Reg. No: 2016/21/P/ST5/03512; Principal Investigator: dr Luca Sancineto

The 2017 will be the second century of the discovery of selenium, the element that for at least the three quarters of its life was mainly considered as a poison. This was probably correlated to the fact that, its toxicity was reported and described before the discovery. It was the 1285 when Marco Polo lost a number of horses crossing the Shanxi Province of China as consequence of an acute selenium intoxication arising from an exceptionally high concentration of the element in forages that was produced in that region. The fear surrounding this element continued for a long time so much so that the term "selenophobia" was coined in 1972.

In the last forty years the interest regarding selenium was renewed because of the identification of a number of selenoproteins endowed with a crucial role in the protection of living systems against oxidative stress. The acknowledgment of selenium as an essential micronutrient and as a key actor within the antioxidant machinery prompted the use of its formulations (mainly inorganic salts) as dietary supplement to prevent the damage of oxidative stress. However, the real positive effects in human health remain to be proved.

Several selenorganic compounds were studied as biological catalysts able to reproduce the catalytic cycle of the antioxidant enzyme glutathione peroxidase (GPx). The effective clinical application generally failed because of the cytotoxicity, which appears at a lower dose than that required for the GPx-mimic activity. Currently, the fine modulation of selenium activity/toxicity is a challenging task and a general poor knowledge of the chemical mechanism of the interaction between selenium and the biological systems represent the main limitation and the main obstacle that need to be overcame.

One of the principal feature that can influence and characterize the activity/reactivity of selenium is its ability to establish nonbonding and weak interactions with heteroatoms and interact with metals and metallic cations. These interactions are relatively poor explored, and the present project proposes a systematic evaluation of their nature and strength. The investigation will be performed on purposely synthesized organoselenium compounds by using spectroscopic analysis with ⁷⁷Se-NMR which will be employed privileged technique and the information will be related to specific structural features.

The main outcome of this study will be the collection of new information for the elucidation of the mechanism of action of organoselenium compounds. Particular interest will be directed to recreate the interaction of the selenium containing compounds with the zinc finger domains of proteins. These could become new targets of organoselenium derivatives for future therapeutic applications or may serve as tools to study and modulate their toxicity.