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Design and synthesis of metal-based chemotherapeutic agents for targeted DNA interactions or DNA repair pathway modulation

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Propositions

accompanying the thesis

Design and synthesis of metal-based chemotherapeutic agents for targeted DNA interactions or DNA repair pathway modulation

1. Although multiple platinum-based anticancer derivatives have been tested in clinical trials, only a disappointing few are suitable for clinical practice.
*A. Florea, D. Büsselberg, **Cancers** 2011, 3, 1351-1371*
2. The exceptional effectiveness of genomic maintenance systems in detecting and repairing DNA defects renders the exclusive reliance on inducing DNA damage for chemotherapy a fantastical approach.
*D. Hanahan, R.A. Weinberg, **Cell** 2011, 144, 646*
3. *In vitro* cell culture models can never accurately reflect the multilayered processes taking place in the skin of real living humans.
N.E. Uzunbajakava, J. Biophotonics, 2023, 16, 202200257
4. Inhibition of DNA repair in cancer cells represents an attractive strategy for potentiating the cytotoxic effects of anticancer chemotherapy and radiation therapy.
*M. Javle, N.J. Curtin, **British Journal of Cancer** 2011, 105,1114*
5. Despite its prevalence in the literature, agarose gel electrophoresis is a surprisingly inadequate method for studying the interactions of small molecules with DNA.
This thesis, chapter 2
6. In crystallization experiments of metal complexes, the use of fully protonated acidic compounds for counterion screening is a superior method and typically leads to more positive outcomes compared to using their corresponding salt forms.
This thesis, chapter 2, 3, 4 and 5
7. Using chiral HPLC to separate enantiomers is particularly challenging when dealing with coordinatively labile ruthenium compounds, as solvents used traditionally in HPLC, such as MeCN or H₂O, have good coordinating properties.
This thesis, chapter 3

8. The light-induced delivery of two distinct inhibitors coordinated to a single molecular scaffold offers unprecedented spatiotemporal control of anticancer treatment.
This thesis, chapter 5
9. Allocating substantial time to obtain a single crystal structure can be seen as inefficient; however, when the obtained structure would be the last one in a series of 24, the investment of time and resources becomes fully justified.
10. If researchers would receive monetary compensation for all compounds labeled as 'promising' based on *in vitro* cytotoxic effects, they would not have to write many grant proposals.
11. A surprising number of experimental challenges can be solved by trifluoroacetic acid.
12. Similar to whisky, acids show superior qualities when their bottles release smokey vapors upon opening.

Corjan van de Griend
Leiden, 27 February 2024