Reviewer's report

Title: A 3D-microtissue-based phenotypic high content screen of chemotherapeutic drugs that overcome tumour resistance to radiation therapy

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Reviewer: Yannick Saintigny

Reviewer's report:

This article from N. Anastasov and colleague is about a new 3D assay to evaluate resistance of breast cancer cell to radiation in combination with chemotherapeutic drugs.

The article is well written and data presented support the conclusions. However, some revisions may improved this paper before it's publication.

Major Compulsory Revisions

The authors need to explain why the T47D line growth as presented in figure 4 (blue lines) looks different than in figure 2B. Indeed, in figure 2B, T47D 3D area show a doubling in 13 days (from 50,000 to ~110,000 µm²). But, in figure 4, the same line seem to triple it size ine 12 days (from ~75,000 to ~210,000 µm²)... 

Minor Essential Revisions

Figure 1C: It is necessary to explain in the legend section why the green color from gfp fluorescence is replace by a "white" color for irradiated 3D models.

Figures 1B, 2B, 3A-C, 4A-B and 5B: The scale of 3D model size (in µm²) is from 50,000 to 250,000 (Fig 1B) or 0 to 300,000 (as in fig 2B) or even 100,000 to 200,000 in fig 5B. Moreover, the "time" axis does not seem to be . Indeed, on figure 1B, the range between 6 and 9 days (3 days interval) is the same length than for 12 to 20 days (8 days interval).

All these graph should be plotted with the same scale in order to ease the understanding of the study.

Discretionary Revisions

I would change the title of this article as it is actually quite difficult to understand the major goal of the study.

In the abstract (results paragraph), i may replace the word "superadditive" by the word "synergy"

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.