Reviewer's report

Title: Involvement of extracellular ATP on the glioblastoma growth in a rat glioma model.

Version: 1 Date: 26 June 2006

Reviewer: cinzia volonte

Reviewer's report:

General

The present work by Morrone and colleagues, entitled “Involvement of extracellular ATP on the glioblastoma growth in a rat glioma model”, submitted to BMC Cancer, analyzes the involvement of extracellular ATP degrading enzymes in cell growth of glioma cells implanted in the rat CNS.

In detail, glioma C6 cells were injected in the right striatum of male Wistar rats and tumor size, immunohistochemical analysis for necrosis, microvascular proliferation (CD31 and VEGF staining), nuclear pleomorphism, glioma cell proliferation (Ki67 immunoreactivity) was performed. Total RNA was also isolated from cultured C6 cells and the cDNA analyzed by Real Time-PCR with primers for the NTPDase family, to study the differential expression of these enzymes in glioma cells versus normal astrocytes.

Notwithstanding the existing abundant literature on the biological consequences and mechanisms of glioma cell proliferation in vivo and in vitro on tumor progression, many key players and signal transduction pathways are still not fully understood and this would therefore justify the interest of the present paper for the readership of BMC Cancer.

Now that the identification of P2 receptors and degrading enzymes for extracellular ATP has obtained full scientific recognition in many physiopathological functions, the in vivo consequences of extracellular ATP metabolism on tumor proliferation/invasivity, as addressed by this manuscript, is therefore a very important and current topic, in tune with the always expanding purinergic field.

In general, in the present study the questions are well posed, the experiments are straightforward, the methods adopted and the results presented are sound and adequately described.

Only in a few cases, the authors should either present further experimental data or add details to the text, in order to confirm or improve the results shown, or to delete accessory or redundant information.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1) The “data not shown” concerning the uptake of glutamate in C6 glioma cells (at the beginning of the Results section) should be omitted, not having direct relevance to the work.

2) Figure 2 and Figure 3 should be combined, since Fig. 2 (Temozolomide sample) is a positive control for the new results depicted in Fig. 3.

3) Conversely, the lack of effect by apyrase on in vitro growth/survival of C6 cells should be presented, providing evidence that apyrase is not toxic to these cells. Do the authors further know if apyrase interferes with cell cycle, cell duplication time in vitro? This could have important mechanistic implications on the results presented.

5) A little editing should eliminate typing or English mistakes.

Discretionary Revisions (which the author can choose to ignore)

6) What happens to glioblastoma growth in the in vivo model if extracellular ATP is added instead of apyrase?

7) Details should be provided directly on Table 1 on how coagulative necrosis, intratumoral hemorrhage, lymphocytic infiltration, and so on were measured.

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.