Permeation of molecules through astroglial connexin 43 hemichannels is modulated by cytokines with parameters depending on the permeant species

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Recent studies indicate that connexin hemichannels do not act as freely permeable non-selective pores, but they select permeants in an isoform-specific manner with cooperative, competitive and saturable kinetics. The aim of this study was to investigate whether the treatment with a mixture of IL-1? plus TNF-?, a well-known pro-inflammatory condition that activates astroglial connexin 43 (Cx43) hemichannels, could alter their permeability to molecules. We found that IL-1? plus TNF-? left-shifted the dye uptake rate vs. dye concentration relationship for Etd and 2-NBDG, but the opposite took place for DAPI or YO-PRO-1, whereas no alterations were observed for Prd. The latter modifications were accompanied of changes in Kd (Etd, DAPI, YO-PRO-1 or 2-NBDG) and Hill coefficients (Etd and YO-PRO-1), but not in alterations of Vmax. We speculate that IL-1? plus TNF-? may distinctively affect the binding sites to permeants in astroglial Cx43 hemichannels rather than their number in the cell surface. Alternatively, IL-1? plus TNF-? could induce the production of endogenous permeants that may favor or compete for in the pore-lining residues of Cx43 hemichannels. Future studies shall elucidate whether the differential ionic/molecule permeation of Cx43 hemichannels in astrocytes could impact their communication with neurons in the normal and inflamed nervous system.

Astrocytes

Connexons

Dyes

IL-1?

Permeability tracers

Permeation

TNF-?

calcium ion

connexin 43

cytochrome b

cytokine

divalent cation

glucose transporter 1

interleukin 1beta

magnesium ion

nucleic acid

tumor necrosis factor

animal experiment

Article

astrocyte

binding site

cell proliferation

confocal microscopy

controlled study

fluorescence imaging

fluorescence microscopy

genetic transfection

IC50

immunofluorescence microscopy

inflammation

male

microglia

modulation

mouse

nervous system inflammation

nonhuman