Most of us are the owners of a dog or a cat and probably would like to have their pet live forever. However, more than 50% of dogs and cats die due to cancer. One of the malignant tumors that can appear in cats after standard vaccination, for example against rabies, are injection-site sarcomas (ISS). Those are malignant skin tumors, the treatment of which is a challenge for veterinary practitioners and a huge problem for their owners, who do not want their pets to suffer due to pain and discomfort strongly connected with the tumors that mainly appear in the cats' back. In 20% of cats they also result in lung metastasis which quickly leads to death of the animal. Methods of injection-site sarcoma treatment include: surgery, radiotherapy and chemotherapy. The most important factor determing the success of treatment or living without the cancer is a clear margin (without neoplastic cells) of the removed tissue after surgery. However, in many cats performing such radical surgery with at least 3 cm margin of healthy tissue is impossible due to the tumor size or localization. Radiation therapy may be used to decrease the tumor size, however, is not accessible in every country. As a result, chemotherapy is considered as an adjunctive therapy enabling the performance of a radical surgery and decreasing the risk of lung metastasis.

The most often used drugs in ISS treatment are: doxorubicin, vincristine, isofosfamide, methotraxate. Both in human and veterinary medicine, doxorubicin is believed to be a drug of choice for sarcomas. However, doxorubicin intra venous injection has many adverse side-effects, for example gastro-intestinal disorders (eg. vomiting). Moreover, it's efficacy is also debatable due to multidrug resistance (MDR) (ineffective treatment after using standard chemotheraopeutics) and low distribution to tumor.

As a result, a novel drug – gold nanoparticles conjugated to doxorubicin (Au-GSH-Dox) has been proposed by the author of the project as a potent therapeutic agent for feline injection-site sarcomas, as in previously performed in vitro studies it has been showed that Au-GSH-Dox enhanced antitumor efficacy (kills more neoplastic cells) of doxorubicin for ISS. Various studies have also demonstrated that gold nanoparticles can act as nanocarriers for oncological drugs as they can be transported into the cell, bypassing glycoprotein P (a protein which can eject anticancer drugs from tumor cells and as a result lead to ineffective chemotherapy treatment). The efficacy of this Au-GSH-Dox was also confirmed by the applicant in the in vivo preclinical studies - by using the chick embryo model (in ovo model in the direct translation meaning "model in the egg").However, in CAM model the tumors exist for not longer than 7-10 days (because the chick embryo development lasts 21 days and the tumor cells are usually implemented between 6-8 day of the chick embryo cycle) so the obtained results suggest the need for further studies on the mice model, which enables to observe mice for a longer time and resembles cats more closely. Should the results be positive, the mechanism of action will be investigated by assessing the cellular uptake of gold nanoparticles and doxorubicin. This is extremely important as this new drug may be used in the future in treatment of various tumors both in human and in veterinary medicine as doxorubicin is one of the most commonly used cytostatic drug. In order to provide the insight into the resistance to standard doxorubicin alone in ISS, the protein analyses of tumors will be made prior to and after the intratumoral injection of colloid gold nanoparticles conjugated to doxorubicin. Further findings in this area could be a basis for personalised therapy as it could help to select in the future patients who would benefit from this treatment.

Moreover, the applicant would like to perform proteome analyses of tumors which could broaden the knowledge about the cause of resistance for standard chemotherapy treatment. The author of the project would also like to compare the activity of glycoprotein P (main protein responsible for ejecting anticancer drugs from tumor cells, what as a result leads to ineffective chemotherapy treatment) in fibrosarcoma cells with its expression in tumors. Further findings in this area could be a basis for personalised therapy both in human and in veterinary medicine as it could help to select patients who would benefit from this treatment. Such a therapy that will take into account the fact that each of us is different and the reaction for treatment also varies for each patient.