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Functionalized hexavanadate exerts antitumor activity against triple negative breast cancer cells

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Triple-negative breast cancer is frequently more aggressive and harder to treat than cancers that are hormone receptor-positive (Luminal A and B) or HER2 positive.[1] Polyoxometalates are considered a prominent class of discrete metallic oxides for many biomedical investigations including anticancer, antiviral, and antimicrobial activities.[2] The hexavanadate functionalized with the tripodal alcohol **H_3L^{Et}** = 1,1,1-tris(hydroxymethyl)propane, $(C_8H_{20}N)_2[V_6O_{13}\{(OCH_2)_3CCH_2CH_3\}_2]$ (**V_6L^{Et}, Fig 1**) was synthesized by using a soft method. ^{51}V NMR spectroscopic studies showed that the compound is stable in water and in RPMI culture medium. The antitumoral activity of **V_6L^{Et}** was assessed *in vitro* against triple negative breast cancer cells by MTT. The IC_{50} values (*i.e.* the dose required to inhibit the growth of 50% of the treated cells) at 24 h are found to be 17.6 and 2.97 µmol L^{-1} against human (MDA-MB-231) and murine (4T1) cancer cells, respectively. For human breast normal cells (HB4a), the IC_{50} value was 9.77 µmol L^{-1}. The previous values have been compared to those determined for decavanadate, $[V_{10}O_{28}]^{6-}$, of 2.53 µmol L^{-1} for MDA-MB-231 and 0,966 µmol L^{-1} for HB4a. The Wound Healing assay using the MDA-MB-231 cells showed that **V_6L^{Et}** reduced the cell migration with a larger gap area (87.6% in 24 h and 79.8% in 48 h). SEM images showed the appearance of vesicles in cells treated with both compounds. However, only **V_6L^{Et}** triggered changes in the cell morphology from fusiform to amoeboid. The gene expression assay with **V_6L^{Et}** in the MDA-MB-231 cell line resulted in an increase in the RIPK3 gene expression by 15 times, which is compatible with a necroptosis mechanism in the presence of the POV. The cytotoxicity assays of **V_6L^{Et}** in both human and murine cell lines are promising for future *in vivo* studies.

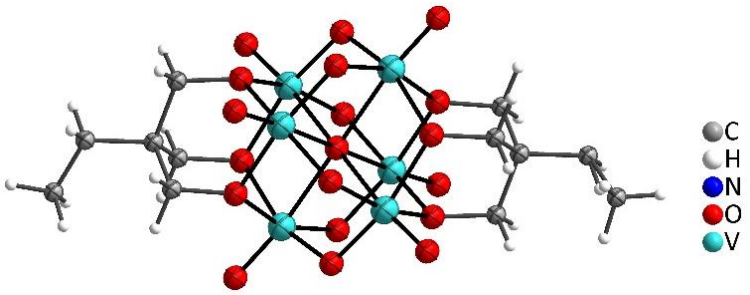

Figure 1. Ball and stick representation of $(C_8H_{20}N)_2[V_6O_{13}\{(OCH_2)_3CCH_2CH_3\}_2]$ **V_6L^{Et}**.

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