Synthesis and structural characterization of new photo-responsive molecular systems endowed with biological activities.

This PhD project is focused on the synthesis of new organic compounds endowed with specific biological activities and/or particular physical properties making them suitable as new "smart materials"–i.e. intelligent materials with one or more properties that can be controlled by external stimuli such as irradiation at selected wavelengths–.

The perspective to realize the *spatio-temporal* control of drug action, to promote the reversible phase-change of materials, to build molecular devices capable of processing and/or storing specific information is the driving force of a high number of cutting edge researches that employ the light to trigger molecular processes. The building of photo-responsive systems requires the incorporation of molecular photo-switches, which undergo a reversible change in their molecular properties upon irradiation.

In this proposal, efforts will be spent on the synthesis and the structural characterisation of new azobenzene analogues and modified nucleosides/nucleotides as molecular tools to study and/or control the function of specific proteins involved in pathological processes, with a special focus on cancer[i] and protein conformational disorders. Some of the obtained molecules will be functionalized to obtain phosphoramidite building blocks useful for the synthesis of new modified aptamers[ii]. The obtained analogues will be characterized for their ability to act as photo-responsive systems in order to realize new ON/OFF switches based on folding/unfolding cycles of aptamer secondary structures, and thus realising a remotely controllable aptamer-target binding capability. The early aptamer sequences will be chosen among those capable of recognising and binding specific marine and freshwaters toxins and/or anthropogenic contaminants[iii]. All the newly synthesised compounds will be structurally characterised by means of spectrophotometric (CD, UV, NMR) and spectrometric (MS, HRMS, MS^n) techniques, using the instrumental analysis laboratories available at UniNa Department of Pharmacy (NMR laboratory and MS laboratory) and the high-resolution mass spectrometry laboratory (LC-ESI-LTQ-Orbitrap-FTMS), the latter being available 50% of its working time to the MarBioTox group. During the training course, the PhD student and the tutors will benefit of interdisciplinary collaborations with the following research groups:

Prof. Carlo Altucci (UniNa, Department of Medical Physics) for the characterisation of the photo-responsive properties of newly synthesized molecules and the production of smart materials,

Dr. Daniela Corda (IBBC, CNR, Naples) for the characterisation of the biological properties of the new molecules,

Prof. Caterina Fattorusso (UniNa, Department of Pharmacy) for the molecular modelling studies aimed at defining the interactions of the synthesized species with their biological targets.

The PhD student will spend a training period at a foreign institution chosen among those currently having International Cooperation Framework Agreement or collaboration in place, in order to acquire skills in the field of structural investigation methodologies through high-resolution mass spectrometry techniques and/or biosensor construction.

The PhD project falls within the ERC sectors PE5 *Synthetic Chemistry and Materials* and PE4 *Physical and Analytical Chemical Sciences*, with particular regards to the subsectors, PE5_17 *Organic Chemistry* and PE4_2 *Spectroscopic and Spectrometric techniques*.

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[i] Imperatore, C.; Scuotto, M.; Valadan, M.; Rivieccio, E.; Saide, A.; Russo, A.; Altucci, C.; Menna, M.; Ramunno, A.; Mayol, L.; Russo, G.; Varra, M. Photo-Control of Cancer Cell Growth by Benzodiazo N-Substituted Pyrrole Derivatives. *J. Photochem. Photobiol. A Chem.* **2019**, *377*, 109-118.
b. Imperatore, C.; Valadan, M.; Tartaglione, L.; Persico, M.; Ramunno, A.; Menna, M.; Casertano, M.; Dell'Aversano, C.; Singh, M.; d'Aulisio Garigliota, M. L.; Bajardi, F.; Morelli, E.; Fattorusso, C.; Altucci, C.; Varra, M. Exploring the Photodynamic Properties of Two Antiproliferative Benzodiazopyrrole Derivatives. *Int. J. Mol. Sci.* **2020**, *21*, 1246.

[ii] Imperatore, C.; Varriale, A.; Rivieccio, E.; Pennacchio, A.; Staiano, M.; D'Auria, S.; Casertano, M.; Altucci, C.; Valadan, M.; Singh, M.; Menna, M.; Varra, M. Spectroscopic Properties of Two 5'-(4-dimethylamino)azobenzene Conjugated G-Quadruplex Forming Oligonucleotides. *Int. J. Mol. Sci.* **2020**, *21*, 7103.

[iii] A. Mazzeo, M. Varra, L. Tartaglione, P. Ciminiello, Z. Zendong, P. Hess, C. Dell'Aversano Toward isolation of palytoxins: Liquid chromatography coupled to low-or high-resolution mass spectrometry for the study on the impact of drying techniques, solvents and materials.Toxins (2021), 13, 650.