Deciphering the antimetastatic potential of naphthalimides and their role as G4-ligands

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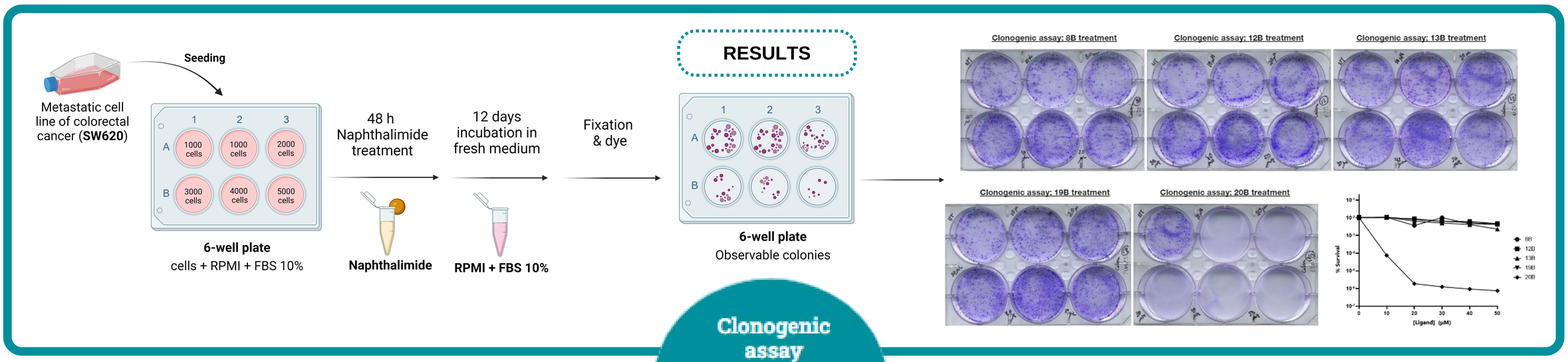
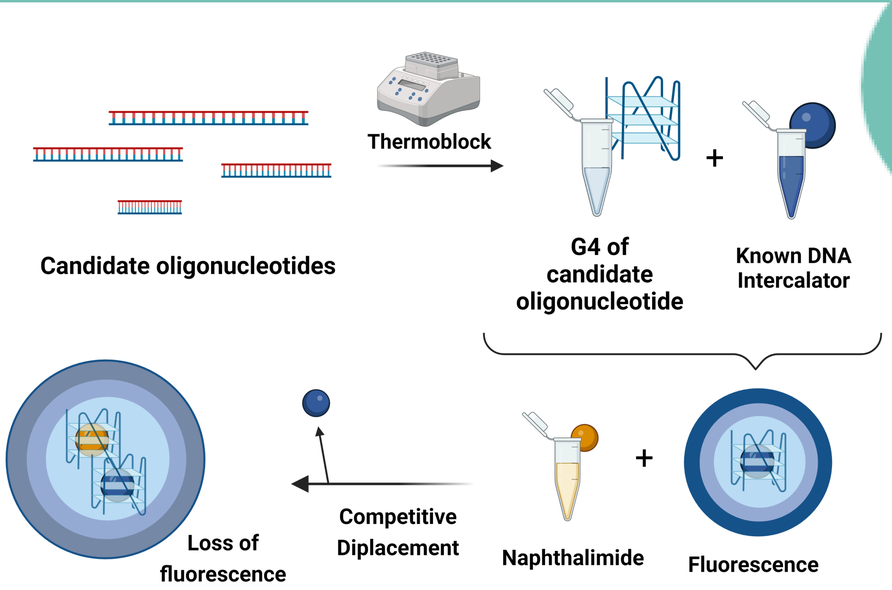
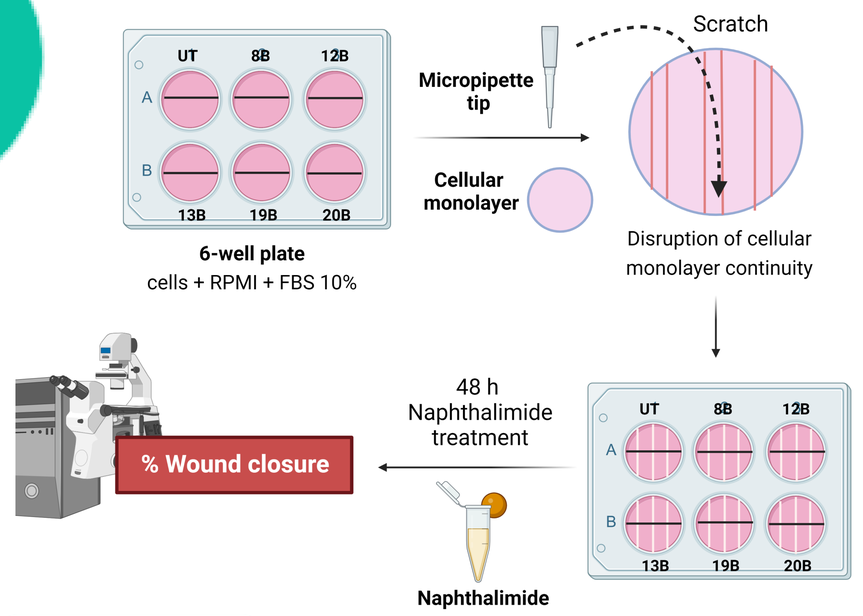
ABSTRACT

