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Editorial

Lighting up neuroscience

Fluorescence has revolutionised the way in which we observe biological processes. As early as the late 19th century high quality optics for transmitted light microscopy were available and the only means to improve resolution was to use light with lower wavelengths. In 1904 Köhler therefore constructed the first ultra-violet microscope. While the use of ultra-violet light was problematic, because the biological specimens fluoresced, it was soon realised that this property could be utilised owing to the contrast between fluorescent and non-fluorescent regions of the sample. Over the next decade these early experiments were extended by attempting to stain non-fluorescent structures with fluorescent materials and, in doing so, making them observable by fluorescence microscopy. By the 1920s the light of the primary light source and the light from the excited object could be separated by suitable filters, opening opportunities for many of the fluorescent methods used today.

We now often see reference to fluorescent tags, labels or probes and read about the development of new methods for scrutinising fluorescent signals. In this special edition of Neuropharmacology we find a rich array of these. In a review by Talwar and Lynch, 2015 (p. 3) we see the bridge between biophysical functions of ion channel activation that can be recorded using electrophysiological methods, and the accompanying structural changes that are reported by covalently coupling fluorophores to regions throughout the ion channel structure. By comparison Ruepp et al., 2015 (p. 13) uses voltage-sensitive fluorophores to directly measure the biophysical changes as an alternative to electrophysiological measurements, and describes an approach to identify new purinergic P2X1 ligands. The theme of fluorescent purinergic P2X1 ligands is further explored by Barden et al., 2015 (p. 22) who are able to observe their binding to membrane receptors in order to monitor binding kinetics, receptor migration and subdomain partitioning of single receptors. Lochner and Thompson, 2015 (p. 31) similarly explore the use of fluorescent ligands for probing the functions and pharmacology of ligand-gated ion channels. Focussing on the 5-HT_3 receptor, they describe the process of developing fluorescent ligands and show how these have been utilised in the 5-HT_3 receptor field to explore everything from single channels to whole animal physiology. McCarron and Chambers, 2015 (p. 41) extends our knowledge of ligand-gated ion channels by providing a review on the use of small molecule fluorescent ligands for imaging NMDA receptors, as well as for dopamine and serotonin transporters. In addition to the ligand-gated ion channels described above, we also see how the fluorescent ligands have contributed important insights into the structure, function and pharmacology of G-protein coupled receptors (GPCRs). Both Stoddard et al., 2015a (p. 48) and Ciruela et al., 2015 (p. 58) review recently reported ligands for β-adrenoceptors, adenosine and P2Y purinergic receptors, and explore the techniques in which they have been used. In relation to this, Stoddard et al., 2015b (p. 68) also provides the first description of a novel and high affinity fluorescently-labelled ligand for one of the members of this family, the adenosine A_3 receptor. In contrast to the synthetic molecules described by many of the authors in this special edition, Hofer et al., 2015 (p. 78) uses immunohistochemistry to identify the origins of endogenous peptide modulators of the GPCRs CB1 and CB2, reminding us that there is still much to be learnt about native ligands. To help with these studies, Merchant et al., 2015 (p. 90) provides a description of probes for studying the anatomy and function of synapses. The fluorescent false neurotransmitters that are used closely imitate the actions of native neurotransmitters, allowing selective imaging of synaptic processes to be visualised.

The methods described in this special edition nicely illustrate some of the diversity of fluorescent methods that are routinely used in laboratories today. We can see from these reports that when incorporated into or onto receptors, fluorescent probes allow us to visualise molecular motions within proteins, watch the movements of receptors within membranes and intracellular compartments, and view their locations in specific structures or whole tissues. In addition they can also be used in drug discovery to identify novel ligands and to determine their pharmacological properties. Importantly, unlike the first fluorescence measurements on preserved biological specimens that were undertaken 100 years ago, we now have unprecedented access to molecular tools for studying the function, pharmacology and physiology of biological systems in live tissues. What is more, significant technical advances in fluorescence microscopy combined with the development of novel bright and photostable fluorescent dyes have made it possible to break the diffraction resolution limit. Live-cell super-resolution microscopy has opened an exciting new door in bioimaging and will undoubtedly provide unprecedented insights into cellular processes in the future.

We would like to thank those who contributed to these advancements and to the researchers who have provided us with new insights in this special edition of Neuropharmacology. All of the original research articles and invited reviews in this Special Issue were peer-reviewed, and we are also very grateful to the reviewers who have given their time to make this possible.

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