Prevention of tumor growth by photo- and X-ray activation of tungsten cluster complex and its conjugate with DNA molecules

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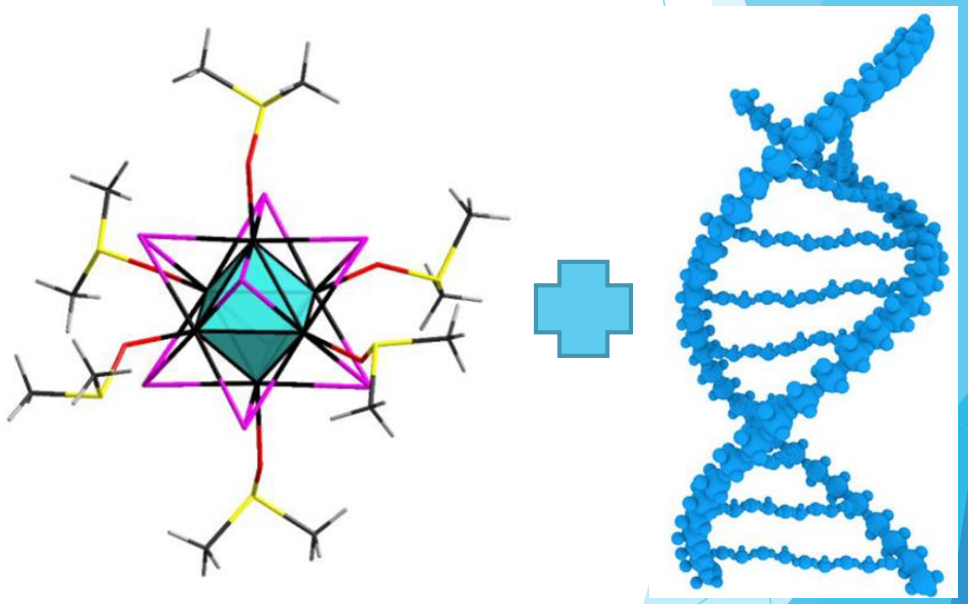
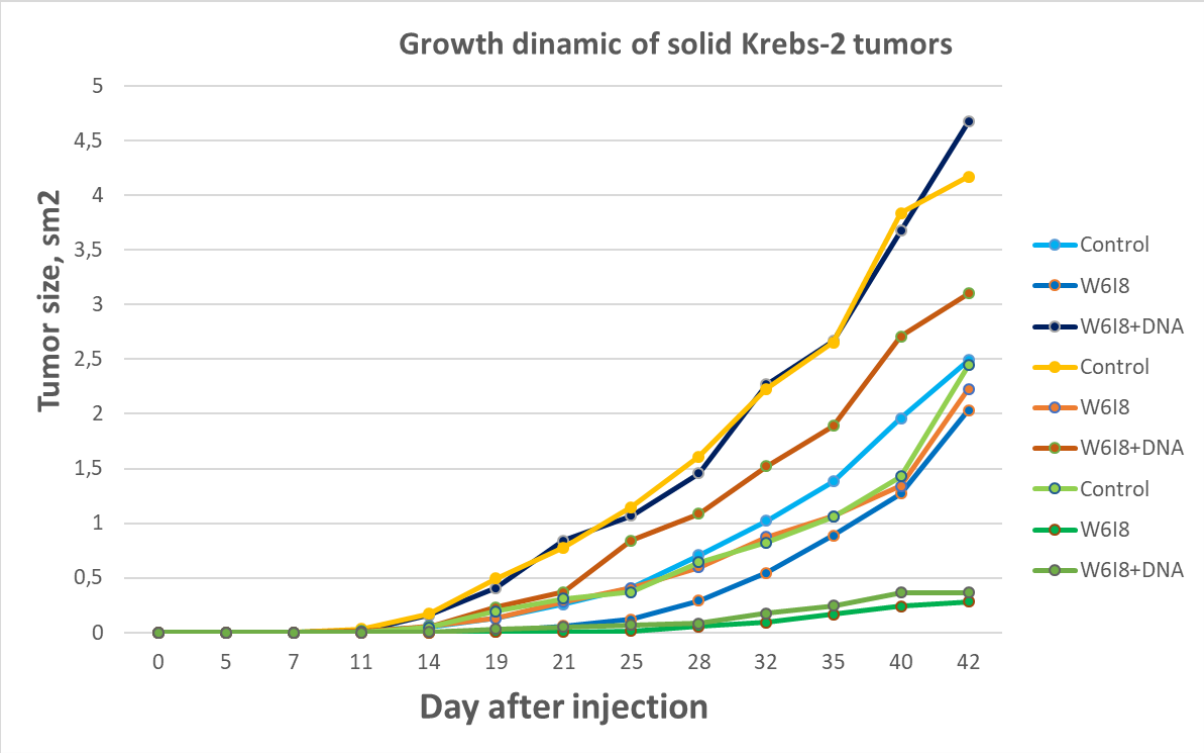
Photodynamic therapy (PDT) is one of the most promising methods of treating cancer, although it has it's limitations due to applying visible light sources with limited exposure depth. To increase the efficiency of the method for treatment of deep lying tumors, it is possible to use other radiation sources, for example, x-rays. In this work a tungsten (W6I8) cluster complex was used as photo- and x-ray-sensitizer and its conjugate with DNA (W6I8DNA) as targeting molecules to eliminate Krebs-2 tumor cells and prevent tumor development in vivo.



