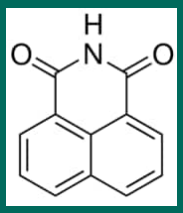

Screening of naphthalimides as antimetastatic agents

Victoria Sánchez-Martín[1,2], Dusan Ruzic[3], Ignacio Castilla-Maldonado[1,2], Matilde Ortiz-González[1,4], Ana Soriano-Lerma[1,2], Ángel Linde-Rodríguez[1,2], Virginia Pérez-Carrasco[1,2], Inmaculada Ramirez-Macias[1,2], Miguel Soriano[1,4], Katarina Nikolic[3] & Jose Antonio García-Salcedo[1,2]

[1]Centre for Genomics and Oncological Research: Pfizer, University of Granada, Andalusian Regional Government, PTS Granada-Avenida de la Ilustración, Granada, Spain.
[2]Servicio de Microbiología, Hospital Universitario Virgen de las Nieves, Granada, Spain. Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain.
[3]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Belgrade. Belgrade, Serbia.
[4]Center for Intensive Mediterranean Agrosystems and Agri-Food Biotechnology (CIAIMBITAL), University of Almeria, Almería, Spain.

Introduction

Treatment options for metastasis are still limited. Naphthalimide (NDI) analogs have been considered as promising anticancer agents against different tumor types. However, their antimetastatic potential has not been investigated before.

Objective

To evaluate the possible antimetastatic activity of a panel of 21 NDIs which were synthesized in the laboratory.

Material and Methods

NDIs were screened in terms of antimetastatic activity. We performed IC_{50} determination, cell cycle analysis and clonogenic assays in SW620 metastatic cells.

Results

We identified 5 NDIs with a potent and selective inhibition of growth in SW620 metastatic cells compared to CRL1790 non-tumoral ones **(Figure 1)**. In addition, these 5 NDIs induced a significant increase at S and G2/M phase in SW620 cells **(Figure 2)**. Finally, we selected the leading compound 20B, which inhibited clonogenic expansion in SW620 cells even at 10 µM **(Figure 3)**.

Conclusion

These results shed light on the NDI 20B as an emerging antimetastatic agent.

Figure 1. IC_{50} values for 21 NDIs in SW620 metastatic cells. Selectivity indexes (SI) were determined dividing the IC_{50} in SW620 by the IC_{50} in CRL1790 non-tumoral cells only for NDIs with IC_{50} < 150µM.

NDI	IC_{50} (µM)	SI
1B	351.5 ± 5.3	-
2B	271.0 ± 3.6	-
3B	201.9 ± 3.2	-
4B	225.9 ± 4.2	-
5B	379.3 ± 5.6	-
6B	190.6 ± 2.6	-
7B	298.5 ± 3.5	-
8B	94.6 ± 2.5	3.7
9B	331.1 ± 4.0	-
10B	365.6 ± 4.6	-
11B	217.0 ± 2.4	-

NDI	IC_{50} (µM)	SI
12B	144.5 ± 2.5	2.3
13B	146.9 ± 6.2	1.9
14B	449.8 ± 9.0	-
15B	194.9 ± 3.0	-
16B	401.8 ± 5.4	-
17B	168.3 ± 4.3	-
18B	158.9 ± 3.8	-
19B	105.2 ± 5.5	4.1
20B	46.2 ± 2.1	2.3
21B	360.6 ± 4.3	-

Figure 2. Cell cycle analysis of SW620 metastatic cells treated with DMSO (non-treated, NT) or NDIs at IC_{50} for 24 h.

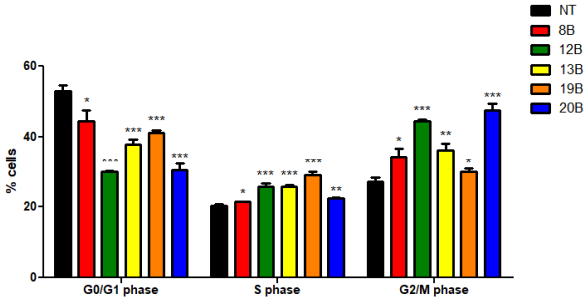

Figure 3. Clonogenic assay in SW620 metastatic cells treated with DMSO (non-treated, NT) or NDIs at increasing concentrations for 48 h.