Goal-oriented research

There is no doubt that the rate of progress has dramatically increased over the past 100 years and has brought with it sudden and pronounced changes, not just for individuals, but also for greater society. Even in our world of research, there are events that bring the words of W.B. Yeats to mind: "...All's changed, changed utterly: a terrible beauty is born." In particular, the Human Genome Project has had a large impact on the way in which biomedical research is now structured. Researchers defined a goal and entered into a contract with society, to deliver the sequence of the human genome. This project also highlighted the potential for the private sector to compete with public research organizations, the consequences of which still rumble in the background. For those who funded the project, the essential facts are that they accepted the goal and they paid for it—I suspect they liked the simplicity of this arrangement, and it is probable that they will wish to have more of this goal-oriented research.

Those of us who benefit from the sequencing effort may still feel that we can continue research in a 'business as usual' manner. However, even suggesting that there could be any research 'directions' gives rise to heated discussions. We all 'know' that top-down defined projects are wrong, because they tend to overlook the brilliant ideas that spark when two unrelated concepts meet in our minds. No committee can have such individual moments of insight, and we are right to resist being reduced to mere providers of bricks of knowledge that contribute to a building planned by some other architect. Our bricks are really sparkling gems, mined with personal skill and produced as individual entities, and it is better to leave it that way. The world has clearly benefited from the unstructured work of academic scientists.

However, the bill for supporting our individualism is increasing. Experiments

are more costly nowadays, and we return to the funding well with ever-larger buckets to fill. In the USA, this has resulted in a twofold increase in funding for some major agencies, driven by the political will to generate more knowledge and thus economic growth. What is sometimes glossed over in the US system is the fact that funding is driven by a presidential agenda—defence-related research can provide fresh money for biomedical research, such as in the case of a smallpox vaccination programme. However, this type of funding comes with some strings attached, which can be manipulated at the whim of the puppet masters.

In Europe, the current hot topic is the need for more support for basic research, an initiative with a multi-billion Euro price tag. Our arguments for this are absolutely correct. High-quality science will give rise to more unexpected and therefore valuable—in all senses of the word—insights. That is less likely to occur if some savants take a 'forward look' and conclude that we should work on bionanotechnology or RNA-control elements or systems biology. Any attempt to predefine knowledge generation will be doomed to failure. Basic research must come from individual investigators and must be open to the wildest ideas, no matter how far they stray from the mainstream. I believe that more support for basic research is needed and timely, but I would be surprised if funding of that magnitude is handed over by some magnanimous Santa Claus with deep pockets and no agenda.

The need for basic research does not mean, in my opinion, that we should ignore the challenge of placing our work in some larger context. Like many others, I could summarize my research goal as trying to understand how a hormonal message triggers the expression of a specific subset of genes. But how should we respond if we were asked the question: "When will you be able to describe this

process in detail for even one gene?" Should we simply say that we do not know and that the journey of research is what intrigues us, not the destination itself? Or should we say that we could have a 'first draft' in, for example, five years' time? We usually give the first answer. But those who fund us, influenced by the Human Genome Project, may put their wallets away if the answer merely implies more unstructured information. If we give the second answer, we may hear the comforting sound of the bank vault opening. We could, of course, lose credibility if we do not reach our self-defined goals, so we should carefully define 'first draft'. Nevertheless, I think that we can accept such goals and continue to work in the way we do at present. The only difference is that we would need to review our data such that we gain a collective view on how close we are to our goal. In addition, this would point to gaps in current knowledge and help others in the area to define their research more clearly.

Such a concept, in which the researchers continue to work in the way we appreciate, but where the randomness of information output is structured *post factum*, arose when I was involved in a discussion on the big challenges for the life sciences. The example mentioned above—understanding how a gene works—could easily be expanded. We could set ourselves new goals to understand how an organelle works and then how a cell works and how an organism works, and eventually we might arrive at what, I believe, is our collective goal: understanding life. This may be a different way of looking at our research, but is it wrong to have such ambitions? And how long will we be able to continue with 'business as usual' before we are being forced to consider such options?

Frank Gannon

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