

Poster presentation

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## LPS-induced down-regulation of NO-sensitive guanylyl cyclase in astrocytes occurs by proteasomal degradation in nuclear bodies

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### Background

We have previously shown that inflammatory agents (LPS, IL-1 $\beta$ ,  $\beta$ -amyloid peptides) that induce reactivity and NOS-2 expression in glial cells down-regulate astroglial soluble guanylyl cyclase (sGC) *in vitro* and *in vivo* [1,2].

### Results

Here we show that the decrease in sGC activity and  $\beta$ 1 subunit protein induced by LPS (10 ng/ml, 24 h) in cultured rat cerebellar astrocytes is prevented by inhibitors of proteasome activity (MG132 5  $\mu$ M; lactacystin 10  $\mu$ M) whereas other protease inhibitors (calpain inhibitor 25  $\mu$ M; ICE inhibitor II 100  $\mu$ M and leupeptin 5  $\mu$ M) were not effective. Furthermore, immunocytochemistry and confocal laser microscopy revealed that in LPS-treated cells a strong sGC  $\beta$ 1 immunoreactivity is evident in aggregates in the cell nuclei where it co-localizes with 20S proteasomes and ubiquitin in clastosomes, nucleoplasmic substructures involved in ubiquitin-proteasome-dependent nuclear proteolysis, but do not colocalize with others proteasome-enriched structures include promyelocytic leukaemia bodies and splicing speckles. In contrast, in untreated astrocytes clastosomes are scarce and sGC  $\beta$ 1 immunoreactivity shows a diffuse cytoplasmic pattern, while in the nucleus it is very weak. A similar distribution is observed when cells are treated with LPS and the protea-

some inhibitor MG132 or the protein synthesis inhibitor cycloheximide.

### Conclusion

LPS orchestrates the recruitment of sGC- $\beta$ 1 protein and components of the ubiquitin-proteasome system to specialized nuclear bodies, clastosomes, suggesting a mechanism for inflammation-induced down-regulation of sGC in astrocytes.

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### References

1. Baltrons MA, Pedraza CE, Heneka MT, García A:  **$\beta$ -Amyloid peptides decrease soluble guanylyl cyclase expression in astroglial cells.** *Neurobiol Dis* 2002, **10**:39-149.
2. Pedraza CE, Baltrons MA, Heneka MT, García A: **Interleukin-1 $\beta$  and lipopolysaccharide decrease soluble guanylyl cyclase in cells of the CNS: NO-independent destabilization of protein and NO-dependent decrease of mRNA.** *J Neuroimmunol* 2003, **144**:80-90.