VIEWPOINT

Science Friction

How to make a science out of drug discovery

Canada really needs a national drug development niche

By Stephen Strauss CBC News

Apparently one of the greatest mysteries in science is how to make a science out of drug discovery.

Let me refer you off the top to Aled Edwards and his blistering critique of today's drug development procedures: "What is crippling the development of new medicines is the fact that as we discover potential new medicines and we start to test them in people, 90 per cent fail.

"And the 90 per cent fail not because scientists are dumb or they make mistakes," Edwards, who is head of collaboration between the University of Toronto, the University of Oxford, and Sweden's Karolinska Institute called the Structural Genomics Consortium, recently told me. "They fail because we have a very poor understanding of human physiology or pharmacology. We just don't know. You could put 82 eggheads in a room, each with eight Nobel Prizes each, and give them 10 medicines and say 'which one is going to work in a person' - and none would be able to predict."

Ouch — but the blistering continues.

"The pharmaceutical industry is less productive every year and has been for the last three decades," he says. "People make chairs more productively, hamburgers more productively, cars more productively, everything else in the world except medicines.

"And it's not a problem with the industry and the structure of industry and the structure of biotechnology or academia. It's that we don't understand human disease, and until we get that done, we ain't gonna make medicines better."

'People make chairs more productively, hamburgers more productively, cars more productively, everything else in the world except medicines.'— *Aled Edwards*

This is not just one basic scientist's reveling in hyperbole.

In 2004, the U.S. Food and Drug Administration dropped a bomb on the pharmaceutical world in a report entitled Innovation or Stagnation. It suggested that while U.S. biomedical research funding had gone to $94 billion in 2003 from $37 billion US in 1994 (a 57 per cent increase when inflation was taken into account), a new drug entering early stage clinical trials had only an 8 per cent chance of reaching market.

This was down from 14 per cent about 15 years before. The year 2004 represented a 20-year low in the numbers of new molecular therapies - truly new drugs reaching market. Failure rates during final-stage clinical trials were as high as 50 per cent, up from 20 per cent a decade before.

All this is within the context of the fact that the cost of getting a drug to market is somewhere between $800 million US and $1.7 billion. The report pointed out if you could weed out 10 per cent of likely failures before they enter clinical trials it would save companies $100 million per drug.

What to do to make the system more rational?

Well, Edwards and his Swedish and English collaborators are studying the shapes of the body's proteins and then making their results freely available on the internet. It turns out the shape of proteins is vital knowledge when trying to develop a drug to block the actions of some disease causing body molecule. And their view is that this is knowledge that all companies need to have for free as a precursor to drug development.

Their analysis suggests they can reduce early drug discovery time by as much as 18 months and do the work at anywhere from a third to an eighth of the price of traditional academic and industrial research.

I like the sound of that, but also fear that things will still get stuck later on. And indeed, the U.S. Food and Drug Administration (FDA), when it looked at the problem, came up with at least six sticking points in the U.S. for rational and efficient drug development.

To my mind, the biggest problem is that even though drug companies have invested billions in trying to make their process more efficient, they are not in the business of unplugging the entire system. Au contraire. If they come up with, say, a cellular assay that lets them choose potential drug winners from losers earlier, it is actually in their financial interest to keep this information from potential competitors. They want their rivals to be inefficient.

Perhaps equally important, they aren't in the "selling-a-more-efficient-process" business. They're drug companies, after all. They want a $5 billion-a-year "treatment" for male impotence and not a bundle of assays or imaging technology to make the whole process better for everyone.

Which leads me in a rather roundabout way to a national pitch.

Canada as a country is great at medical research - per capita we're right at the top in the world - but we ain't so great at turning those drugs into products. Sure, there was insulin and the three-drug cocktail for AIDS, but the reality is that we are a branch-plant economy for foreign drug companies. And this is extremely worrying in an age when the best future jobs are seen to be in places like biomedicine and not, um, well, car plants in Ontario or clothes-manufacturing plants in Quebec.

A few places in this country - Montreal, the new MaRS facilities in Toronto, Vancouver, Alberta, Nova Scotia, Saskatchewan and even little Prince Edward Island - understand this and have tried to create what are called bioclusters. These are centres of excellence that integrate research and industry. But the truth is there are dozens and dozens and dozens of these bioclusters in every developed and developing country around the world. If we were a relentlessly entrepreneurial country we might forge ahead, but well, again, we ain't.

So what I think Canada really needs is a national drug development niche.

OK, maybe the earliest of the drug development stuff is best left to Open Access, a la Edwards's model, but we could make it our national calling to nourish companies that specifically try to improve the rational discovery process down the pipeline: companies that try to come up with things like heart stem cells you can test drugs on to see if they might ultimately cause heart damage, or new kinds of imaging technology to watch how living human cells respond to treatment and how living animals experience them.

Take aim at the boring middle ground of rational drug development and not the sexy billion-dollar final product. That won't be easy.

"Convincing scientists that an assay has a commercial value is tough, and patenting an assay is very tough," Mark Poznansky, former president and scientific director of the Robarts Research Institute in London, Ont., recently warned me when I ran the idea past him.

Nonetheless, it seems to me in a highly competitive world where good jobs slip away in a blink, Canada needs to mark out a patch of medical research and say, "This is us. This is our national expertise. And we're betting this is where our biomedical BlackBerry will come from."