Reviewer's report

Title: Influence of gold nanoparticles on Collagen Fibril Morphology Quantified using Transmission Electron Microscopy and Image Analysis

Version: 1 Date: 20 April 2006

Reviewer: Nily Dan

Reviewer's report:

The focus of this paper is on the characterization of collagen networks crosslinked via gold nanoparticles using electron microscopy. The authors use image analysis to determine the length of fibrils and their shape complexity of the networks when compared to collagen in the absence of particles.

1. Is the question posed by the authors new and well defined?
   Yes.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
   No.

This referee is not a microscopy or cellular network expert; Therefore, it is possible that the points listed below are addressed in the text in a manner that is clear to experts. However, if the paper is to be available to most people interested in the topic these issues must be, in my opinion, clearly discussed.

a. The images were obtained using TEM, but no details are provided regarding the method of sample preparation. Was this done in an aqueous environment? Dried? Cryo-TEM? The methodology of sample preparation in this case is essential, since the structure of a network is significantly different in the presence or absence of a solvent (water) (see any basic polymer textbook that has a chapter on gels). Thus, such parameters as the fibril length or the density distribution as measured from the micrographs may be inapplicable to the water-swollen network.

b. Microscopy is a useful tool, and can provide some insights into the properties of networks and gels. However, it is very limited in scope and accuracy. Important parameters such as the network elastic (Young) modulus, for example, cannot be determined from microscopic image analysis. Yet, the network modulus is an important parameter for issues in synthetic tissue and implants such as cell adsorption, as listed below. Therefore, I find this study partial at best and the results not very illuminating.

(see for example, Study on physical properties and nerve cell affinity of composite films from chitosan and gelatin solutions
Author(s): Cheng MY, Deng JU, Yang F, Gong YD, Zhao NM, Zhang XF
Source: BIOMATERIALS 24 (17): 2871-2880 AUG 2003,
Polyelectrolyte multilayers with a tunable Young's modulus: Influence of film stiffness on cell adhesion LANGMUIR 22 (3): 1193-1200 JAN 31 2006
Cell organization in soft media due to active mechanosensing
Author(s): Bischofs IB, Schwarz US

c. In Figure 6 it seems to me that the results for the two systems- nanoparticle and control- are within the standard deviation of each other, and are thus not statistically significant.

3. The authors develop a method for image analysis. It will be useful to compare to similar works (see, for example Quantification of biopolymer filament structure
Author(s): Shah SA, Santiago P, Rubin BK
Source: ULTRAMICROSCOPY 104 (3-4): 244-254 OCT 2005

Quantitative analysis of keratin filament networks in scanning electron microscopy images of cancer cells
Author(s): Beil M, Braxmeier H, Fleischer F, Schmidt V, Walther P
3. Are the data sound and well controlled?
No (see 3).

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?
Moderate.

6. Do the title and abstract accurately convey what has been found?
Yes

7. Is the writing acceptable?
Yes

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests