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AN AUDIENCE WITH…

Stephen Frye

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Nearly 175 scientists and drug developers gathered in Lake Tahoe in March for a Keystone meeting on novel targets and new chemical space. Key topics on the programme included advances in epigenetics and toxicology, but some of the most interesting themes emerged unplanned. Conference co-organizer Stephen Frye, who works at the University of North Carolina in Chapel Hill, USA, but previously led discovery medicinal chemistry at GlaxoSmithKline, told **Asher Mullard** that one unexpected success was in highlighting the emerging capabilities of academic drug discoverers. Another theme, covered by SciBx, was the renewed interest in phenotypic screening (see go.nature.com/9l2mO8).

You are among a growing cadre of researchers who have moved from industry to academia. Why did you make the switch 5 years ago?

Most fundamentally, at a professional level, I thought that I could make a bigger contribution in academia than I could at a pharmaceutical company.

I had gone to GlaxoSmithKline — although when I had started it was Glaxo — believing exactly the opposite. But so much has changed over the past 20 years, and I thought that pharma was too busy doing mergers and acquisitions to actually focus on long-term strategies for drug discovery or to let a project exist for the 10–12 years that are needed to get from idea to patient. So I felt like it was time to do something different.

How has academic drug discovery changed since you made your move, and how was this reflected at the meeting?

What I saw was great scientific advances and individual success stories from within academia, juxtaposed against people who are really concerned about the model for success in the industry, where it is all doom and gloom.

As noted last year in an article in *Nature Reviews Drug Discovery*, since 2003 there have been 50 or so drug discovery centres created in academic or non-profit organizations in the United States. So whereas most biological laboratories in academia have not had the skills or the scientific knowledge to address the challenge of ligand discovery, what is changing is that these skills are now being fostered within academia. The optimist in me says that the story that Scripps' Jeff Kelly told at the meeting — about how he took the extremely novel high-risk concept behind the small-molecule protein stabilizer tafamidis all the way through to licensing by Pfizer — will become a path that will be available to more academic researchers. The growing number of academic drug discovery centres will enable more and more investigators to test their hypotheses with small molecules in *in vitro* and *in vivo* models.

What are the outstanding hurdles to more successful academic drug discovery?

A huge bottleneck in academia is the lack of models for funding projects that have passed the animal proof-of-concept stage. Perhaps industry is going to start licensing things or partnering earlier though, and perhaps the US National Institutes of Health's National Center for Advancing Translational Sciences will also help us to move from a lead molecule to something that can be used to test a hypothesis in humans.

The other really huge problem — for both industry and academia — is how to test more novel hypotheses in humans without spending a billion dollars to get every drug out. A lot of the problem is redundancy and overlap, because people consider the early stages of drug discovery to be part of the competitive landscape. Companies in parallel all work on the same hot targets, all go into Phase II clinical trials and most of the time they all fail. We need to come up with different models to test our hypotheses, in the open, where everybody can learn and benefit together.

How do academic drug discovery centres work with one another?

Working within academia has been really refreshing. We share anything with anybody, with basically no limitations. Discovery work is accelerated enormously if nobody has intellectual property.

Barbara Slusher, at Johns Hopkins University, is also in the process of creating an academic drug discovery consortium in the United States, and the founding members will include my centre. We want to build networks and have people share things even more readily, without the organizational and legal encumbrances that can hold us back. The website should go live within the next few months.

As an academic you need to train Ph.D. students and postdoctoral researchers. What are the prospects for your trainees?

It's a great question: what is the next generation going to do? My students are headed into a field where they need to be flexible. Job security is not working for the same company, but is building a skill set that is valuable. So far, our students have been able to get the positions they wanted, but it hasn't been like it was during the heyday of the industry.

But I have this hope that things will re-equilibrate. The United States, the United Kingdom and Switzerland have been hotspots for innovation in drug discovery, and I think in the long term that will still be the case.

What other themes came out of the meeting?

One topic that came up was the human organizational psychology of drug discovery, which is fascinating. There were some questions, for example, about whether project champions are good or whether a 'fail fast and fail cheap' approach is better. From my perspective, if you focus on failing fast and failing cheap, all you will end up with is failure, especially as every project is on the chopping block at some point in time.

I think project champions play a huge part in success. And that's one of the things I like about academia. The biologists I work with are pretty much unconditionally committed to their hypothesis.