

## Funding for knowledge-sake – Letter

In his recent editorial, Roland Kozlowski wondered ‘what attraction academia still offers for the academic interested in applied research’<sup>1</sup>. His portrayal of academia as a *de facto* niche for industrial research at a much lower salary ignores important philosophical issues in the way funding sources are evolving. While I share an enthusiasm for improved academic–industrial relations, I emphatically disagree with the implication that the research community should accept the academic–industrial relationship as a research funding model because no real alternatives exist.

Kozlowski has observed the benefits that academically minded scientists receive from an industrial employer and collaborator relative to a University employer and governmental sources of research funds. The differential results in ‘few young scientists (who) are tempted to remain in academia’<sup>1</sup>. The argument that academics (at heart) are becoming more inclined towards industry and industrial funding, however, is depressingly attributed to an:

- Increasingly vague distinction between the motivations and purpose of industrial versus non-industrial funding sources
- Adaptation of academics to the paucity of funding sources for work that does not meet the expectations of particular industries, charities or governments.

Academics have found relationships with industry rewarding, but sometimes through necessity rather than consciously deciding that the best research will come from a com-

promise of the academic and industrial approaches to research. I worry that the politics of science creating these motivations for academics are an early warning of a serious threat to the diversity of research.

### Pure and applied research

The sense in which Kozlowski uses the terms ‘applied’ and ‘pure’ research is a false distinction between industrial and academic research. Both the academic and industrial sectors do both types of research. Whether the work is applied or not does not determine how it addresses fundamental issues or bear upon its conduct and quality. If anything, when research is too pure, it can be neglected even by the academic research community<sup>2,3</sup>. Whether the research has application is a non-issue for academics. My reluctance to accept the industrial funding model has nothing to do with the research being applied.

### Knowledge-driven research

The relevant characteristic defining different approaches to research has more to do with the options for discovery than application. The sense in which ‘knowledge-driven’ research differs from that traditionally stereotyped as industrial research is that knowledge-driven questions do not need to be relevant to a desirable outcome (everything from profit to the public good). Applied research is not automatically embraced by either industrial or government sponsors at present because some applications are not what the sponsor desires.

### Industrial funding by default?

I do not accept that because govern-

ments are adopting the industrial funding model that I should embrace it. My own government in New Zealand requires that requests for research funds from most of its contestable research money (sought by academics) is blessed by an existing industry<sup>4</sup>. Thus, to propose an applied project with no benefit (and possibly a threat) to existing vested interests would have been a wasted effort, regardless of the project’s merit.

I begrudgingly concur that governments are adopting the industrial funding model. The public good fully substitutes for corporate profit as a motivation to pose, and oppose, certain questions. Whether industry, government or charity funds the research, or whether the research is applied or pure, does not matter if the questions are constrained to those that will further existing interests. A recent article reviewing the biomedical research on salt and blood pressure provides an excellent example<sup>5</sup>. Some researchers perceive they have an obligation ‘to push for universal salt reduction’ while the research is conducted ‘to bring scientific certainty’ to the issue of the effects of dietary salt on blood pressure. What worries me, as a committed academic, is not the compromises of the academic–industrial relationship, but the apparent loss of funding opportunities for research that could discover something our sponsors might rather not know.

By contrast to Kozlowski, I believe our industry-bound young researchers are following jobs rather than endorsing the academic–industrial bond. For all their apparent disinterest in academic careers, my recent experience with the job market tells

me that good academic positions are not vacant for the taking. There are benefits to the academic-industrial relationship to be sure, but its popularity among job and fund seekers, and emulation by non-industrial funding bodies, is not evidence of its success. In a world with no alternatives, I concede Kozlowski's point that industrial relations do not disproportionately impact academic research. However, I fear for the advancement of science in such a world.

Jack A. Heinemann  
Senior Lecturer

Department Plant and  
Microbial Sciences  
University of Canterbury  
Christchurch, New Zealand  
tel: +64 3 364 2926  
fax: +64 3 364 2083  
e-mail: j.heinemann@pams.  
canterbury.ac.nz  
URL:  
<http://www.pams.canterbury.ac.nz/>

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# Beyond uHTS: ridiculously HTS?

Newcomers to the world of HTS attending the back-to-back High-Throughput Screening/Miniaturization Technologies conferences at Monterey, CA, USA (28 February-3 March 2000) could have been forgiven for thinking that the industry was struggling a little to get to grips with where its priorities should lie. While some speakers were presenting exciting glimpses of technological developments far beyond the 1536-well plate with ever greater potential throughputs, many others were starting to acknowledge that primary screening is no longer the bottleneck in the pursuit to discover novel lead candidate molecules with therapeutic potential. What has emerged are bottlenecks both upstream, notably assimilating target information emerging from the Human Genome Project into screenable assays, and downstream, coping with the 'rich seam' of hits that ultra-HTS (i.e. that performed in 1536-well plates) is uncovering.

## Coming up with the goods

A solution to the hit characterization perspective was offered by Bill Janzen

(Sphinx Pharmaceuticals, Research Triangle Park, NC, USA) in his keynote speech, who reminded the audience just how far the HTS industry had come in a relatively short time (Table 1). Before the audience could become too self-congratulatory, he reminded everyone of the key obvious limitation to HTS: it usually identifies only hits rather than leads. He suggested the following definitions:

- Hit – A molecule with confirmed activity from the primary (HTS) assay, with a good profile in secondary assays and with a confirmed structure.
- Lead – A hit series for which the structure-activity relationship (SAR) is shown and activity demonstrated both *in vitro* and *in vivo*.

Janzen offered Sphinx's solution to the dilemma of how to prioritize upwards of thousands of active molecules now being produced from uHTS. He proposed that the solution lies in close co-operation between compound library managers, HTS biologists and discovery chemists under the umbrella

'hits to leads'. Key features are rapid delivery of 'cherry-picked' active compounds for batch potency/selectivity testing and fast cyclical library synthesis based on screen results to see if SAR exists. A key requirement is having access to powerful data analysis software tools to assimilate the vast quantities of data being generated. For Sphinx, results so far are very encouraging, with two-thirds of the projects having yielded leads.

## Exploitation of virtual screening

Building on the theme of possibilities downstream of HTS, Andy Good (Bristol-Myers Squibb, Wallingford, CT, USA) contended that virtual screening techniques and HTS have much to offer each other. He claimed that the industry had been slow to exploit fully the extensive quantities of HTS data it had now accumulated. The prerequisite is for the generation of high-quality screen data through maintenance of compound integrity, rigorous compound handling and testing of samples in duplicate to improve reproducibility, which becomes economically more viable