

“Site Specific Hydrogen Deuterium Exchange Mass Spectrometry in ‘Real World’ Drug Development”

Hydrogen Deuterium Exchange Mass Spectrometry (HDX-MS) has quickly risen to become one of the most important structural biology methods in drug development. This came as quite a surprise to crystallographers/CryoEM people because, compared to what they can do, conventional HDX-MS really doesn't provide a high resolution picture of what is going on – you get at best ‘peptide level’ structural information so you can say things like ‘aha! It binds somewhere around here!’. To really stick it to crystallographers, we'd need to achieve ‘site specific’ HDX-MS, meaning that we can see exactly what is going on at each backbone amide hydrogen in the protein target, but that is hard because... well it's a long story, but CID doesn't work so you have to use ETD/ECD and you have to detune your instrument which means your experiment is about as sensitive as Elon Musk. Fortunately, some clever people at SCIEX developed a Zeno ECD cell that allows for efficient ECD and good ion transmission even after we detuned the hell out of it. This allowed us to demonstrate for the first time site specific HDX-MS for a real-world, drug-binding context which – you'll just have to just take my word for this until you see the talk – transforms the HDX-MS experiment, increasing its analytical power to the point where we can explore not only binding sites, but now also binding modes, ligand specific allosteric effects and K_d .

Biography: Derek Wilson originally desired to be an actor/singer, but for lack of talent and (let's face it) social graces, he instead tried his hand at Biochemistry. This went surprisingly well – he completed an undergraduate thesis that (sort of) led to a paper in the laboratory of the moderately tall Steven Rafferty (Trent) followed by a PhD in the lab of the very tall Lars Konermann (Western) where he eventually got the hang of things (Lars will tell you – it was touch and go there for a while) and published some papers. The next thing he did was interview at York, which – in a pretty questionable move – hired him before he'd even done a post-doc (which he did over the next year under the gentle... and by gentle I mean mostly absentee... tutelage of Chris Dobson at Cambridge). Armed with a pretty sorta good understanding of MS and a totally inadequate understanding of NMR ‘professor’ Wilson launched his independent lab in 2007, starting out inauspiciously by failing to get even a basic discovery grant... twice... But since then he's done pretty well. He's authored or co-authored over 100 publications (some of which are pretty good), led about \$35M in successful grants from all over the place (including discovery), founded (made up) the “Technology Enhanced Biopharmaceuticals Development and Manufacturing Initiative” and even won an award or two (including a fancy NSERC Synergy) and has generally been kicking butt. If you want to talk about bioanalytical mass spectrometry for drug development, he is possibly one of many people you may want to meet.