Rod Porter

From: Rod Porter [News@rodporterconsultancy.emailmsg.net] on behalf of rod.porter@rodporterconsultancy.com
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To: roderick.porter@btinternet.com
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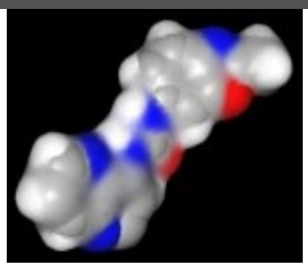


Medicinal Chemistry News from Rod Porter

September 2013 vol 4. no. 4

Dear Dr Porter,

1. Welcome

Welcome to the September edition of the Medicinal Chemistry newsletter from RodPorterConsultancy.Features this month include several items on pipeline approvals, attrition and industry costs, chronobiology, weak bases and absorptiona nice example of atropisomerism in action, constrained dipeptides, his phosphorylation and a brief consideration of RAS.

My thanks to Cyclofluidic and ChemPharmaServe for sponsoring this issue of the newsletter - this allows me to keep issues rolling out.

I am looking forward over the next few weeks to trying out software from Elixir software designed to securely optimise communication and collaboration across a remote project team.

Do have a look at the CompChem Solutions services a range of complementary activities to those of RodPorterConsultancy.

Please forward this newsletter to your colleagues – just follow the link at the bottom of this mail. Any comments, criticisms or suggestions for future articles are very welcome please mail Rod Porter - I am happy to give attribution.

My next mailing is planned for mid October. In the meantime I am looking forward to meeting up with friends and former colleagues at ELRIG (Manchester) and at the Cambridge Medicinal Chemistry conference over the next couple of weeks - do say hello if you are going to either of these meetings.

Wishing you every success with your research.

In this issue:

Cyclofluidic

Cyclofluidic is working with collaborators in the pharmaceutical industry to optimise hits to quality leads using its proprietary CyclOps™ microfluidics platform. CyclOps™ allows biological data to be collected on each compound minutes rather than weeks after it has been designed allowing true integrated data driven medicinal chemistry - saving time and money. A Cyclofluidics scientist will be presenting some of the companies research findings at the 2nd SCI/RSC Symposium on Continuous Processing and Flow Chemistry, 24th/25th September 2013 meeting and for a recently published example of the companies work please click here. For more information or to discuss evaluation and collaboration opportunities please contact Elizabeth Farrant, Business Development Director at Cyclofluidic.

ChemPharmaServe is an innovative chemistry solution provider, established in Cambridge UK in 2004, helping biopharmaceutical companies to fast-track their drug discovery and development projects. Their core expertise spans preclinical development and cGMP production of drug substances.

One of their most popular services is the provision of metabolites, custom-made compounds and labelled molecules.

They take the risk out of compound supply by investing in the chemistry, solving the technical issues and taking the responsibility for compound delivery to their clients allowing them to focus on drug discovery challenges. The costs are borne by them and they get paid only when products are delivered to the client's satisfaction. For more information and contact details please visit ChemPharmaServe.

SMR - next meeting

The next Society of Medicines Research meeting on 3rd October is "Kinases: New Horizons" will be held at the National Heart and Lung Institute South Kensington.The final meeting of the year is on December 12th From "Targets to candidates: Emerging Strategies in Drug Discovery" also at the NHLI

2. State of the industry

FDA approvals for first half of 2013

Analysis of FDA drug approvals over the first six months of the year has just appeared **1** with 13 novel compounds approved. So is this time to start worrying over low numbers of approvals again – remember 39 approvals for 2012. Answer is no – at least not yet - at the half way point last year only 14 drugs had been approved, apparently the FDA tends to approve more drugs in the second half of the year than the first. Five of the approved compounds are predicted to achieve (multi)billion dollar sales by 2018. From a scientific perspective its good to see ado-trastuzumab emtansine a second antibody drug conjugate approved; antisense representation with mipomersen; the first sodium-dependent glucose co-transporter 2 (SGLT2) inhibitor to be approved in the United States canagliflozin and the first MAPK/ERK kinase inhibitor trametinib. Oncology dominates the target indications as might be expected with COPD, diabetes, hypercholesterolaemia and imaging/contrast agents also represented. The full list of approvals is here. At some point there should be a surge of products coming through from the FDA breakthrough categorisation although that (presumed) surge will mean a dipin approvals in subsequent years.