(Bu4N)2[{W6I8}(NO3)6] was synthesized in Laboratory of Bioactive Inorganic Compounds (Nikolaev Institute of Inorganic Chemistry SB RAS)

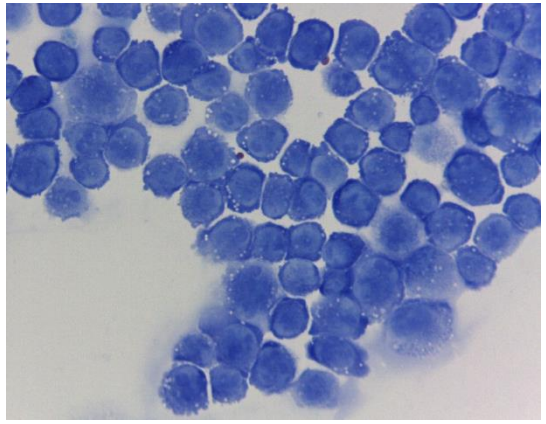
Results



Pic. 1. Growth dynamic of solid Krebs-2 tumors (sm2) in mice CBA/Lac 4-6 month old. Quantitative data were expressed as mean ± s.e.m. N=6. A nonparametric Mann-Uitny test was used for comparing the treatment groups and the control groups. (* - p <0.05) – X-ray compared to light, (# - p <0.05) – x-ray compared to control, ($ - p <0.05) – (W6I8) and (W6I8DNA) compared with control in X-ray group.

Irradiated with X-ray Krebs-2 cells, incubated with W6I8 and W6I8-DNA, give later tumor growth or its absence

