Molecular mechanisms involved in the protective actions of Selective Estrogen Receptor Modulators in brain cells

Baez-Jurado E.

Rincón-Benavides M.A.

Hidalgo-Lanussa O.

Guio-Vega G.

Ashraf G.M.

Sahebkar A.

Echeverria V.

Garcia-Segura L.M.

Barreto G.E.

Synthetic selective modulators of the estrogen receptors (SERMs) have shown to protect neurons and glial cells against toxic insults. Among the most relevant beneficial effects attributed to these compounds are the regulation of inflammation, attenuation of astrogliosis and microglial activation, prevention of excitotoxicity and as a consequence the reduction of neuronal cell death. Under pathological conditions, the mechanism of action of the SERMs involves the activation of estrogen receptors (ERs) and G protein-coupled receptor for estrogens (GRP30). These receptors trigger neuroprotective responses such as increasing the expression of antioxidants and the activation of kinase-mediated survival signaling pathways. Despite the advances in the knowledge of the pathways activated by the SERMs, their mechanism of action is still not entirely clear, and there are several controversies. In this review, we focused on the molecular pathways activated by SERMs in brain cells, mainly astrocytes, as a response to treatment with raloxifene and tamoxifen.

Astrocytes

Brain pathologies

Estrogen receptors

GRP30

SERMs

Tamoxifen

afimoxifene

cre recombinase

droloxifene

drug metabolite

endoxifen

estrogen receptor

G protein coupled receptor 30

hydroxytamoxifen

inositol 1,4,5 trisphosphate receptor

inositol 1,4,5 trisphosphate receptor 2

Notch1 receptor

raloxifene

selective estrogen receptor modulator

tamoxifen

unclassified drug

estrogen receptor

neuroprotective agent

selective estrogen receptor modulator

astrocyte

brain cell

brain damage

cell differentiation

cell fate

cell function

cell interaction

central nervous system disease

drug mechanism

drug response

human

LoxP site

memory

microglia

nerve cell

nervous system inflammation

neural stem cell

neuroprotection

nonhuman

priority journal

Review

animal

brain disease

drug effect

metabolism

Animals

Astrocytes

Brain Diseases

Humans

Neuroprotective Agents

Raloxifene Hydrochloride

Receptors, Estrogen

Selective Estrogen Receptor Modulators

Tamoxifen