1. Nature Reviews Drug Discovery 2013, 12, 568 doi:10.1038/nrd4097

Attrition in Phase II and III

A new analysis of failure rates in PhII and PhIII for 2011-2012 **1** compares with similar analyses for PhII (2008 – 2010) **2** and PhIII (2007-2010) **3**. Between 2011 and 2012 there have been 148 failures in PhII and PhIII/submission for which 105 had reported reason for failure. In PhII failure is dominated by lack of efficacy (59%) and safety(22% a figure that includes those compounds with an inadequate TI) slightly higher than 2008 – 2010. However strategic considerations showed a reduction to 16% (still high in my view) compared with a staggering 29% in 2008 – 2010 (effect of mergers and "right-sizing"?). In contrast for PhIII failures due to efficacy has declined from two thirds to about half although failure due to safety issues has increased. In a trend analysis of companies accounting for two thirds of global R&D expenditure it appears that PhII successes is still running at below 20% although there is apparently a modest 7% increase in PhIII success rate. Still if this is a sign that better decisions are being around the output from (relatively) cheap PhII trials prior to entering PhIII that has got to be considered progress.

1. J. Arrowsmith and P. Miller Nature Reviews Drug Discovery 2013, 12, 569 doi:10.1038/nrd4090
2. J. Arrowsmith Nature Reviews Drug Discovery 2011, 10, 328
3. J. Arrowsmith Nature Reviews Drug Discovery 2011, 10, 87 doi:10.1038/nrd3375

First in class v. best in class and target duplication

First in class v. best in class - a report addressing this question suggests that being first in class and best in class, not surprisingly, gives most commercial success. However being first in class even if not quite as effective is about as commercially successful as a more effective second in class compound. Being second in class or later with markedly worse therapeutic outcome than first in class is heading for commercial disaster. Generally also fast follower compounds need to be launched within the first two years after the first compound has launched ie the window for commercial success is relatively narrow and effectively the follower compounds will probably have to be in PhII when the first compiound is launching. The analysis proposes a few exceptions to this - firstly that favourable differentiation of a follow-on compound such as aripiprazole (arguably) 6th antipsychotic to launch in its class but commercially successful offering a subtle differentiation of mechanism and extended range of indications. A second factor may be where cycling of drugs is required to identify the best compound for the individual - such as in the SSRI anti-depressant area. Third is that marketing can make a big difference to commercial success. While the analysis can be subject to some criticisms it does rather look like offering real therapeutic advantage first is the place we would all want to be if not can we quickly get to market with a superior or differentiated product or can we argue that one of the exceptions applies. If not should that compound really still be in development?

Following on from first v. best there has been quite a lot of discussion about the duplication of research effort on the same molecular targets by pharma. However, a recent analysis, albeit with a number of caveats, suggests the duplication may not be quite as bad as all that. Using Pharmaproject as a source the GSK authors found that the 247 "proven" targets (targets with a drug already on the market) did have 5 or more companies working on about two thirds of them - that is a lot of duplication. However, for the 712 "novel" targets (with no approved agent) the picture is rather different with over 70% having only one or two companies investigating them. Furthermore in this "novel" category of the 83 targets with a compound in PhIII 34 are being pursued by five or more companies while preclinically of the 304 identified targets 267 are being followed by one or two companies only. Within therapeutic areas neurodegeneration targets, perhaps not surprisingly, tend to see a lot of duplication probably due to the paucity of targets and the high stakes being played for. One problem acknowledged by the authors is the known unknown of those companies working on a target who have not revealed their interest via either the literature - patent or other.

