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Oral presentation

NO-sensitive guanylyl cyclase β1 subunit interacts with chromosomes during mitosis: novel role in the regulation of chromatin condensation

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Background

NO-sensitive guanylyl cyclase (GC_{NO}), the major NO target, exists as an obligate heterodimer of one α and one β subunit. Two types of each subunit have been cloned (α1–2, β1–2), but only β1 and α subunit expression has been reported in the CNS. In this tissue, in situ hybridization studies have shown that β1 is more widespread than α subunits and in some areas is the only GC_{NO} subunit expressed [1]. Since β1/β1 homodimers are catalytically inactive the possibility of β1 having functions other than GC_{NO} activity has been suggested. GC_{NO} is predominantly cytosolic, however recent studies suggest that it can associate to membranes and other intracellular structures including nuclei [2,3].

Results

In the course of our studies on the cellular and sub-cellular distribution of GC_{NO} subunits in CNS glial cells we have found that the β1 subunit is localized in the cytoplasm and the nucleus in cells that also express α subunits and present GC_{NO} activity (astrocytes), as well as in cells devoid of α subunits and GC_{NO} activity (microglia). In both cases GC_{NO} β1 associates peripherally to chromosomes in all phases of mitosis and appears to regulate mitotic chromatin condensation independent of cGMP formation. Moreover, silencing by siRNA increases the percentage of cells in the S phase of the cell cycle and enhances proliferation.

Conclusion

The GC_{NO} β1 subunit associates to chromosomes during mitosis and regulates chromatin condensation and cell cycle progression decreasing cell proliferation. This actions of GC_{NO} β1 are independent of NO-dependent cGMP formation.

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