



Seminarios internos del IBFG

Brain neovascularization mediated by p53 signaling pathway determines functional recovery after intracerebral hemorrhage

Cristina Rodríguez

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Salón de actos del IBFG

Intracerebral hemorrhage (ICH) is the most severe type of stroke and associates with high mortality rates and risk of disability of affected patients. So far there is no effective treatment, which, added to the lack of accurate prognosis, evidences the need to deepen the mechanisms that regulate brain repair after ICH. We previously showed that the human *Tp53 Arg72Pro* polymorphism modulates brain endothelial cells survival after ICH, which is essential for the secretion of growth factors and cytokines (i.e. VEGF) that mediate the mobilization of endothelial progenitor cells (EPCs) from the bone marrow to the peripheral blood. EPCs promote brain vascular repair after ICH. Then, pro-apoptotic p53 would be a negative regulator of EPC mobilization, thus affecting the functional outcome after ICH.

Since p53 is accumulated in the brain after ICH, we speculate that p53 destabilization not only will promote cell survival, but also vascular recovery and brain repair. To confirm this hypothesis, p53 KO mice were subjected to an experimental model of ICH *in vivo* by injecting bacterial collagenase into the basal ganglia. Proliferative markers and perfusion status of newly-formed blood vessels in the brain were also analyzed. Thus, we observed that loss of p53 reduced lesion volume and increased levels of circulating EPCs. As a consequence, an improved vascular response was achieved in p53 KO mice, in comparison with those expressing an active p53 protein.

Our results point out the impact of the p53 signaling pathway in the balance between brain damage and repair, which might condition functional recovery after ICH.