Of course another question is how much duplication of effort across the industry is sensible – certainly it seems to me that some duplication makes sense after all the majority of projects end in failure for various reasons and being first to market doesn't guarantee best at least when later compounds have additional advantages. I guess this is one of those – how long is a piece of string questions.

Cost of producing new drugs - again

A crude but intriguing analysis of drug discovery costs (with data here) sees an extended reprise of of an earlier survey highlighted in FierceBiotech and further discussed by Derek Lowe in which total R&D budgets are divided by the number of products produced by that organisation during the same 10 year period. One problem with the survey is that different companies include different items in their budget like post marketing follow-up safety and use extensions, a smaller burden for one product companies. In the case of Abbvie all the money spent on devices as opposed to drugs makes them stand out as apparently by far the least efficient company unless you take that tangential expenditure into account. 65 companies had developed only one product at a mean cost of $765M, however the spread is enormous – from $15M - $4,325M a 288 fold range. Hidden by the survey is how much money have big pharma put into in-licensed projects from those companies that apparently managed to develop a product so cheaply. Furthermore for those companies with one product, in reality they represent the lucky ones who made it and this ignores the large number that failed including those failures would be a truer reflection of cost. Amongst the 19 companies who launched 4 or more drugs the mean cost per drug was around $5,100M a fair bit higher than one launch companies. While some factors have already been considered perhaps another is that larger companies can and do run some particularly expensive clinical trials which of course have a nasty habit of failing- perhaps that's another debate. While there is some spread in cost Sanofi $10,000M/cpd (ouch!) to Shire $957M/cpd the 10 fold spread is clearly less than for one product companies. BMS Genentech, Biomarin and Regeneron also look pretty effective. I guess getting a bit lucky (OK so you can at least in part make your own luck) inevitably introduces a spread in the costs for comparable companies one failure or success makes a big difference to the numbers

Another aspect that isn't considered in this review (and perhaps correctly) is the value of the portfolio generated – Dendreon coming in at 59th having spent $509M must be wandering if that relative success was worth the cost!

Bottom line remains - this is an expensive game with no easy fixes although a few suggestions are made why some companies at least appear more effective than others.

3. In Brief

Chronobiology and chronotoxicity

Readers are referrred to a recent blog entry relating to the discussion of relevance of dose timing to efficacy and the role of circadian rythm on biology and toxicity.

hERG channel blockers and phospholipidosis inducers?

Analysis of hERG and phosphlipidosis data generated for a set of 4,000 compounds **1**, showed that a substantial majority of phosphlipidosis inducing compounds (77%) were also hERG inhibitors. Of this set almost all were positively charged. In contrast those compounds that were phospholipidosis inducers half were steroids perhaps reflecting the amphoteric surfaces that a steroid tends to present.

Perhaps none of this is a major surprise but yet again highlights the downsides of trying to mitigate solubility issues by whacking on a basic centre – you may solve one problem but others come out of the woodwork see my discussion below on absorption of weakly basic drugs and elevated stomach pH.

1. H. Sun et al Bioorg. Med. Chem. Lett., 2013, 23, 4587

Back to top

4. Medicinal Chemistry

Absorption and high stomach pH

A review **1** highlights some of the problems of variable exposure that can be encountered with weakly basic drugs given to

patients with elevated gastric pH (causes of which can include H. pylori infection, AIDS, use of proton pump inhibitors (PPI) or H2 (H2R) antagonists, age). One example cited was ketoconazole where patients receiving PPI or H2R therapy alongside ketoconazole had >80% reduction in AUC and Cmax relative to patients not receiving PPI/H2R antagonist treatment. Conversely weak acids can show improved exposure. Some practical clinical or formulation solutions (excuse the pun) to the problem included consuming an acid drink (Coca-Cola was the example) with the drug, pretreatment with an organic acid (glutamate which sounds even worse than Coca-Cola in my opinion) or solid dosage formulations containing an organic acid such as fumarate or HCl. While these strategies can work they also tend to lead to significant inter-patient variability. Also reviewed are ways of examining formulations of such compounds in vitro and in preclinical models not quite as straightforward as you might expect in the absence of agreed standard protocols.

