

petri dishes. Following mixing of the tetra-amino PEG and tetra SE-PEG, the dishes were tilted repeatedly; the gelation time was considered to be the point at which the formulation ceased to flow. The effect of pH on gelation time of the various tetra-amino PEG/tetra SE-PEG formulations at room temperature is shown in Table 6, below.

TABLE 6

Effect of pH on Gel Formation of Tetra-amino PEG/Tetra SE-PEG Formulations			
Tetra-amino PEG Conc. (mg/ml)	Tetra SE-PEG Conc. (mg/ml)	pH	Gelation Time
20	20	6	>90.0 min
20	20	7	20.0 min
20	20	8	1.4 min
50	50	6	24.0 min
50	50	7	3.5 min
50	50	8	10.0 sec
100	100	6	9.0 min
100	100	7	47.0 sec
100	100	8	10.0 sec
200	200	6	2.0 min
200	200	7	9.0 sec
200	200	8	5.0 sec

The time required for gel formation decreased with increasing pH and increasing tetra-amino PEG and tetra SE-PEG concentrations.

Example 7

Culturing of Cells in Crosslinked Multi-amino PEG Matrix

Thirty (30) milligrams of tetra-amino PEG (10,000 MW, obtained from Shearwater Polymers, Huntsville, Ala.) was dissolved in 0.6 ml PBS, then sterile filtered. Thirty (30) milligrams of tetrafunctionally activated SE-PEG ("tetra SE-PEG", 10,000 MW, also obtained from Shearwater Polymers) was dissolved in 0.6 ml of PBS, then sterile filtered.

The solutions of tetra-amino PEG and tetra SE-PEG were mixed together with a pellet containing human skin fibroblast ("HSF") cells (CRL #1885, passage 4, obtained from American Tissue Type Culture Collection, Rockville, Md.). Two hundred fifty (250) microliters of the resulting cell-containing tetra-amino PEG/tetra SE-PEG (PEG-PEG) solution was dispensed into each of two wells on a 48-well culture plate and allowed to gel for approximately 5 minutes at room temperature. One (1) milliliter of Dulbecco Modified Eagle's Media (supplemented with 10% fetal bovine serum, L-glutamine, penicillin-streptomycin, and non-essential amino acids) was added to each of the two wells. The concentration of cells was approximately 3×10^5 cells per milliliter of tetra-amino PEG/tetra SE-PEG solution, or 7.5×10^5 cells per well.

To prepare a control, a pellet of HSF cells were suspended in 1.2 ml of complete media. Two hundred fifty (250) microliters of the control mixture was dispensed into each of three wells on the same 48-well culture plate as used above. Each well was estimated to contain approximately 7.5×10^5 cells. Each well was given fresh media every other day.

Initially, the cell-containing tetra-amino PEG/tetra SE-PEG gels were clear and the cells were found to be densely populated and spheroidal in morphology, indicating that there was little adhesion between the cells and the PEG/PEG gel (the cells would normally assume a flattened, spindle-shaped morphology when adhered to a substrate,

such as to the treated plastic of the tissue culture plates). After three 3 days incubation at 37° C., the media in the wells containing the PEG/PEG gels was found to have lightened in color (Dulbecco Modified Eagle's Media is normally red in color), indicating a pH change in the media. This indicated that the cells were alive and feeding. At 7 days incubation at 37° C., the cells were still spheroidal in morphology (indicating lack of adhesion to the gel) and the media had lightened even further, indicating that the cells were still viable and continued to feed.

On day 7, the contents of each well were placed in a 10% formalin solution for histological evaluation. According to histological evaluation, an estimated 75% of the cells in the wells containing the PEG/PEG gels appeared to be alive, but did not appear to be reproducing.

The results of the experiment indicate that HSF cells are viable in the tetra-amino PEG/tetra SE-PEG crosslinked gels, but did not seem to adhere to the gel and did not appear to reproduce while entrapped within the gel matrix. As described above, adherence or non-adherence of cells to a substrate material can influence the cells' morphology. In certain types of cells, cellular morphology can, in turn, influence certain cellular functions. Therefore, non-adherence of the cells to the PEG-PEG gel matrix may be an advantage in the delivery of particular cell types whose function is influenced by cell morphology. For example, the ability of cartilage cells to produce extracellular matrix materials is influenced by cellular morphology: when the cells are in the flattened, spindle-shaped configuration, the cells are in reproductive mode; when the cells are in the spheroidal configuration, reproduction stops, and the cells begin to produce extracellular matrix components.

Because the PEG-PEG gels are not readily degraded in vivo, the gels may be particularly useful in cell delivery applications where it is desirable that the cells remain entrapped within the matrix for extended periods of time.

What is claimed is:

1. A method of forming a three dimensional synthetic polymer matrix on a first tissue surface, comprising the steps of:
 - (a) providing a first synthetic polymer containing m nucleophilic groups and a second synthetic polymer containing n electrophilic groups, wherein the electrophilic groups react with the nucleophilic groups to form covalent bonds therewith, wherein m and n are each greater than or equal to two, and wherein m+n is greater than or equal to five;
 - (b) contacting the first synthetic polymer and the second synthetic polymer to initiate crosslinking; and
 - (c) simultaneous with or subsequent to step (b), applying the first synthetic polymer and the second synthetic polymer to the first tissue surface; and
 - (d) allowing the first synthetic polymer and the second synthetic polymer to become crosslinked to one another to form a three dimensional matrix.
2. The method of claim 1, further comprising contacting the first tissue surface with a second surface after step (c) but before step (d) to effect adhesion between the first tissue surface and the second surface.
3. The method of claim 2, wherein the second surface is a native tissue surface.
4. The method of claim 2, wherein the surface is a non-native tissue surface.
5. The method of claim 4, wherein the non-native tissue surface is a synthetic implant.
6. The method of claim 5, wherein the synthetic implant is selected from the group consisting of: a donor cornea, an