Unlike other tissues, the regeneration in the central nervous system during adulthood is limited due to the lack of neurogenic niches and the toxic microenvironment after an injury or degenerative disease. For this reason, the loss of neuronal populations and axonal connexions results in most cases irreversible. Nowadays, there are therapies focused on the regeneration of the central nervous system after an injury or disease, and they consist in cell implantation, drug delivery and electrical stimulation using electrodes. Despite these methods have shown some improvements in the regeneration and the recovery of the loss functions, they do not produce complete recovery of the loss functions or are transient. In the present work, the efforts have been focused on the development of structured materials (scaffolds) to provide a support for the different cells from the central nervous system, especially, from the brain tissue after stroke or similar damages. Besides, these materials could act as vehicles for cells being a neuronal source and/or growth factors providing substances to create a more permissive environment for axon regrowth.

In this work, the scaffolds are mainly composed of the sodium salt of hyaluronic acid, hyaluronan. This material has been chosen because of its natural origin in many tissues, including the brain one. Besides, some formulations based on hyaluronan and derivatives thereof are currently employed in clinical applications, and they have shown good biocompatibility and similar properties to the brain tissue. However, the unmodified hyaluronan have shown short residence times in the physiological environment because of its high solubility and fast degradation rate, lack of the control over mechanical properties, high swelling degree and hard handling to develop structured materials. In the present work, in order to develop stable and structured hydrogels, the hyaluronan has been modified following two strategies: crosslinking with divinyl sulfone, and the copolymerization of a hyaluronan derivative with ethyl acrylate to develop semi-degradable copolymer networks.

The crosslinking of hyaluronan with divinyl sulfone has been characterized by physical, mechanical and chemical methods with the aim of determining the effect of the degree of crosslinking on the properties of the hydrogels. This chemistry has been employed to develop porous scaffolds by a repetitive method. Besides, the posterior treatments after the crosslinking reaction have been evaluated in terms of their effect on the enzymatic degradation. On the other hand, the cytotoxic and inflammatory effects of these materials on different types of cells from the central nervous system environment (astrocytes, neurons and endothelial cells) have been studied. Moreover, the influence of the degree of crosslinking on the initial colonization of these cells has been evaluated.

The copolymer networks based on hyaluronan and poly(ethyl acrylate) have been synthesized with the aim of developing novel semi-degradable materials, which combine the biological properties of hyaluronan and good compatibility of poly(ethyl acrylate) with different cells, including those of the central nervous system. However, the use of hyaluronan in polymerization reactions required its previous modification, and hence the degree of modification was determined after synthetizing the hyaluronan derivative. Moreover, the opposite properties of both materials permit to obtain copolymer networks with tuneable mechanical properties and swelling degree in aqueous environments. The experimental composition of each component, as well as some physical and mechanical properties were determined by the appropriate methods in each case. Besides, the enzymatic degradation of the copolymer networks was evaluated, determining the scissed fragments and the structural stability of the different materials with the aim to guarantee the integrity of the materials through a hypothetical regenerative process. On the other hand, the cytotoxic and inflammatory effects of these materials on cells from the central nervous system environment were evaluated. Additionally, preliminary studies of cell colonization on the copolymer networks were performed.