Synovial membrane: reaction to collagen scaffold implanted into the articular cartilage.

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Keywords: synovial membrane, scaffold, biomaterials, synoviocytes.

Background: Biomaterials are conceptually divided into three different types according to the response they provoke in cells and tissues: inert, bioactive and biodegradable materials (Hence & Polak, 2002). Hyaline articular cartilage is the tissue that most frequently needs to be repaired or replaced during life and several biomaterials have been proposed and tested on this tissue. Interestingly, the articular cartilage does not contain blood and lymphatic vessels and nerves, and receives nutrients and cytokines by diffusion from the overlying synovial membrane. Therefore, the synovial membrane is the reactive tissue that can manifest the effects of a biomaterial inserted into the articular cartilage.
Aim: To study the biocompatibility and biodegradability of a peculiar collagen scaffold to be used to repair the articular cartilage, by examining the reaction of invitro human macrofages and of the rabbit synovial membrane after different times of contact with the scaffold.
Material and Methods. Scaffolds made of horse collagen type I (75%) (from Achille's tendon) and type II (25%) (from trachea) (Opocrin-Corlo, Formigine-Modena-Italy) were either used as substrate for culturing J111 human macrophages or implanted into the articular cartilage of the medial femoral condyle in adult rabbits. Sham operated contro-lateral paws were used as the controls. Macrophage structure and cytokines produced by were analyzed after 24 and 48 hr. Synovial membranes were taken from sacrificed rabbits after 2 days, 3, 6 and 9 months since the insertion of the collagen scaffold and examined by light and electron microscopy.
Results: The scaffolds of mixed horse collagen type I and II were not immunogenic, as they allowed macrophages to adhere and grow without appreciable production of interleukin 1 and 12 (Fig.1). The structural organization of macrophages was normal after 48 hr contact. As to the synovial membrane, the surgical intervention induced an inflammatory response with increase of the number of macrophages and of dilated vessels in both the subintima and the subsynovia during the first three month from the intervention. Later, with age, there was a slight increase of the multilayered cell areas in the superficial lining and an increase of collagen in the subintima and in the subsynovia, with no clear signs of inflammation.
The synovial membranes of the articular joints receiving the collagen scaffolds did not reveal dramatic changes compared to the age-matched controls. Signs of inflammation were present during the first 3 months (Fig.2), which later were less evident. By contrast, with time, there was an increase of the areas of the superficial lining with multilayered synoviocytes and a well evident vascular network in the underlying connective tissue. Moreover, synoviocytes, especially those with macrophage appearance (type A), exhibited a high number of lysosomes containing electron dense material. After 6 and 9 months from implantation, the multilayered lining and the slight increase of the number of cells and vessels in the subintima

DOI: 10.3217/978-3-85125-062-6-264,

and in the subsynovia, compared to age matched controls, were indices of a light permanent inflammatory process. In a number of sections debris of collagen scaffold were also present.
Conclusions: Scaffolds made of mixed collagen type I and type II from horse were shown to be not dramatically immunogenic when assayed on human macrophages and in vivo in the articular joint of rabbits. Moreover, EM observations indicate that scaffolds are degraded and ingested by macrophages. This could suggest that these scaffolds might be used “to lodge" and "to implant" stem cells, and that macrophages might cooperate to release cells without eliciting a strong inflammatory process.

1. Hench LL., Polak JK. Science **295** (2002) p1014-7.
2. This research was supported by Opocrin. The aid of Bruna Parma is gratefully acknowledged.