In my experience the extent of stomach pH change and the sort of drug drug interaction relating to antacids/PPI's/H2R antagonists isn't always appreciated sufficiently during the research phase. Indeed I have often heard the advice of "just put any sort of basic centre into your molecule to "solve" solubility issues". Ultimately however all this does come down to the medicinal chemists (doesn't everything in small molecule drug discovery!) being able to work with appropriate templates with adequate intrinsic solubility so that a greater or lesser degree of ionisation doesn't impact absorption substantially.

1. A. Mitra and F. Kesisoglou Mol. Pharmaceutics, Article ASAP Publication Date (Web): July 22, 2013 DOI: 10.1021/mp400256h

Back to top

NMR 3D structural information in drug design

An account **1** of a new NMR method to determine high definition unbound conformations of ligands and their dynamic motion, discusses application of the approach to streptomycin. Two major conformational families are observed the most populated of which corresponds to the crystallographic conformation in complex with the 30S ribosomal subunit. The method can be applied in physiologically relevant solvents and is independent of molecular modelling using multiple datasets, much greater quantities of data than previous NMR approaches and a dynamic model during refinement. The authors argue that, in the absence of a target crystal structure the unbound conformation – particularly of high affinity ligands, can be used to deduce the target site binding pocket shape and, at least to some extent, electrostatics of interaction. Clearly the data can be used to help improve predictions of conformational constraint as well – which does call on the molecular modelling for support. The C4X team have also just reported the solution structure of an antagonist for a class B GPCR, CRF **2**.

1. C. D. Blundell et al Bioorg. Med. Chem. Lett., 2013, 21, 4976.
2. C4X Discovery press release 20th Aug 2013

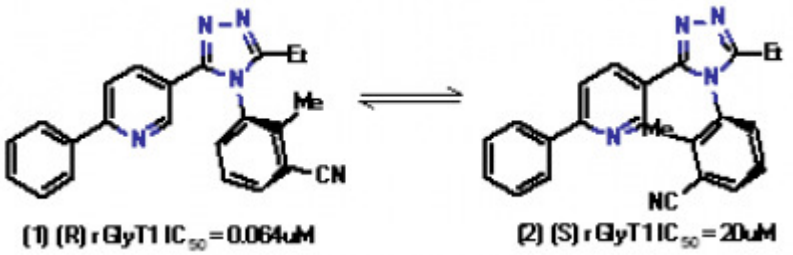
Back to top

Atropisomerism and GlyT-1 inhibitors

Sticking with the theme of conformation a nice example of atropisomerism **1** that I came across during the early stages of preparing to write a chapter on Glycine Transporter inhibitors for a book on Schizophrenia. Reported is a series of substituted phenyl triazoles, one of which was separated into atropisomers by chiral HPLC and shown to be stable – Gibbs free energy for racemizatioin estimated at 31.4kCa/mol giving a 37 year half-life. The R-enantiomer (1) was potent and selective in vitro as a GlyT-1 inhibitor and showed good in vivo activity and reasonable PK with no evidence of efflux transporter liability. Plasma free fraction was 10%, higher than I might have expected based on the number of congruent aromatics but perhaps reflecting the "conformational "enrichment" due to the steric crowding/atropisomerism.

1. T. Sugane et al J. Med. Chem 2013, 56, 5744

Back to top



Plasma protein binding: From discovery to development.

