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Optimizing *in vitro* sphaeropsidin: A-induced anti-melanoma effect by means of computed determination of optimal chemocombinations

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Statement of the Problem: Despite the major advances in their treatment over the last five years, stage III and IV melanoma patients still have a poor prognosis. Indeed, most patients develop resistance within 6-8 months after their treatment initiation with targeted therapy or chemotherapy. To reduce resistance, combinations of therapies with different mechanisms of action/targets are encouraged and studied. Natural products derived from plants have been widely used as source of drugs for diverse medicinal purposes including cancers. We identified sphaeropsidin A as an interesting candidate regarding its specific activity against melanoma. This fungal metabolite revealed to be a modulator of ionic transporters. Thereby it can disrupt the regulatory volume increase process that contributes to protect cells from apoptosis via the regulation of the intracellular chloride concentration. The co-administration of sphaeropsidin A with pro-apoptotic agents could potentially reduce therapies resistance.

Aim & Methodology: Leaning on this assumption, we evaluated sphaeropsidin A in combination with cytotoxics, e.g. cisplatin or temozolomide with the aim to obtain the maximal cytotoxicity against melanoma cell lines. Owing to the complexity of optimizing the experimental method, we developed a predictive model based on response surface methodology to determine the optimal concentrations of drugs.

Findings & Conclusions: We found 75 µM of cisplatin and 850 µM of temozolomide combined with 4 to 6 µM of sphaeropsidin A reached maximal *in vitro* cytotoxic effects. Those concentrations are in line with the *in vitro* active concentrations of these anti-cancer drugs. Importantly, sphaeropsidin A acted with cisplatin and temozolomide in a synergistic manner. We are now undertaking to compare the cytotoxic activity of sphaeropsidin A with hemisynthetic derivatives with the aim to improve its efficiency *in vitro* and/or develop chemical combined drug.

Biography

Aude Ingels is a PhD student in Laboratoire de Cancérologie et de Toxicologie Expérimentale in Université Libre de Bruxelles (Belgium). She started her career in Laboratory of Bone and Metabolic Biochemistry (ULB) where she studied the physiopathology of nonunion fractures and bone cell therapies. After a short passage as Study Coordinator (oncology section) in Cliniques Universitaires Saint-Luc (Brussels, Belgium), she started in 2013, a thesis focusing on the use of natural product as anticancer therapy.

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