Subject: Finasterid-neuroprotektiv-schützt vor neurodegenerativen Krankheiten?
Posted by fixt on Thu, 29 Nov 2007 15:42:48 GMT
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We've speculated often here that because of its (weak) inhibition of brain 5AR type I, finasteride may have deleterious effects on the brain that are mediated by some sort of allopregnanalone deficiency. Seemingly in opposition to this, following patent document claims that finasteride actually has neuroprotective effects:

http://www.wipo.int/pctdb/en/wo.jsp?IA=WO2006058781&wo=2 006058781&DISPLAY=DESC

"Due to these previously unknown neuroprotective effects, Finasteride, Dutasteride and related compounds are suitable as cytoprotective and particularly neuroprotective drugs and new lead structures for the development and optimization of new therapeutic compounds."

"Whereas control cells had a surviving rate 4.8 ± 3.4% (number of cells at first stimulation: 189 and number of cells at second stimulation after chemical ischemia: 9), Finasteride-treated (1 uM) cells had a surviving rate of 72.1 ± 4.4%..."

2.7 Conclusions

Our results clearly show that Finasteride, Dutasteride and related compounds can exert neuroprotective effects in different experimental paradigms, related to human neurodegenerative diseases and conditions, like epilepsy, Morbus Alzheimer, Morbus Parkinson and others, via a novel mechanism which involves voltage-gated potassium channel beta subunits (Kvbeta) and several members of SLC family, (in particular Ant1 of the MPTP) as, previously unknown targets of the compound. The direct effects

on functional potassium channels are relatively small, but measurable. We have indications, that the AKR6-function of Kvbeta is important in modulating other ionotropic ligand-gated channels, like GABAA-, ?7-nicotinic and NMDA receptors, from the latter in particular those with NR2B subunits (which are supposed to be regulated by steroids). In the brain this target may play an important role, whereas the original target, 5-?-dehydrogenase plays a minor role in the brain.

A clear effect can however be quantified on the level of the MPTP by a fluorescent assay employing Rhodamine-123, the most important major factor in the induction of the so-called intrinsic apoptotic (mitochondrial) pathway. Finasteride and Dutasteride clearly inhibit in a dose-dependent manner the opening of the mitochondrial pore, moreover in a concentration range which corresponds to the respective range of neuroprotective effects in in vitro and in vivo assays (Figs. 2 & 3, . Without wishing to be bound by theory, we conclude that the binding of Finasteride and Dutasteride to various members of the solute carrier family 25 (SLC 25) is responsible for this effect, in particular binding to Ant1 , an essential constituent of the MPTP is assumed to underlying the neuroprotective effects and the inhibition of MPTP opening, and thus induction of intrinsic mitochondrial apoptotic pathways.

This property of Finasteride, Dutasteride and related compounds was previously unknown and allows the conclusion that Finasteride/Dutasteride/Dutasteride and related compounds may be used as cytoprotective, e.g. neuroprotective agents for medical applications.

The neuroprotective properties of Finasteride, Dutasteride and related compounds are rather due to this hitherto unknown multiple mode of action, which became apparent by a focussed drug repositioning program.

Es drängt sich so langsam die Frage auf wieviel man überhaupt noch auf solche Studien geben sollte nachdem wir vor einigen Wochen das GENAUE Gegenteil diskutierten.
Diese Studie scheint einen protektiven Effekt von Finasterid/Dutasterid vor Krankheiten wie Alzheimer/Parkinson etc. zu demonstrieren....also das genaue 100% Gegenteil von dem vorhin diskutierten.
