

**XV Congresso Nazionale della SOCIETA' ITALIANA DI RICERCHE  
CARDIOVASCOLARI (SIRC)  
Imola (BO), 9 - 11 ottobre 2008 - Fondazione Cassa di Risparmio di Imola**

**Title** DEVELOPMENT OF A NEW TECHNOLOGY FOR 3-D NANOSTRUCTURED SCAFFOLDS WITH POTENTIAL CARDIOVASCULAR APPLICATIONS

**Authors:** Monica Lemmi, Enrica Briganti, Angela Magera, Roberta Arici, Chiara Ristori, Elisa Simonetti, Federica Chiellini, Giorgio Soldani, Alberto Balbarini, Rossella Di Stefano

**Aims** The *in situ* release and maintaining of cells to promote revascularization is a new goal of cardiovascular therapy. Endothelial progenitor cells (EPC) may contribute to the process of vascular repair. Medical devices realized according to tissue engineering are composed by a cellular component and by an artificial component, usually made of a biocompatible polymer. Scaffolds may be coated with bio-polymers like fibrin to enhance cell adhesion and growth.

Aim of this study was to realize nanocomposite 3D scaffolds composed by a synthetic polymer coated with fibrin to support EPC growth and to promote *in vivo* angiogenesis.

**Methods** 3D PEtU-PDMS scaffolds were studied *in vitro* for their biocompatibility (viability and proliferation tests; cytokine release). *In vivo* biocompatibility was studied by intramuscular implant in a rabbit model. The scaffolds were fabricated by spray-phase inversion technique. 25U/mL thrombin was sprayed during the fabrication process. The composite scaffold was then incubated o.n. at 37°C with 18mg/mL fibrinogen. The scaffold morphology was analysed by stereomicroscopy and by scanning electron microscopy (SEM).

EPC obtained from peripheral blood were cultured for 1 week on the scaffolds at the concentration of  $1 \times 10^6$  cell/ml. Fibronectin coating was used as a control. Cell viability was assessed by confocal laser (Calcein-AM incorporation).

To test *in vivo* angiogenesis, EPC-seeded scaffolds were subcutaneously implanted into the back of rats for 14 days. After harvesting, the scaffolds were examined histologically and immunohistochemically to evaluate inflammatory response and neovascularization.

**Results** *In vitro* and *in vivo* biocompatibility data demonstrated absence of any cytotoxic effect, immunocompatibility and a slight inflammatory reaction without any sign of encapsulation and implant rejection. Morphological analyses showed an homogeneous fibrin coating of the scaffolds, tightly bound and interconnected to the PEtU-PDMS surface. SEM showed the presence of a well organized layer of fibres in a nm scale (mean diameter ~140nm). Cell viability and phenotype were not affected when EPC were seeded on PEtU-PDMS/fibrin scaffolds. The histological observation of explanted scaffolds revealed a slightly inflammatory response and a significant increased numbers of neovessels in tissues surrounding the EPC-seeded scaffold as compared to the scaffold without cells.

**Conclusions** Our data suggest that PEtU-PDMS/fibrin scaffold obtained with a new spray manufacturing technology can support *in vitro* EPC growth and promote *in vivo* neovascularisation. Further studies are currently under way in an ischemic hindlimb rat model.