Comparing Bioactivity between Biomaterials

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Statement of Purpose: Biomaterials designed for surgical implantation, such as the meshes investigated presently, are designed to provide mechanical stability to an area of tissue weakness while remaining immunologically accepted by the host system. Yet if a material can only provide strength without regenerating native tissue, the normal function of a defect area will not be restored. This may result in unwanted, post-operative complications. Thus the ideal biomaterial should be bioactive. That is, it must interact with the host system to stimulate functions associated with tissue regeneration. Materials are derived from different sources and processed in different fashions, giving each a unique molecular composition. One molecule known to have bioactive properties is fibroblast growth factor 2 (FGF-2). This factor has previously been shown to stimulate angiogenesis and cell migration, processes that accompany tissue formation. This study compares the FGF-2 content and also the relative bioactivity in six different biomaterials used for surgical applications.

Methods: The materials compared were: Surgisis® and Surgisis® Gold™ (Cook Biotech Inc., West Lafayette, IN), Permacol® (Tissue Science Laboratories, Covington, GA), Veritas® (Synovis Surgical Innovations, St. Paul, MN), AlloDerm® (LifeCell, Branchburg, New Jersey), and SurgiMend® (TEI Biosciences Inc., Boston, MA). A quantitative sandwich enzyme immunoassay technique was used to measure the FGF-2 content of each material. To prepare the tested extracts, samples were cut from each material and ground in 1X PBS for three, thirty second intervals. The extracts were then tested for FGF-2 content using the Quantikine® Human FGF basic Assay from R&D Systems (Minneapolis, MN). In the presence of FGF-2, PC-12 cells exhibit the differentiated phenotype of neurite outgrowth. Thus the cell line is an ideal to model to test the bioactivity of biomaterials. Bioactivity is measured as a percentage of differentiated PC-12 cells in response to media conditioned by the materials. Samples were incubated at 37 degrees C for 24 hrs. with vigorous shaking in sterile media. 20,000 cells were seeded per well and the conditioned samples were added in triplicate along with a positive control of unconditioned media with 10 ng/ml FGF-2. Unconditioned media alone was used as a negative control. Cells in conditioned media were incubated for 48 hrs. The number of cells with significant neurite outgrowth were counted over the total number of cells in three random fields per well as a measure of bioactivity.

Results/Discussion: The analysis of FGF-2 content (fig. 1) and corresponding bioactivity (fig.2) reveals that Surgisis and Surgisis Gold contain an adequate amount of bioactive FGF-2 to induce differentiation of the PC-12 cells. The other products tested do not have detectable levels of FGF-2 and have no observable bioactivity. Surgisis is prepared from porcine small intestinal submucosa (SIS) in a process that removes cellular and nuclear contents, while maintaining the natural structure of the extracellular matrix (ECM). The process is gentle enough to retain many of the ECM-bound factors, such as FGF-2, that stimulate tissue regeneration. Permacol is a crosslinked porcine dermis collagen mesh, Veritas is derived from bovine pericardium, AlloDerm is processed cadaveric dermis, and SurgiMend is a collagen matrix made from fetal bovine dermis. The fact that none of these latter materials induced the FGF-2 dependent differentiation of the PC-12 cells indicates that these materials do not promote the active remodeling of tissue as quickly or efficiently as the SIS derived products.

Figure 1: Results of FGF-2 Assay

Biomaterial (n=3)	Average FGF-2 content (pg/g)	Standard deviation (pg/g)
Surgisis	50,700	4900
Surgisis Gold	36,000	2300
Permacol	not detectable*	n/a
Veritas	not detectable*	n/a
AlloDerm	not detectable*	n/a
SurgiMend	not detectable*	n/a

*the assay lacks sensitivity to detect FGF-2 below a concentration of 3 pg/ml (or 120 pg/g).

Figure 2: Results of Bioactivity Assay

Sample (n=9)	Average Bioactivity*	Standard deviation
Surgisis	20.9%	1.4%
Surgisis Gold	23.0%	5.7%
Permacol	0.2%	0.1%
Veritas	0.1%	0.1%
AlloDerm	0.7%	1.3%
SurgiMend	0.5%	0.2%
Positive control	11.3%	1.4%
Negative control	0.6%	0.7%

*bioactivity is measured as the number of cells with significant neurite outgrowth over the total cell count.

Conclusions: Surgisis and Surgisis Gold were the only two products with a detectable level of FGF-2 content. These two products were also the only to have an observable level of bioactivity. This lack of FGF-2 and bioactivity should raise question to the tissue regenerating potential of Permacol, Veritas, AlloDerm and SurgiMend.

References:

(Presta M. Cyto Gr Fac Rev. 2005; 16(2):159-78.)