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Combined oxaloacetate and dehydroepiandrosterone treatment: a new neuroprotective startegy

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Stroke is accompanied by the development of neuronal and functional loss. Under ischemic brain pathological conditions interstitial glutamate (Glu) concentration increases to an excitotoxic level. Decreasing blood Glu concentration enhances the brain-to-blood efflux of Glu. The so called Glu scavenging from the brain moderates Glu excitotoxicity which contributes to the neuronal loss and long-lasting neurological deficits seen in stroke. Inflammatorical events take place in the affected area a few days after the excitotoxic period. In the aspect of therapeutic window Glu scavenging has to be done immediately after ischemic insult whereas antiinflammatory treatement is effective in the following 48 hours after cerebral ischemia.

4VO (four-vessel occlusion) as a global cerebral ischemic model was used to evaluate the neuroprotective effects of oxalocetate (OxAc) as a Glu scavenger and Dehydroepiandrosterone (DHEA) as antiinflammatic agent and the combined treatement.

ECoG recordings were carried out for the validation of the global ischemic intervention and for the detection of the effect of OxAc on post-ischemic ECoG pattern and on Burst-Supression ratio (BSR). Furthermore, power spectral density (PSD) and changes in ratio of frequency bands were measured. *In vitro* extracellular field-EPSP amplitudes were measured, LTP induction and I/O curves were recorded in the CA1 subfield of rat hippocampal brain slices.

FlouroJade C staining was used to visualize the degenerated CA1 neurons, Cresil-violet staining was used to estimate the thickness of the CA1 pyramid cell layer.

OxAc (20mg/100g bw) administered right after the ischemic insult decreased the formation rate of post-ischemic ECoG pattern. In the in vitro experiments both OxAc (20mg/100g bw) and DHEA (2mg/100g bw) resulted in a mild increase of the impaired synaptic plasticity in the CA1 region. The combined OxAc mediated glutamate scavenging and the DHEA treatement together were able to moderate the ischemic damage in the 4VO group and increased synaptic plasticity.

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The biosynthetic pathway of PGE2 and its role in the virulence of *Candida parapsilosis*

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Candida parapsilosis is often the second most commonly isolated *Candida* species from blood cultures, and it even outranks *Candida albicans* in some European, Asian, and South American hospitals. *C. parapsilosis* is an opportunistic human pathogen, that can colonize and cause disease on immuno-compromised patients (with AIDS, organ transplantation ect.) or in particular patient groups such as neonates or elders

Despite the increasing clinical importance, little is known about the virulence factors of *C. parapsilosis*. Thus, in our recent study we investigated the biosynthetic pathway of prostaglandin E2 (PGE2), a putative virulence factor of *C. parapsilosis*. Prostaglandins are fatty acid metabolites build up of 20 carbon atoms. Mammalians produce immune response regulator prostaglandins from arachidonic acid by the contribution of *COX1* and *COX2* cyclooxigenases. Although fungi do not possess cyclooxigenase homologes, several pathogenic species are able to produce prostaglandins from host originated arachidonic acids. In case of *C. albicans* the fatty acid desaturase homolog ole2 and the multicopper oxidase homolog fet3 enzymes were identified as potential key factors of the prostaglandin biosynthetic process. Due to its ability to block Th1-type, and promote Th2-type immune response, fungal Prostaglandin E2 can move the host's immune response towards helping the fungi to colonize and to carry out chronic inflammation. In our recent study we investigated the role of the putative fatty acid desaturase CpOle2 in the prostaglandin biosynthesis of the emerging human pathogen *C. parapsilosis*. We generated a homozygous *OLE2* deletion mutant through repeated application of a caSAT1 flipper KO cassette. We characterized the pseudohypha production, FBS utilization ability, growth ability on different pH and temperature of the *OLE2* deletion mutant in comparison to that of the wild type strain and we found that mutant strain showed the same characteristics as the wild type. First we characterized the prostaglandin profile of *C. albicans* and *C. parapsilosis* with HPLC and it showed that *C. parapsilosis* do produce PGE2, similarly to *C. albicans*, from the supplemented arachidonic acid. Than we purified *C. albicans* and *C. parapsilosis* PGE2 and we examined the immune modulating effect of these purified prostaglandins on human peripheral blood mononuclear cells derived macrophages (PBMC-DM) with the help of qRT-PCR. When the PGE2 production of *C. albicans* SC5314 and *C. parapsilosis* GA1 wild type, *CpOLE2* heterozygous deletion *(ole2 /OLE2)* and homozygous deletion mutant *(ole2 /ole2)* was measured after the treatment of arachidonic acid by Enzyme-linked immunosorbent assay