# Critical evaluation of three abstracts and titles – Jeremy

# Look at the three attached abstracts and titles from early drafts of Brazilian research papers. Please be prepared to discuss what you like and do not like about each one.

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# For each article indicate, would you be encouraged to take the time to read the article if this was in your area of research?

# What problems do you see with the English writing and presentation style? Indicate in the texts.

*Can you detect phrases or sentences that could be improved? I have highlighted some text at the beginning of the first abstract that I changed in the next draft.*

# Can you try to improve one of these abstracts?   Show what you think can be improved.

As explicações e melhorias podem ser escritos em Português.

# 1) Euphol from *Euphorbia tirucalli* induces autophagy and sensitizes temozolomide cytotoxicity on gliobastoma cells

**Abstract**

Glioblastoma (GBM) is the most frequent and aggressive form of brain tumors. The therapeutic options for GBM patients are scarce, so, it is imperative the development of new and effective agents. The tetracyclic triterpene alcohol, euphol, is the main constituent of the sap of *Euphorbia tirucalli*, a plant known for its use in traditional medicine. We have previously screened euphol anti-cancer activity through a cytotoxicity evaluation in a large panel of 73 human cancer cells. Here, we expand the toxicological screening by analysing the inhibitory effect of euphol in two additional glioma primary cultures, and assess euphol effects in a large array of biological mechanisms, in order to understand it anti-neoplastic activity in gliomas. Euphol exposure showed a similar cytotoxicity effect against glioma primary culture compared to commercial glioma cells. Concentration-dependent cytotoxicity effects of euphol were seen on the 14 cancer cell lines and normal cells tested, but varied significantly between individual cell lines, with up to a more than five-fold difference in the IC50 values (IC50 range: 5.98 – 31.05 μM). The treatments with euphol exhibited the highest selectivity indexes, from 0.64 to 3.36 compared to temozolomide (TMZ), which selectivity indexes ranged from 0.11 to 1.13. Moreover, euphol was able to promote reduction in proliferation, as well as cell motility inhibition. No effect was found on cell cycle distribution, invasion and colony formation. A proteome cell death-array revealed that euphol promotes changes in anti-apoptotic and pro-apoptotic protein expression, and alters the state of several components of stress pathway. Importantly, the expression of the autophagy-associated protein LC3-II and acidic vesicular organeles formation were markedly increased; yet, the inhibition of autophagy by Bafilomycin A1 potentiated it cytotoxicity activity. Finally, euphol also exhibited antitumoral and antiangiogenic activity in vivo, by chicken CAM assay and revealed a synergistic interaction with TMZ in most glioma cell lines. In conclusion, euphol exerted an in vitro and in vivo cytotoxic activity against glioma cells, acting in several cancer pathways, including the activation of autophagy-associated cell death as a mechanism of action. These findings suggest euphol, either as a single agent or in combination with chemotherapy, as an antineoplastic compound interesting for GBM treatment.

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**2) Somatic Copy Number Aberrations in Clear Cell Renal Cell Carcinoma of Brazilian Patients**

**Abstract:**

Somatic copy number aberrations (SCNAs) are often associated with the clear cell renal carcinoma (ccRCC) pathogenesis and have been a source for new potentially useful diagnostic, therapeutic and prognostic applications. Recurrent SCNAs include loss of crhomossomes 3p, 14q, 9p and gains of 5q and 8q. Some of them are suspected to interfere on gene expression and can influence clinical outcomes. Despite multiples studies on RCC CNAs, there is currently no description of chromosomal alterations in a Brazilian ccRCC cohort. The aim of the present study was to evaluate the chromosomal profile of Brazilian ccRCC patients and explore clinical associations. Therefore, a total of 92 ccRCC Brazilian patients that underwent nephrectomy at Barretos Cancer Hospital were analyzed for SCNAs by array comparative genomic hybridization.The cohort was mainly consistent of patients with early stages and localized disease. Most significant alterations included loss of 3p (87,3%), 14q (35,8%), 6q (29,3%), 9p (28,6%) and 10q (25%), and gains of 5q (59,7%), 7p (29,3%) and 16q (20,6%). Gene annotation and enrichment analysis were performed. In silico analysis revealed 19 genes mapped to CNA significant regions, including (*SETD2*, *BAP1*, *FLT4*, *PTEN*), (*FGFR4* and *NSD1*). A fraction of the CNA genes correlated with gene expression on TCGA data and worse survival. Overall, this study provides the CNA profile of 92 ccRCC Brazilian patients and highlights regions potentially worthy of further investigation

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3) **Rapid DNA methylation changes in promoter region of *CDKN2A* gene in workers exposed in construction environment**

**Abstract**

The population of construction workers are exposed to a mixture of substances in the workplace considered carcinogenic for humans. Gene-specific changes in DNA methylation in this population have not been studied extensively. This study aims to compare the DNA methylation profile of *CDKN2A*, *RASSF1A*, *MLH1*, *MGMT*, *APC*, *ALU* and *LINE-1* from peripheral blood nucleated cells in the group of construction in a short time exposure. In 39 male constrution workers, we evaluated the DNA methylation in 4 gene-promoter regions (*CDKN2A*, *RASSF1A*, *MLH1* and *APC*) and 2 repeat elements (*ALU* and *LINE-1*) in blood samples obtained on the 1st and 5th day of the same work week. DNA methylation was measured by bisulfite-PCR-Pyrosequencing. We also measured the levels of metals detected in these blood samples. In the analysis of methylation levels, we only observed significant difference in the average between the 1st and 5th day for the *CDKN2A* gene. Metal levels were detected, but based on correlation analysis, we found no significant correlation with the average methylation levels of all CpG sites for the *CDKN2A* gene. In summary, the data suggest that changing the standard of *CDKN2A* methylation in construction workers may be a potential biomarker in populations exposed in construction environment.