Evaluation of the anti-tumor effects of artesunate on Circulating Tumor Cells (CTCs)

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Background & objectives

Repurposing the anti-malarial drug artesunate (AS) or other artemisinin derivatives as anticancer therapeutic agents has lately attracted a lot of attention. Indeed, AS has demonstrated antitumor activity in numerous cancer types. Metastasis is a hallmark of cancer and circulating tumor cells (CTCs) are notorious for their involvement in establishing metastases in distant organs, provided they survive the harsh journey in circulation. Another characteristic of CTCs is the acquisition of resistance to therapeutic regimes.
The aim of the study was to evaluate the effect of AS on non-adherent cancer cells, such as CTCs

Methods

Poly(2-hydroxyethyl methacrylate) was used to prevent cell attachment and spreading and hence establish the desired CTC model. Breast, lung, and colon cancer cell lines were evaluated, as well as the first patient-derived colon CTC-MCC-41 cell line. Adherent and non-adherent cell cultures were used for side-by-side comparisons. Cell viability was examined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-dimethyltetrazolium bromide (MTT) assay, following treatment with different concentrations of AS.

Results

AS decreased viability of all adherent cell lines in a concentration-dependent way and IC_{50} was shifted to the right in the non-adherent lung and breast cells. While AS (10 μM, 48 h) inhibited the viability of all adherent cell lines, the effect was less prominent in the non-adherent model. AS effects were more pronounced on lung (63 ± 1 and 27 ± 6 inhibition of adherent *vs* non-adherent respectively; n = 4) and colon (57 ± 3 and 36 ± 7 inhibition of adherent *vs* non-adherent respectively; n = 4), compared to breast cancer cells (49 ± 3 and 11 ± 9 inhibition of

adherent *vs* non-adherent respectively; n = 3). In respect to CTC-MCC-41 cells, AS inhibited the viability of adherent cells (68 ± 2), but also significantly decreased the viability of their counterparts in suspension (47 ± 6, n = 4).

Conclusion

The present model, whereby the free-floating cells mimic CTCs, is promising for identifying drug efficacy. AS seems to exert antitumor activity with different effects on cancer cells depending on their adherent status and tissue origin. Moreover, AS is potentially effective on patients' metastasis-initiator CTCs.

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