Another review **1** on plasma protein binding, effective drug concentration – for efficacy and for potentially precipitating off-target effects or DDI's and cross species differences in plasma protein binding. The influence of plasma protein binding on behaviour of compounds in vivo has been an area of misunderstanding. A still seminal paper in this field must be the one from Smith/Li/Kerns **2**, featured in a previous newsletter, on misconceptions surrounding plasma protein binding in drug discovery. While this tends to focus on the research end of drug discovery clinical impact has also been considered on many occasions e.g. **3**.

1. T. Bohnert and L. S. Gan J. Pharm. Sci., 2013, doi: 10.1002/jps.23614

2. D. A. Smith, L. Di and E. H. Kerns Nature Reviews Drug Disc., 2010, 9, 929
3. L. Z. Benet and B-a Hoener Clin Pharmacol. Ther., 2002, 71, 115

Back to Top

Redox chemistry and drug discovery

A paper just out **1**, that set me thinking a bit, discusses redox potentials of hydroxycinnamic acids such as caffeic and ferulic acid these are of particular current interest in health because of their anti-oxidant activity. It's estimated that this class may constitute one third of the phenolic compounds in our diet. The paper determines redox potentials for a range of these acids alongside their antioxidant activity showing that the two properties correlate with each other and allows development of structure property activity relationships.

All this is well and good assuming stuffing ourselves with anti-oxidants really is a good thing, though I will keep drinking the red wine just in case, but what about use of redox potentials more generally in drug design – are we missing a trick? My past experience and from what I see in the literature I generally read is very little use of the technique to help understand how our molecules will behave – when I tried to get some redox potentials measured while working in big pharma I was told the kit was no longer available – note the no longer. I guess where I am coming from is can we use measured redox potentials as part of our understanding of improving stability of molecules in aggressive redox environments particularly within metabolic enzymes. A quick look on google did pick up this thesis sponsored by Roche **2** looking at developing high throughput redox measurement techniques. The starting point they come from is that redox potentials can be considered equivalents of ionisation potentials **3**. So could we be looking at some sort of cascade of calculated ionisation potentials during in silico design followed by redox potentials after synthesis and who knows perhaps exploit electrochemistry during synthesis another under used area perhaps? It would be good to hear people's thoughts on this.

1. J. Teixeira et al BioMed Research International Volume 2013 (2013), Article ID 251754,
2. A. Felix Redox Potential and Metabolic Stability: Development of High Throughput Assays for Early Compound Profiling Dissertation Univ Basel 2008
3. F. B. Guengerich and T. L. MacDonald The FASEB Journal 1990, 4, 2453

Back to top

RAS inhibition

Somatic mutations of RAS are present in one-third of all human cancers which can lead to aberrant activation of downstream signaling pathways involving RAF/MEK/ERK kinases. There has been little success in trying to identify direct RAS binding inhibitors to block downstream aberrant signalling effects of mutants **1** nor have efforts so far proved successful in blocking obligate prenylation via farnesyl transferase inhibition due to shunt mechanisms kicking in. Now reported **2**, however, is a strategy to block the farnesylated RAS from reaching cell membranes by competing for the PDEδ carrier protein used by the RAS to reach the membrane. The team identified a benzimidazole (1) that bound to the PDEδ that prenylated RAS binds to. Interestingly crystallographic studies revealed that two molecules of the benzimidazole bound to the PDE pocket Fig. 1 which allowed the development of more potent compounds by a simple dimerisation although the dimerisation doesn't look like its optimal based on the drop in ligand efficiency of the dimeric molecule Deltarasin (2). Certainly it looks like there will be plenty of room for further optimisation. Despite these comments (2) does show activity in cell based assays consistent with its proposed mechanism of action and reduction in the rate of growth of tumours in a Panc-Tu mouse xenograft model 10mg/kg bid

