

## **How use micro structured scaffolds and nano tags to control cell differentiation and improve tissue regeneration**

**Jose Iñaki Alava**, Nerea Garagorri, Patricia Gracia Parra.

Tecnalia Research and Innovation Co. Ciber BBN, ITUS-INASMET group, Paseo Mikeletegui 2, San Sebastián –Donostia, 20009 SPAIN  
inaki.alava@tecnalia.com

Furthermore, the extracellular matrix plays a key role in controlling the differentiation of progenitor cells into the cell lines that will be replaced. Depending on the signals that these cells receive from their environment, their capacity for differentiation is enhanced or limited. In last 15 years, many researchers have tried to control neural growth and differentiation by using a wide range of approaches - micropatterned scaffolds [1], conductive biomaterials [2], electrospinning [3] and many others [4,7,8,9]. The appearance in 2002-2003 of new micro-technologies such as microcontact printing and others in the field of neurobiology, (we will comment on them in the next paragraph) have led to competition aimed at obtaining optimum micro (or nano) patterning of guidance molecules for neural cell growth and differentiation [4].

With the appearance of nanotechnology on the scene, the biocompatibility and special properties of some nanoparticles have led to the use of single wall carbon nanotubes in cell cultures [5] as a way of improving neural signal transfer [6]. In 2006, multiple-channel biodegradable scaffolds were used to promote spinal cord regeneration [7] with Schwann-cells as feeder-cells

The ability to replicate patterns at the micro to nanoscale is crucially important for the progress of micro and nanotechnologies and the study of nanosciences. The planar manufacturing technology used by the semiconductor industry means that integrated circuits are built by stacking one layer of circuit elements on top of another. Each layer is manufactured according to a sequence of well-characterized processes. Lithography is used over and over again to create desired patterns in all these processes. Considerable industrial effort has been devoted to the leading-edge optical methods and the so-called next generation lithography (NGL) techniques, exposing the material to energy beams from UV, electron beam, ion-beam or x-ray sources. However, there are many other non-traditional microelectronic applications that require nanoscale features and demand low-cost nano and micro patterning technologies. One of the main areas is the biological field, with applications in micro and nanofluidic devices for labs-on-a-chip, biosensors, DNA or protein arrays and the alignment of biomaterials for cell patterning or tissue engineering related applications. Surfaces with micro and nanopatterns are being used as cell culture substrates to develop new assays for monitoring cell adhesion and cell proliferation or differentiation on different surfaces [10,11].

Patterned surfaces and their chemical landscape provide cues for cells to attach, migrate and assemble into functioning tissue. Tissue engineering is a multidisciplinary/interdisciplinary field that applies the principles of biology and engineering to develop tissue substitutes that restore, maintain, or improve the function of diseased or damaged human tissues. One approach to tissue engineering involves seeding biodegradable polymeric scaffolds with donor cells and/or growth factors and then culturing and implanting the scaffold to induce and direct the growth of new, healthy tissue. Unfortunately, current polymeric biodegradable scaffolds have several drawbacks: However, most biodegradable polymers being used in clinical practice do not exhibit clearly biocompatible behaviour and their mechanical properties are usually not enough to allow them to be used for load bearing parts of the body. No single material, however, can satisfy all the goals required for creating optimum scaffolding. On the other hand, the extra cellular matrix (ECM) is a complex and strange material. In fact, is impossible for a single material to mimic all ECM properties. A composite multi-material matrix is the natural solution to the different requirements of the wide range of ECMs needed for tissue regeneration [12]. Therefore, the incorporation of nanoparticles such as carbon nanotubes or carbon nanofibers and nanohidroxiapatite to the polymer matrix for increasing the safety of the polymer appears to be very important [13]. We show some examples of micro-structured scaffolds, with nano-tags (molecular signals), that may be used for cell differentiation and tissue repair.

## References

- [1] Schmalenberg, K.E., Uhrich, K.E., *Biomaterials* 26, (2005), 1423-1430
- [2] George, P.M., Lyckman A.W., LaVan, D.A., Hegde, A., Leung, Y., Avasare, R., Testa, C., Alexander, P.M., Langer, R., Sur, M., *Biomaterials*, 26, ,(2005), 3511-3519
- [3] Yang, F., Murugan, R., Wang, S., Ramakrishna, S., *Biomaterials*, 26, (2005), 2603-2610.
- [4] Oliva, A.A. Jr, James C.D., Kingman, C.E., Craighead, H.G., Banker, G.A., *Neurochemical Research*, Vol 28, (2003), 11,1639-1648.
- [5] Gheih, M.K., Sinani, V.A., Wicksted, J.P., Matts, R.L., Kotov, N.A. *Adv. Mater.* 17, (2005), 2663-2670.
- [6] Lovat, V. Pantarotto, D., Lagostena, L., Cacciari, B., Grandolfo, M., Righi, M., Spalluto, G., Prato, M., Ballerini, L. *Nano Letters*, Vol 5, 6, (2005), 1107-1110.
- [7] Moore, M.J., Friedman J.A., Lewellyn, E.B., Mantila, S.M., Krych, A.J., Ameenuddin, S., Knight, A.M., Lu, L., Currier, B.L., Spinner, R.J., Marsh, R.W., Windebank, A.J., Yaszemski, M.J., *Biomaterials*, 27, (2006), 419-429.
- [8] Recknor, J.B., Sakaguchi, D.S., Mallapragada, S.K., *Biomaterials* 27. (2006), 4098-4108.
- [9] Tsai, E.C., Dalton, P.D., Shoinet, M.S., Tator C.H., *Biomaterials*.27. (2006), 519-533
- [10] Falconnet D. et al., *Biomaterials* 27, (2006) 3044-3063.
- [11] Zhang SG, et al, *Biomaterials* 20, (1999), 1213-20.
- [12] Alava, J.I., Jurado, M.J., García, A., and Murua O. *Joint Meeting of the Tissue Engineering Society International and the European Tissue Engineering Society, Congress Abstracts, Lausanne, Switzerland, (2004).*
- [13] Meike van der Zande, Balaji Sitharaman, X. Frank Walboomers, Lesa Tran, Jeyarama S. Ananta, Andor Veltien, Lon J. Wilson, Jose Inaki Alava, Arend Heerschap, Antonios G. Mikos, and John A. Jansen. *Tissue Engineering: Part C* Volume 17, Number 1, (2011), 19-26