

Glioblastoma: Looking at the Currently Marketed Sigma-1 Agonists and Antagonists

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Megalizzi et al.'s data showing reduction of glioblastoma cells' motility by the experimental sigma-1 agonist 4-IBP [1] is delightful news. Since we already have several approved and marketed drugs with potent sigma-1 agonist activity we can start looking at treatment consequences of their data now.

The antidepressant drug fluvoxamine is an old, generic, selective serotonin reuptake inhibitor with quite potent sigma-1 agonist activity [2,3]. Donepezil is a cholinesterase inhibitor used for over a decade in the treatment of Alzheimer's disease that has coincidentally high affinity and agonist activity at the sigma-1 receptor [4]. Dextromethorphan is an old anti-tussive that although weak in that role, does have sigma-1 agonist activity [5,6]. Memantine, FDA approved for treatment of Alzheimer's dementia, also has some agonist activity at sigma-1 [7].

Caution is warranted though because sigma-1 antagonists have shown pro-apoptosis effects in breast cancer and other cancer models [for example ref. 8].

Haloperidol, one of the oldest drugs still in wide use as an anti-psychotic medicine, is also used commonly to treat delirium, including post-operative delirium. This would perhaps be ill-advised after glioblastoma surgery if the data of Megalizzi et al. [1] mean that sigma-1 agonism can restrict this cancer's extreme motility. Haloperidol in low and commonly used doses, shows high affinity antagonism of the sigma-1 receptor [9,10].

So we have available drugs to inhibit or stimulate the sigma-1 receptor as the clinical situation requires. Given the easy tolerability of the above sigma-1 agonists, careful follow-up studies should be done to explore the conclusions of Megalizzi's work.

References

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