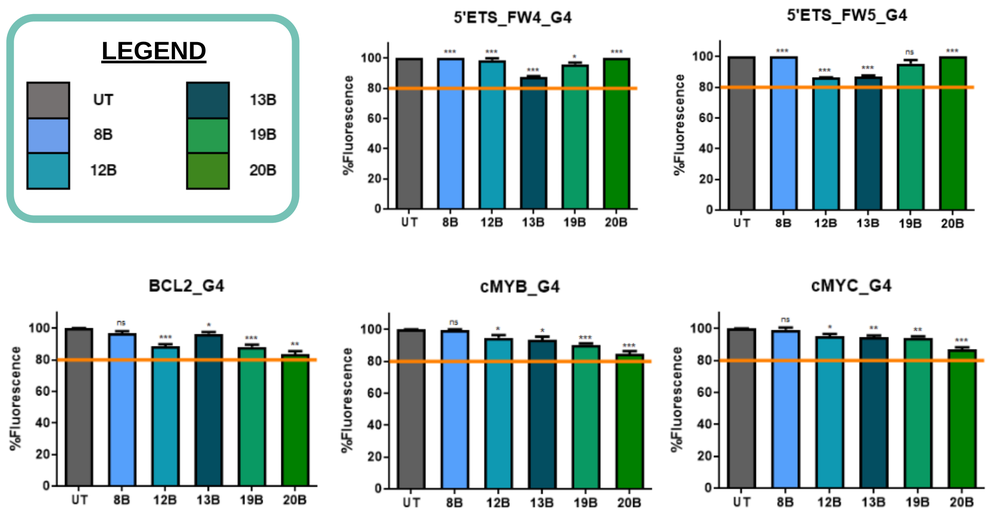
G-quadruplex (**G4**) is a non-canonical secondary structure of nucleic acids linked to the regulation of transcription, replication and telomeric homeostasis. These phenomenoms are highly dysregulated in cancer, being the reason why we considered G4s as a riveting pharmacological target. In this research we evaluated the possible antimetastatic potential of a group of five naphthalimides, denominated 8B, 12B, 13B, 19B and 20B; as well as its capability to bind to G4s. In order to solve these aspects, we performed a clonogenic assay and wound-healing assays using a metastatic colorectal cell line (SW620). Fluorescent intercalator displacement assays (FID) were carried out as well, deeming G4-oligonucleotides with a paramount role in cancer. The results shed light on 20B naphthalimide as an emerging antimetastatic agent, due to its inhibition in SW620 clonal expansion and cellular migration, as well as its higher capability to bind to the G4s-oligonucleotides.

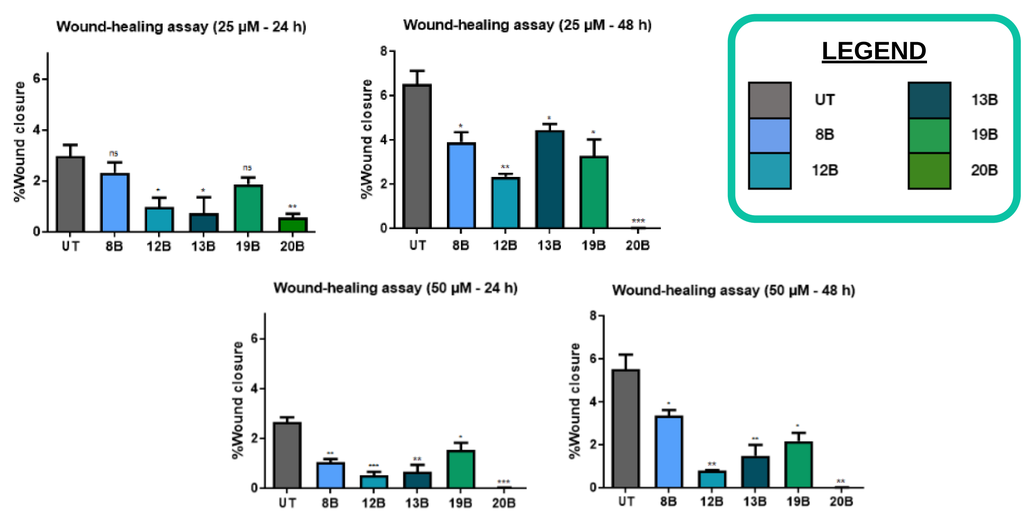






RESULTS





Conclusions

The capability of the studied naphthalimides to specifically bind to DNA-G4s has been demostrated by FID assay. **20B naphthalimide** is responsible for making the biggest displacements, among which *BCL2*, *cMYC* and *cMYB* G4-containing oligonucleotides have to be highlighted. This naphthalimide also showed the highest repression over SW620 clonal expansion as well as over cell migration.

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