HYALURONIC ACID GRAFTING MODULATES THE BIOTOLERABILITY OF NEW ELECTRODE ARRAYS FOR CEREBRAL APPLICATIONS DEVELOPED IN THE FRAMEWORK OF THE NEUROPROBES PROJECT

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Intracortical electrodes could provide new directions of therapy for several central nervous system diseases and are of great interest for neuroscience research. The NeuroProbes Integrated Project aims to develop a new generation of highly biocompatible 3D arrays of multifunctional microprobes for high temporal and spatial resolution brain studies that include freely moving subjects. This project is not limited to guaranty the non-toxicity of the arrays, but also encloses the optimization of the physical and chemical surface properties for long term biotolerability.

This study was designed to investigate the effects of coating the silicon based neural probes by a constituent of the extracellular matrix, namely hyaluronic acid (HYA). The HYA was chemically functionallised with reactive S-S-Pyridin groups. In parallel, three different types of silicon samples with different degree of oxidation were derivatized by merkaptopropyldimethoxisilane, terminated by thiol groups. The samples were then exposed to the modified hyaluronic acid and tested in vitro with three different cell lines (neurons, glial cells and fibroblasts). Furthermore we implanted HYA coated probes in the cerebral cortex of rabbits for up to 1 month. The implanted sites were removed and processed by immunocytochemical techniques. Digital images were collected for each stained sample and analyzed using a computer-assisted image analysis program.

Our *in vitro* results show a preferential growth of neuron cells onto the HYA treated surfaces independently of the degree of oxidation of the original surface. The growth of glial cells and fibroblasts was less influenced by the surface coating. The *in vivo* results showed a limited glial proliferation around probe tracks. The absence of hemorrhages in chronic experiments indicates that injury to the blood vessels occurs early and that it is usually limited. Although the coating of the neural probes with HYA did not have clear and significant effects on neuronal density on the proximity to the electrode surface, it seems that coated probes have a reduction in GFAP staining compared with control uncoated probe sites. These results show that the new multiple intracortical microelectrodes can be used in long-term studies and suggest that, although more studies are needed, the coating of Si probes surfaces with HYA could help to improve long-term biotolerability.