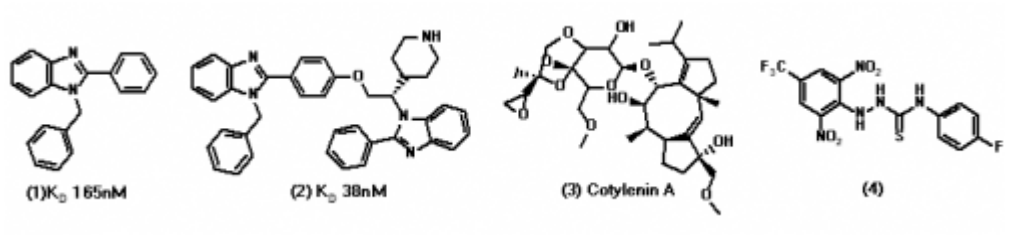
A second interesting approach recently out **3** is use of Cotylenin A (3), a plant growth regulator, to stabilise RAF/14-3-3 interactions by binding to inhibitory 14-3-3 interaction sites but not activating sites. Cotylenin-A on its own is inactive in RAS mutant models but combination with an anti-EGFR antibody shows synergistic effects in vitro and in vivo. Cotylenin-A in conjunction with rapamycin has previously been reported 4 to cooperatively inhibit tumour cells through induction of G2.

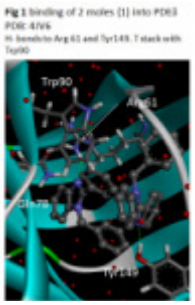
Finally another new development **5** is the identification via virtual screening against a pocket in RAS identified by the authors that inhibits effector binding. Compounds e.g. (4) "inhibit both anchorage-dependent and -independent growth and induce apoptosis of H-rasG12V–transformed NIH 3T3 cells, which is accompanied by down-regulation of downstream molecules such as MEK/ERK, Akt, and RalA" Furthermore compounds were active via oral administrattion on a xenograft of human colon carcinoma SW480 cells carrying the K-rasG12V gene. I have to confess I am not totally enamoured of the structures but it establishes an interesting precedent which could lead to new directions perhaps **1** will need rewriting in due course!

1. W. Wang et al Bioorg. Med. Chem. Lett. 2012, 22, 5766
2. G. Zimmermann et al Nature 2013, 497, 638
3. S. Kasper et al, ACS Chem. Biol. 2013, Article ASAP DOI: 10.1021/cb4003464
4. T. Kasukabe et al, Cancer Sci. 2008, 99, 1693. doi: 10.1111/j.1349-7006.2008.00867.x
5. F. Shima et al, Proc. Natl Acad. Sci. 2013 29 Apr doi:10.1073/pnas.1217730110

Back to top

RAS inhibitors





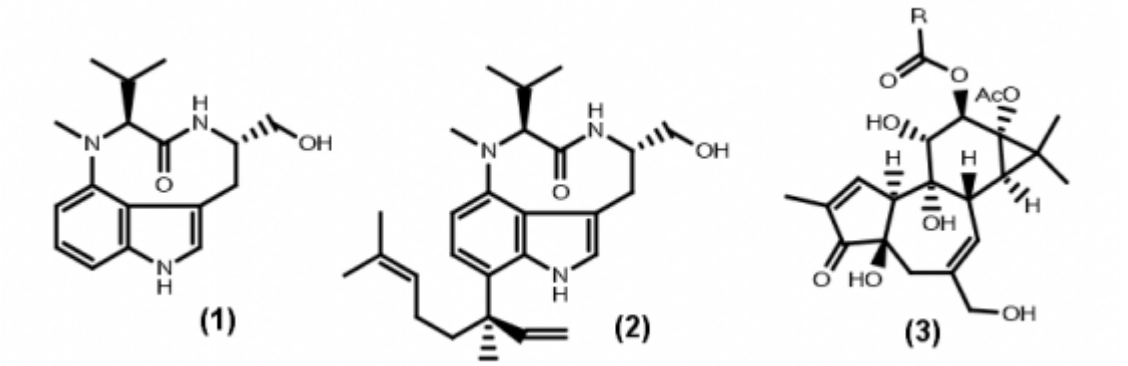
Dipeptide – conformationally constrained 9-membered rings

