaffolds, with the preloaded cells, are then fused using CO_2. Eventually the construct can be developed into a complex tissue or organ. We found that CO_2, even at low pressures, could manipulate the chain mobility and reduce the glass transition of polymers at the nanoscale, which makes it possible to fuse polymeric micro/nanostructures at biologically benign temperatures. Furthermore, CO_2 could diffuse into the media and fuse the scaffolds with cells grown in it, while the cells (e.g. NIH 3T3 fibroblasts, mouse embryonic stem (ES) cells and human mesenchymal stem cells) kept their viability, growth, and functions. For example, after saturated with CO_2 at 37^{o}C and 200 psi for 1.5 hours, poly(lactide-co-glycolide) scaffolds with different microstructures were fused and the mouse ES cells grown in them were viable, kept their proliferation ability, formed embryonic bodies, and showed the potential to differentiate into multiple cell lineages. This demonstrates that a complex tissue with localized cell types could be constructed.