

## Restoration versus reconstruction: how cell anatomy and extra-cellular matrix influence tissue regeneration

Dario Coletti<sup>1,2</sup>, Laura Teodori<sup>3</sup>, Zhenlin Li<sup>2</sup>, Jean Francois Bernaudin<sup>4</sup> and Sergio Adamo<sup>1</sup>

<sup>1</sup> Sapienza University of Rome, Department of Anatomical, Histological, Forensic & Orthopaedic Sciences, Section of Histology & Medical Embryology, 00161, Rome, Italy and Interuniversity Institute of Myology

<sup>2</sup> UPMC Univ Paris 06, UR4 Ageing, Stress, Inflammation, 75005, Paris, France

<sup>3</sup> ENEA-Frascati, UTAPRAD-DIM, Diagnostics and Metrology Laboratory, 00044 Rome, Italy

<sup>4</sup> UPMC Univ Paris 06, Hôpital Tenon, Histology and Tumor Biology, 75020, Paris

Tissue regeneration replaces damaged cells and is involved in tissue remodeling. In order to investigate the existence of a leitmotif of tissue regeneration, we compared the cellular aspects of regeneration of epidermis, neurons and skeletal muscle, characterized by different types of histological and functional organization. Following damage, all the tissues here analyzed go through three phases: inflammation, regeneration and maturation. Another common feature is the occurrence of cellular de-differentiation and/or differentiation events, including gene transcription, which are typical of embryonic development. Nonetheless, various strategies are used by different tissues to replace their lost parts. The epidermis regenerates *ex novo*, whereas neurons restore their missing parts; muscle fibers use a mixed strategy, based on the regrowth of missing parts through reconstruction by means of newborn fibers. The choice of either strategy is influenced by the physical, chemical and structural features of the cells as well as by the extracellular matrix typical of a given tissue, which points to the existence of differential, evolutionary-based mechanisms for specific tissue regeneration. Taking skeletal muscle as a model, we present evidence about the importance of the fiber niche to direct and favour tissue regeneration, a phenomenon of particular relevance for highly hierarchized tissues such as striated muscles. Niche properties are accounted for by cell-cell contacts, cell-matrix interaction and paracrine effects in skeletal muscle. The ordered sequence of steps that characterizes the regeneration processes, shared by several tissues, suggests it may be possible to model this extremely important phenomenon to improve guided *in situ* regeneration interventions.

### References

Coletti et al. (2013) BMC Regenerative Medicine Research, in press.

### Key words

tissue regeneration, stem cells, extracellular matrix, Vasopressin, Tumor Necrosis Factor.