Non-ribosomal peptides synthesised by non-ribosomal peptide synthetases are a class of peptide secondary metabolites often with interesting biological activities whose synthesis is independent of mRNA and thus can use non-proteinogenic amino acids. They often contain cyclic structures and modified e.g. formylated, methylated residues. A database **1, 2** has been put together with over 1,000 entries for non-ribosomal peptides. Two examples are indolactam-V (1) and its prenylated analogue Lyngbyatoxin-A (2) isolated from blue green sea algae in small quantities. A recent report **3** now describes producing these molecules from E. coli at upto 150mg/l for indolactam-V. These two compounds are protein-kinase C activators/tumour promoters similar to the perhaps better known phorbol esters (3). I have to confess this particularly caught my eye as being very akin to my PhD work (total synthesis in my case) on the Teleocidins/Lyngbyatoxin.

Perhaps more important (these compounds have been totally synthesised after all **4**), is however, that these represent 9-membered ring compounds which have always been regarded as tricky beasts - in my hands I tended to achieve around 30% yields for the cyclisation using high dilution and others have done better since **4**. One would imagine the chemistry is helped here by the rigidity provided by the three atoms of the indole ring. Rather more to the point is that these are conformationally constrained cyclic dipeptides – amide E/Z isomers being evident by NMR with the cis isomer thought to be the PK-C activator relevant conformation **5**. It is fairly easy to see how indolactam V analogues (or similar aryl ring constrained ring templates) could be used as constrained peptidomimetics – preferably losing the PK-C activator/tumour promoting activity at the same time! Conformationally constrained dipeptides have featurted strongly in drug discvoery over the years not least the diketopiperazines **6**.

1. S. Caboche et al Nucleic Acids Res. 2008 36(Database issue): D326–D331. doi: 10.1093/nar/gkm792 x
2. NORINE: a database of nonribosomal peptides
3. S. E. Ongley et al ACS Chem. Biol., 2013 Publication Date (Web): June 17 DOI: 10.1021/cb400189j, 2013
4. Z. Zhu et al Org. Biomol. Chem., 2011, 9, 2512
5. K. Irie et al J. Am. Chem. Soc., 1996, 118, 10733
6. A. D. Borthwick Chem. Rev., 2012, 112, 3641

Back to top



Histidine phosphorylation - a therapeutic target?

I have mentioned phospho-his post translational protein modification in the past highlighting that one of the issues in advancing the field has been the difficulty in detecting phosphorylated histidine due to chemical lability. Progress has now been reported with the presentation of a polyclonal antibody with high affinity for a range of his phosphorylated proteins 1 , 2 that used a stable phosphohis as the hapten . It has previously been estimated that about 6% of phosphorylated amino acids are histidine 3, 4 making it about 100 fold more abundant than phosphotyrosine 4 so clearly this is a significant path of post translational modification, however, it does seem to have been largely neglected as a point of drug intervention perhaps in no small part due to the difficulties in working in the area.

An additional recent development is the report 5 of a crystal structure for bacterial histidine kinase with signal transducer and sensor domains which may represent a target for novel antibacterials. Thus the field continues to move forward although as yet I am unaware of anyone addressing his phosphorylation therapeutically or indeed what effects existing S/T kinase inhibitors are

having on His phosphorylation - please let me know if I have missed something.

