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Many interesting targets in drug design are membrane-bound proteins. These proteins are often difficult to deal with since they lose their structure and hence their functionality when removed from their natural membrane environment. Therefore it is of great interest to study membrane-bound proteins directly on living cells. The G-protein coupled receptors (GPCRs) are an important subclass of membrane-bound proteins. In fact, between all clinically marketed drugs, greater than thirty percent are modulators of GPCRs.

To target membrane-bound receptors, as GPCRs, directly on living cells, a few homonuclear NMR experiments, such as saturation transfer difference (STD), WaterLogsy (WL) and transferred NOESY (trNOESY) can be used, detecting binding events and providing information on the bound conformation of the ligands. Those are also called ligand-based NMR techniques since only the ligand signals are observed. STD and WL are the most used ligand-based NMR techniques. These techniques are based on the transfer of saturation from the protein to the ligand or from the water to the ligand, respectively. In favorable cases, STD and WL experiments allow to establish if interaction occurs and which are the groups of the ligand in closer contact with the receptor (Group Epitope Mapping). Ligand-based NMR can also give quantitative information on the interaction strength (Kd). Finally, 2D trNOESY spectra are useful to gain information on the bound conformation of the ligand.

The group of Prof Carotenuto and others have successfully applied those techniques to study ligand-receptor interactions directly on living cells using NMR sample containing suspensions of cells which overexpress the desired receptor.

Melanocortins (MCRs) are a group of peptide hormones including adrenocorticotropin (ACTH) and α-, β-, and γ-melanocyte stimulating hormones (MSHs). To date, five human melanocortin receptors (MC1R-MC5R) have been characterized as GPCRs. As MCRs mediate a plethora of biological functions including, among others, feeding behavior, pain modulation, cardiovascular effects, and skin pigmentation, they can be considered potential drug targets for treating pain, food intake, and body weight.

In this context, prof Carotenuto, thanks to the above described NMR techniques, will contribute to the study of some MCRs analogues developed at the University of Cergy-Pontoise, aiming to obtain information on the bound conformation of these synthetic ligand at the different receptor subtypes.