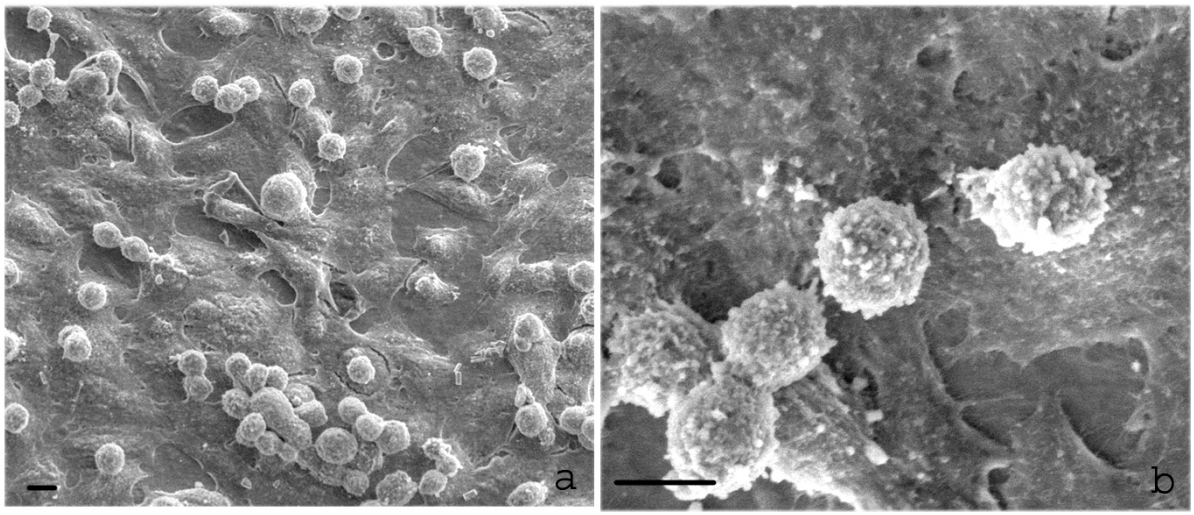

Figure 1: Macrophage scattered on C2T25 collagen membrane observed by ESEM. A: macrophages were identifiable as round cells and they were numerous (bar 1μ). B: Cells was covered with developed microvilli and microplicae (bar 1μ).

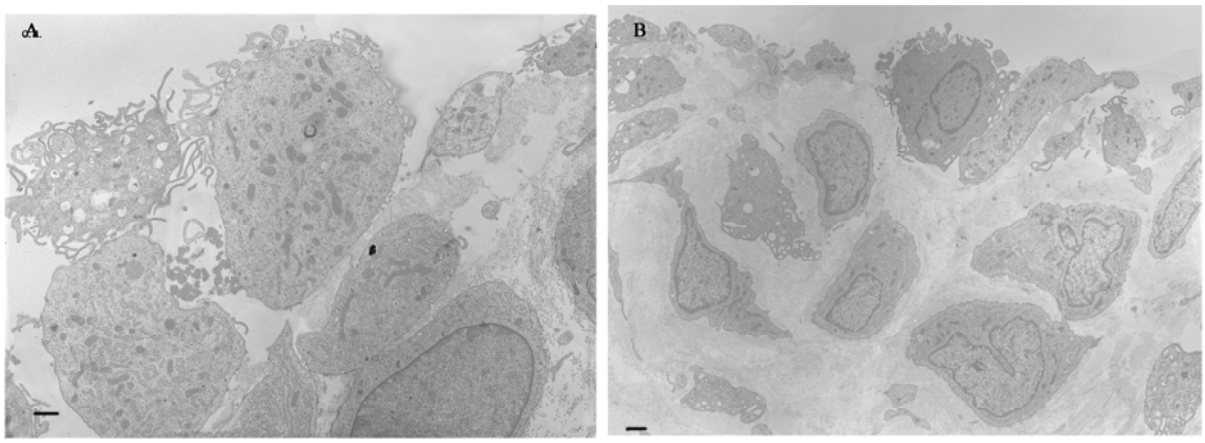

Figure 2: Synovial membrane after two days by implant with collagen scaffold observed by TEM. A: control rabbit, cells display an epithelium like nature (bar 1μ). B: treat rabbit, cells was broadly distributed throughout the lining (bar 1 μ).

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