ABSTRACT EN

The objective of this work was to study novel synthetic iron chelators and to study their potential use in inhibition of TET1 (ten-eleven translocation methylcytosine dioxygenase 1) protein. Epigenetic mechanisms, such as hydroxymethylation of DNA, are promising target in many serious pathologies, including oncological disorders. In the presented study, we intended to discover novel inhibitors by screening small libraries of heterocyclic molecules, such as pyrrolo[3,2-b]pyrrole derivatives with hydrazide (compound **1**) or hydrazone (compound **2-6**) iron-binding group and hydrazone-based iron chelators (compound **7-10**).

Within the scope of this study, we used various analytical and biochemical techniques for the purpose of characterization of novel cancer therapies based on TET1 protein inhibition. The absorbance and the complexation of tested compounds with Fe(II) ions was studied by UV–Vis spectroscopy. Inhibition of TET1 protein was studied by fluorometric assay based on ELISA and further supported by microscale thermoporesis and *in silico* docking. The cytotoxicity of compounds on cancer cell lines was measured by MTT assay and intracellular distribution was determined by live-cell imaging.

This study presents a biochemical analysis of potential TET1 protein inhibitors and brings significant insights that could possibly lead to the discovery of innovative anticancer treatments based on targeting of epigenetic mechanisms.

Keywords: TET1 protein inhibitor, hydrazide, hydrazone, Fe(II) chelators, epigenetics, anticancer therapy