Experiment model

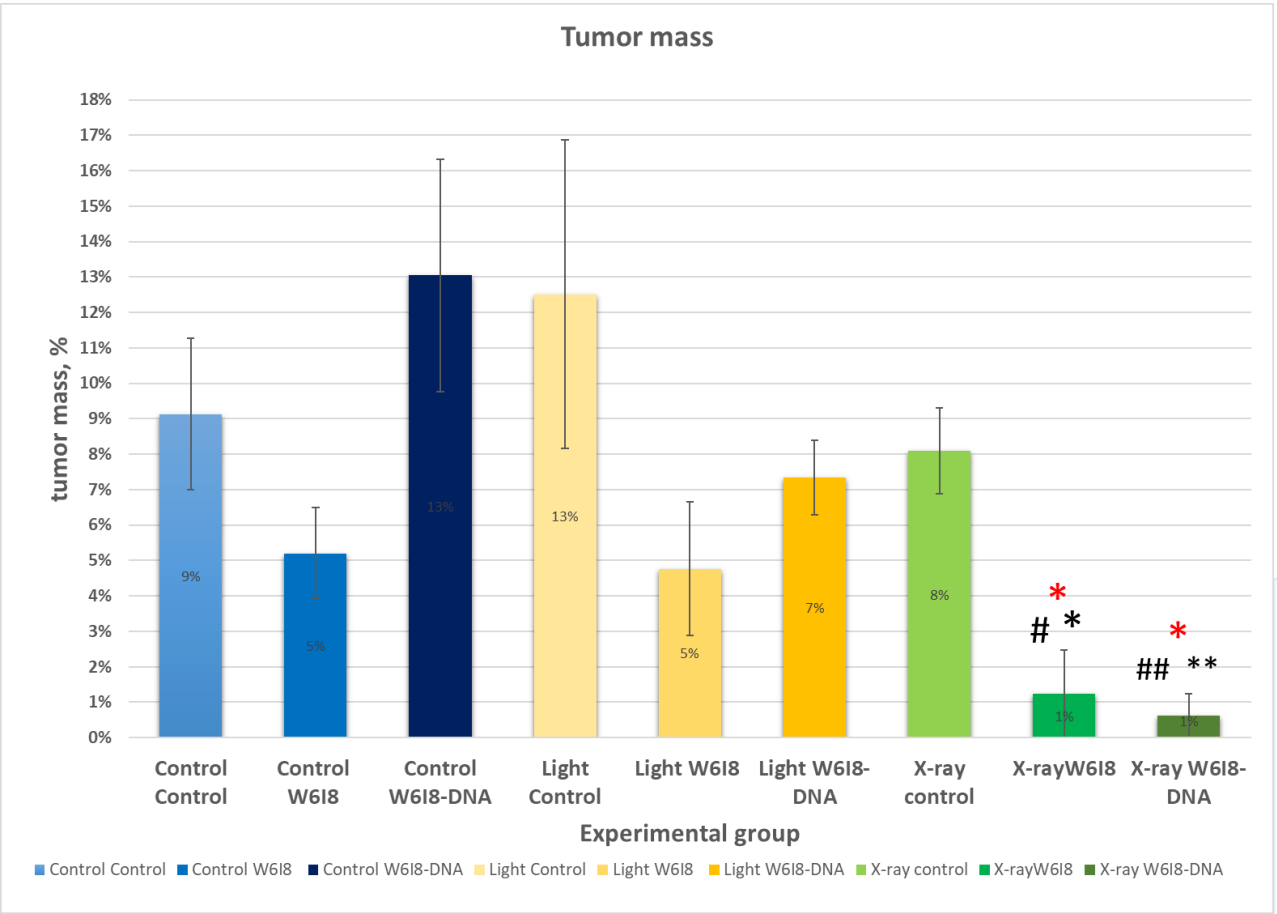


2 hours incubation at 37°C, 5% CO2 with W6I8, W6I8-DNA

Irradiation with halogen lamp, 500 W
30 min

Irradiation with X-ray source, 15000 MU
30 min

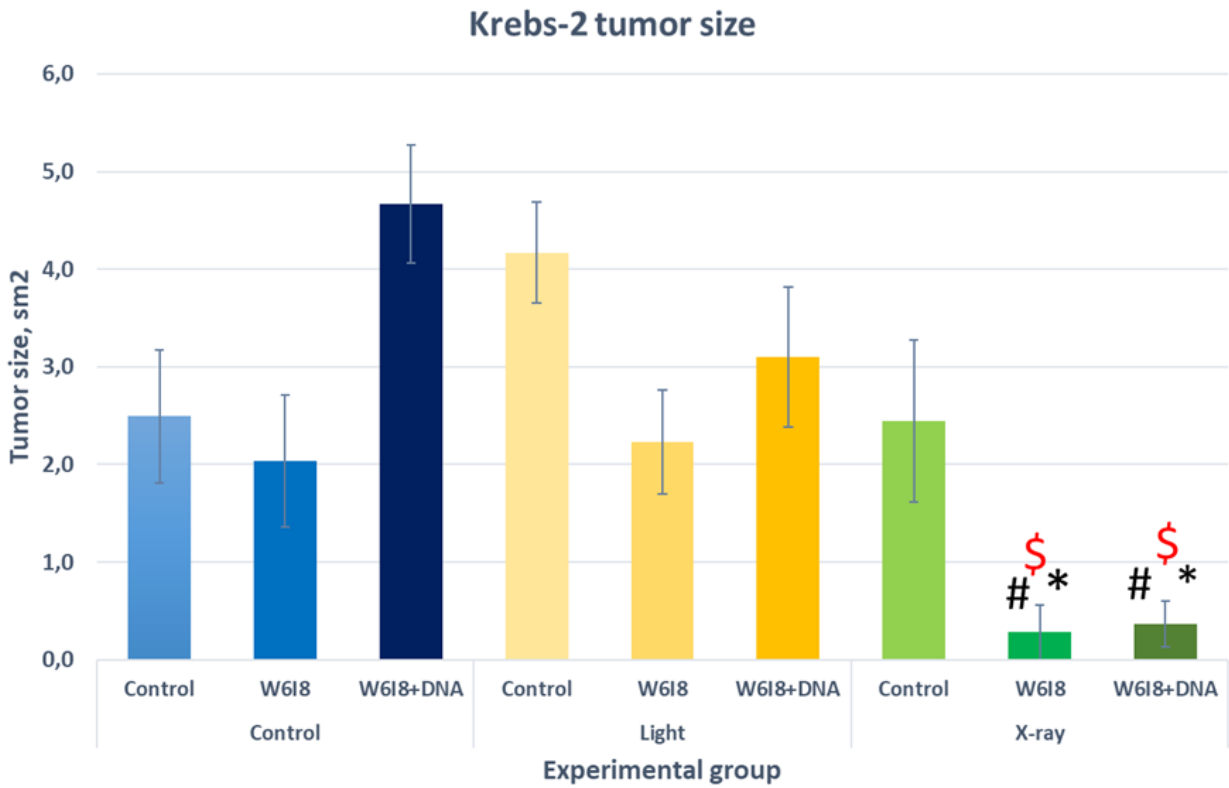
Krebs-2 cells were previously incubated with (W6I8) and (W6I8-DNA) for 2 hours in standard culture conditions (37°C, 5% CO2). After that, cells were irradiated with 500W halogen lamp for 30 minutes or with x-ray source. Cells were injected intramuscularly



Pic. 2. Krebs-2 tumor size (sm2) after 42 days of cultivation in mice CBA/Lac 4-6 month old.

Pic. 3. Ratio of Krebs-2 tumor mass to body mass (%) after 42 days of cultivation in mice CBA/Lac 4-6 month old.

Quantitative data were expressed as mean ± s.e.m. N=6. A nonparametric Mann-Uitny test was used for comparing the treatment groups and the control groups. (* - p <0.05) – X-ray compared to light, (# - p <0.05) – x-ray compared to control, ($ - p <0.05) – (W6I8) and (W6I8DNA) compared with control in X-ray group.



CONCLUSIONS

- We found out that Tungsten cluster complex (Bu4N)2[{W6I8}(NO3)6] and its conjugate with DNA (W6I8DNA) can be activated with x-ray which leads to elimination of Krebs-2 cells.
- X-ray irradiation of Krebs-2 cells reduce tumor growth or leads to its absence when injected intramuscularly.