The nicotinic acetylcholine receptor (AChR) has been the first ion channel to be isolated and characterized electrophysiologically, identified biochemically, cloned and imaged by electron microscopy, and remains the prototype of ligand-gated ion channels (LGICs). Most basic knowledge on the pharmacology, biochemistry and biophysics of LGICs comes from the study of the so-called “muscle-type” nAChR, a receptor that is highly enriched at the neuromuscular junction and in the electric organ of *Electrophorus* eels and *Torpedo* rays.

It is now known that nAChRs are members of the cys-loop LGIC family and are made of 5 subunits, each comprising 4 transmembrane domains (M1-4). The nAChR subunits are distinguished into  (1-10) and non- (1-4, , , ) subunits, that, as a first approximation, represent ligand binding and structural subunits, respectively. In general, a functional receptor is made up of 2 (or 3)  and 3 (or 2) non- subunits, with the exception of a few subunits (7 and 9) that can form homopentamers.

A further major distinction, related to their cellular expression pattern, is between skeletal muscle-type (1, 1, , , ) and neuronal (2-10, 2-4) subunits, though more and more neuronal subunits are shown to be expressed by a number of non-neuronal non-muscle cells.

The presence of such a large family of proteins makes it theoretically possible the existence of a very large number of different nAChR subtypes containing specific subunit combinations. In the first part of the talk I will present studies on the composition of actual nAChRs expressed by different cell types, in particular, in different brain circuits.

Due to their wide distribution in the body, nAChRs are involved in a wide number of functions. In the second part of the talk, I will discuss the involvement of specific nAChR subtypes in the pathophysiology of neuronal circuits of the central nervous system, with particular reference to reward circuits.

Finally, in the last part of the talk I will briefly discuss the rapidly expanding field of nAChR involvement in the physiology and pathology of non-muscle non-neuronal tissues.