Drug Targets

The Cannabinoid Receptors

Edited by *Patricia H. Reggio.*

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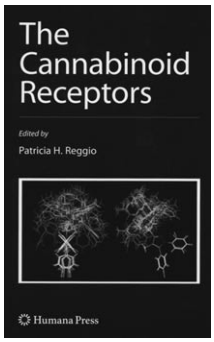

The process of reviewing a book (at least in the Selwood household) goes something like this—an email arrives out of the blue offering a free copy of an interesting sounding title (at least to me), I agree, thinking I could be reading the latest opinions of the leaders in the field and wanting to do my bit for the scientific community. Then the book hits the desk with a thud and the idea doesn't seem so good anymore. It is like reviewing a dozen mega papers all at once, do I check every reference? Of course, it is always bottom of the list behind that grant application, paper, safety assessment, and bedtime reading doesn't seem to get it done. Then there are the misgivings, what if I don't like it? These people have probably put months into writing it, suppose they review one of my grants/papers later, I might be on *the* list. Oh well, here goes…

This book is great if you want a lot of information about the cannabinoid receptors in one place; from evolution to molecular biology and medicinal chemistry, it is all here. There is a beautiful cameo article about cannabinoid receptor evolution (Elphick and Egertova), though I feel that this otherwise excellent chapter would have been better if it had been written in a more accessible style as not everyone is a molecular evolutionary biologist (I had to sit with Wikipedia to work out the ancestral fish line). The chapter describing the structure–activity relationships of classical cannabinoids (Raj Razdan) is another little gem; everything you need to know is here. It is clearly laid out and also includes those bits that are often missing from reviews, such as the numbering system of the compounds. Generally, I do wonder if summarizing large and complicated datasets is really the province of reviews in this format, surely this data needs to be in a database so that it can be searched by substructure. The StARLITe database, designed by Inpharmatica (now Galapagos/Biofocus) and transferred to EMBL–EBI with funding from the Wellcome Trust, is just such a database. Unfortunately, at the time of writing this review, StARLITe is not yet available to the scientific community; let's hope this changes in the near future.

In some ways this book is a monument to hundreds of years of publishing, nicely bound, quality printing, good illustrations, some colour prints (not many); but now if we look at the chapter by Thomas and co-workers we can see the limitations of the historical format. This is a nicely written piece presenting molecular modelling analyses of the cannabinoid ligands. The authors show the chemical structures with stick views of the 3D conformations (in black and white). It is okay, but how much better would it have been as an e-book with models you could rotate and enlarge to inspect properly. The authors have these models readily available. This is not the fault of the authors; it is an old-fashioned approach to publishing that has not yet been jettisoned. The mechanics of the book, the index and contents work fine, and there are plenty of references. It is good stuff, but could have been done better in the 21st century. Of course, any book of this type is just a snapshot in time and this one looks to have been put to bed in late 2006.

In part, interest in cannabinoids stems from the potential to manipulate the cannabinoid system for therapeutic uses. Unfortunately, this book was printed before the withdrawal of rimonabant (Acomplia, EMEA, October 23, 2008) because of a doubling of psychiatric disorders in patients, and because of a lack of efficacy in clinical practice as opposed to clinical trials. The fallout from this decision is likely to affect development of all CB1 antagonists (or inverse agonists), even those that are CNS excluded.

The main problem with this book is the focus, how can you have a discussion about "the cannabinoid receptors" and not cover the Edg receptors and the other lipid receptors such as GPR55. Plant cannabinoids certainly have affinity for these other receptors if that is the criterion. More to the point, the definition of the cannabinoid system looks to have had its day. We can now see the endocannabinoid system (surely more relevant than the plant cannabinoids) as simply part of the wider array of lipid mediators, a substantial set of molecules acting through multiple GPCRs. So is it correct to discuss rimonabant without mentioning its GPR55 activity? Already we can see new therapies emerging from the lipid field—fingolimod, the new multiple sclerosis drug works by inhibiting the sphingosine 1-phosphate receptor, but also has effects on other lipid receptors and CB1. Either you limit your discussion to a single receptor or, at least in my view, you have to discuss the entire system, by picking out CB1 and CB2 this book draws artificial boundaries.

This book is intended for newcomers to the cannabinoid field; it is certainly not a student text and assumes a high level of technical knowledge in which ever field is under discussion. That said, it is a useful repository of knowledge and as long as you are aware of its limitations, it is a good book to have.

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