Highly Moldable "Clay"-Like Fluffy Biodegradable Nanofibrous Scaffolds for 3D Tissue Engineering

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Statement of Purpose: Electrospinning has been shown as a versatile method to fabricate the nanofibrous structures. It has known electrospinning has many advantages to be used in fabricating tissue engineering applications, however, to be used in actual medicinal practice, conventionally fabricated electrospun matrices have a critical disadvantage: it can only be fabricated into two-dimensional, sheet-like structures with small pore size. Several methodologies have been attempted to fabricate three-diemensional electrospuns caffolds. However, according to our paper searching, the major challenges of recently developed advanced methodologies are i) difficulty of fiber alignment, ii) difficulty in shaping the scaffolds freely, iii) requirement of additional equipment and iv) long fabrication time (a couple of hours). In the present study, a novel and rapid methodology for fabrication of 3D scaffolds by employing clay-like electrospun matrices that can be shaped freely with a mold, a wire and even a finger is presented.

Methods: Co-axial electrospinning was employed to fabricate 3D fluffy fibrous scaffolds composed of polystyrene (PS) and polycaprolactone (PCL). Each nanofibers were composed of two layers, core and sheath, and each core and sheath are composed of PCL and PS, respectively. It is also possible to apply the uniaxial alignment of the fibers in the resulting scaffolds with a conventional rotating mandrel. Using the 'selective leaching' technique developed in our group, only PS was leached out and biodegradable polymer, PCL, was remained.

Results: Even after rigorous washing and shaping steps, intact fibrous structures of the outer surface and inner space were confirmed by scanning electron microscopy (SEM). Alignment using rotating mandrels was also confirmed. From a stress-strain curve of tensile strength tests, 'rubber clay'-like property of electrospun clay-based scaffold was confirmed. Importantly, different from traditional electrospun matrices, cells were fully infiltrated into the 3D electrospun clay-based scaffolds both *in vitro* and *in vivo* experiments. Furthermore, we investigated the further potential to be used as inductive tissue engineering scaffolds using adeno-associated viral vectors (AAV) to transduce the adherent cells in the scaffolds. By conventional substrate-mediated gene delivery system, viral vectors were delivered to the cells and transduced into the cells. The cellular infiltration and transduction in the three-dimensional manner were observed in both randomly oriented and uniaxially aligned scaffolds.

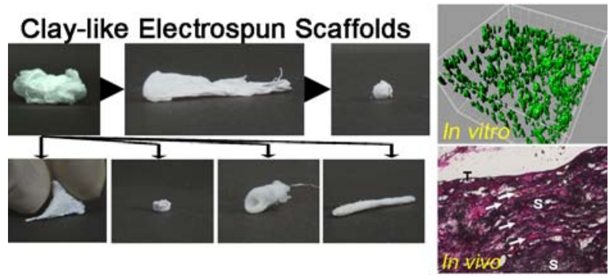

Figure 1. 'Clay'-like properties and cellular infiltration of PCL electrospun clay

Conclusions: In conclusion, we have developed 3D electrospun biodegradable scaffolds with 'rubber clay'-like properties by co-axially electrospinning polystyrene (in the outer layer) and poly (ε-caprolactone) (in the inner layer) followed by selectively leaching the polystyrene out of the scaffolds. The resulting process generated highly fluffy PS-PCL composite structures within 30 minutes, which is relatively very short time compared with conventional electrospinning. The leaching process to remove the PS shell yielded highly flexible, PCL-clay fibrous scaffolds. Because of the 'clay'-like properties of PCL scaffolds, the scaffolds could be formed into any desired shape without compromising the micro- and macroscopic structural integrity. Importantly, cells cultured in the 'clay'-like PCL fibrous scaffolds both *in vitro* and *in vivo* infiltrated homogeneously throughout the entire scaffolds and maintained their phenotypic morphologies and viabilities, all of which can be regarded as significant improvements compared with conventional 2D electrospinning. Microfibrous and biodegradable scaffolds with any desirable three-dimensional shapes have great potential to contribute to tissue engineering and regenerative medicine.

References: [1] Sun B. Nanoscale. 2012; 4; 2134-2137, [2] Lee S. Acta Biomater. 2011; 7;11; 3868-3876