universität wien

FAKULTÄT FÜR CHEMIE

Einladung zum Vortrag von

Prof. Dr. Andriy Mokhir
Friedrich-Alexander-Universität Erlangen-Nürnberg

N-Alkylaminoferrocene-based prodrugs responsive to reactive oxygen species: potential applications in chemotherapy of cancer diseases

A basal level of reactive oxygen species (ROS) in malignant cells is higher than that one in normal cells. Therefore, the former cells are more vulnerable to the oxidative stress. For example, when malignant and normal cells are treated with exogenous compounds increasing cellular ROS amount, the malignant cells die first. Known ROS generating drugs exhibit dangerous side effects. In particular, apart from killing cancer cells, they also increase ROS amount in normal cells. High ROS stimulates transformation of the cells and induce secondary tumors. We develop prodrugs, which increase ROS concentration in cancer cells, but do not affect ROS concentration in normal cells. These compounds are non-toxic, stable molecules or nano-sized constructs. In the ROS-rich microenvironment of cancer cells they are transformed into cytotoxic agents of two types: type 1 agent impairs an antioxidant system of the cell; type 2 agent generates ROS catalytically. Type 1 agent is an organic electrophile reacting with glutathione (GSH) or other nucleophilic (-SH or -SeH-containing) biomolecules. Type 2 agent is an electron rich organometallic compound (e.g. ferrocene), which is able to cycle between reduced and oxidized states without decomposition. These species act synergistically by inducing strong oxidative stress that leads to apoptosis or necrosis of cancer cells. Our prodrugs are not activated in the microenvironment of normal cells containing low ROS concentration. The excellent antitumor effects were confirmed in cell free settings, experiments with cell cultures and primary cells as well as *in vivo* in several mouse and one rat models. We are currently working on further chemical modification of these prodrugs to achieve their targeting to particular organelles of cancer cells (lysosomes, mitochondria, Golgi, endoplasmic reticulum and nucleus) to potentiate their antitumor activity. Our progress in this project will be highlighted in the presentation.

Freitag, 29. März 2019, 15:00 Uhr
Seminarraum 2 der Fakultät für Chemie
Währinger Straße 42, 1090 Wien

Vladimir Arion
Institut für Anorganische Chemie

Veronika Somoza	Bernhard Keppler	Lothar Brecker
Vizedekanin	Dekan	Vizedekan