1. J. M-Kee et al Nature Chemical Biology 2013, 9, 416 doi:10.1038/nchembio.1259
2. M. J. Piggott and P. V. Nature Chemical Biology 2013, 9, 411
3. H. R. Matthews Pharmacology & therapeutics 1995, 67, 323. DOI: 10.1016/0163-7258(95)00020-8
4. A. Kowluru J. Cell. Mol. Med. 2008, Vol 12, No 5B, 1885
5. C. Wang et al PloS Biol 2013 (11(2) e1001493 doi:10.1371/journal.pbio.1001493

Back to top

5. Chemistry

Asymmetric glycans

Picking up from carbohydrates as templates for lead discovery a significant development in the synthesis of asymmetrical branched glycans has now been reported **1, 2**. Glycans including oligosaccharides, glycoproteins and glycolipids are key elements in recognition between proteins and the full complement of glycans has never been determined for any cell type. While there are synthetic routes to linear and symmetrical branched glycans (along with microarray plates) the more prevalent asymmetrically branched glycans are much less accessible. Reported by Wang **1** is a route exploiting both synthetic chemistry and biochemistry using glycosyl transferase mediated diversification of a key pentasaccharide core intermediate present in all mammalian glycans. Microarrays prepared using asymmetric glycans showed different protein binding profiles relative to linear or symmetrically branched microarrays and are more likely giving a truer reflection of what is happening physiologically. Perhaps new microarrays containing asymmetric branching may give a clearer guidance on potential for intervention.

1. Z. Wang et al Science 2013, 3451, 379
2. Perspective L. L. Kiessling and M. B. Kraft Science 2013, 341, 357

Back to Top

6. Conferences

Conferences Rod Porter Consultancy will be attending - click on the links for the agenda.

- Drug Discovery, ELRIG, Manchester 3rd, 4th September
- RSC/SCI Medicinal Chemistry Symposium Cambridge 8th-11th Sept
- Kinases: New Horizons, SMR NHLI London, 3rd Oct
- From Targets to candidates: Emerging Strategies in Drug Discovery, SMR NHLI, London 12th Dec

Meetings Attended

Meetings attended during June included Partnerships: future models for drug discovery SMR Lily Horsham, 20th June. If you spot any items from these meetings that you would like to know more about I should be able to supply some notes to you. Of course nothing compares with actually attending the meetings and speaking with old and new friends.Slide packs are now available for talks from the SCI meeting "Choosing the Right Target"

Back to top

7. Also of interest

Using the web, all sorts of interesting resources appear. If you come across any resources that you would like to share please contact Rod Porter.

Perfect papers for perfect journals

Picked up by my friend and colleague Steve Smith (Stortmedchem) an item from Derek Lowe's blog - perfect papers for different journals - well we shouldnt take our selves too seriously all the time should we!

These sites are featured because Rod Porter has found them of interest - featuring these sites does not reflect any endorsement or accountability for their use from Rod Porter Consultancy

Back to top

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8. About RodPorterConsultancy

Established in 2009 RodPorterConsultancy offers medicinal chemistry consultancy services to a widening client base of small biotechs, academic and charitable bodies. Services offered include assistance with or proposal of medicinal chemistry strategies, with a particular interest in CNS targets, independent, expert review of ongoing programmes and projects, review, critique and refereeing of research proposals, third party due diligence and more. If I can't help you perhaps my informal network of contacts can. Visit the RodPorterConsultancy website, see my linked-in page or contact Rod Porter directly for more information.

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About CompChemSolutions

CompChem Solutions offers computational chemistry & computational biology services to academic and industrial researchers involved in drug discovery and development. Established in 2004 and based in Cambridge, UK, CompChem Solutions has a wealth of experience across the range of chemoinformatic and computational chemistry disciplines, having worked extensively in many therapeutic areas, particularly oncology, inflammation and pain. Recent publications from CompChem Solutions have exemplified the use of in silico methodology for target validation and identification, particularly within the context of phenotypic screening. Services can be provided in virtual screening, rational ligand design, protein homology modelling, library design, ADMET property prediction, and many other areas.

We are currently offering fixed-price virtual fragment screening services for a limited period. Please contact Susan Boyd at CompChem Solutions for more details on any aspect of CompChem Solutions services.

Back to top