

COMMENT

Dominoes

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Somewhere in Washington, DC (or maybe London, or Brussels, or Tokyo), a science administrator makes a decision. A group of well-known scientists from prestigious institutions has recommended a new Big Science Program. It will generate reams of data, they say, that will lead to new insights into an important biomedical problem. It will impress Congress with our vision and productivity. It will garner great press. And it will only cost US\$100 million, less than 3% of the budget of the administrator's agency. The administrator realizes what being associated with such a big, important activity will do for his prestige and chances for advancement. He goes to see his boss, the head of the agency, and recommends to her that the project be approved. She, too, recognizes the opportunity that such a project represents to enhance her own standing among her peers, and to facilitate the advocacy for her budget with political leaders. The Big Science Program even has a sexy name and a memorable acronym. She approves it, funding it at \$100 million a year for 5 years. What she doesn't realize is that, in so doing, she has tipped over a little black rectangular tile, with a line dividing its face into two square ends, each end being marked with a number of spots.

That tile is next to a long row of others, unseen in Washington (or Berlin, or Paris, or Beijing), and one by one they start to fall over. In a small university town in the Midwestern USA, a young scientist submits a research grant to that same agency. It's not big science, just an individual research project driven by the curiosity of that investigator to see if a hypothesis she has formulated is true or not. The grant makes its way through the peer-review system where, eventually, it receives a score in the 7th percentile range, meaning that it is in the top 7% of all grants reviewed, but not in the top 6%. This is the sort of score that would normally cause a young investigator to break out the champagne. However, because the Big Science Project has consumed \$100 million of the budget, this year the agency is only able to fund applications in the 5th percentile or better.

You see, \$100 million is only 3% of the agency's budget, but it represents the funding of at least 100 individual investigator-driven grants. Because her proposal did not get funded, the young investigator has to let three postdocs and two technicians go. Only one of them is able to find a job elsewhere in science. The young investigator, unable to get her project funded, is not given tenure at her institution and decides to leave science. A pity; her project, had it succeeded, would have identified a new target for the treatment of an incurable form of cancer. The discovery of that target is thus delayed by 11 years, and during that time, 42,000 people will die of the disease.

Not every one of those 100 grants that didn't get funded would have had such repercussions, of course, but in aggregate, they would have meant employment in science for over 1,000 trained people. Meanwhile, the heads of the Big Science Program are busy hiring their 100 employees, and garnering lots of publicity at their institutions for the money they are bringing in and the jobs it has created.

In a small town in China (or maybe India, or Russia), a young science student receives an email from a department at a university in the USA (or maybe the UK, or Italy). It says that the sender is sorry, but they are unable to offer the young science student a place in their graduate program in cell biology (or biochemistry, or neuroscience, or immunology). A training grant that usually funded their domestic graduate students was not renewed because the funding agency didn't have enough money to fund all the worthwhile training grants, and so the university is going to have to support its domestic students with money usually reserved for foreign applicants. The Chinese student's foreign language score wasn't very good, so this was his only chance to study abroad. He ends up going to his local university instead. A pity because, had he gone to the US university, he would eventually become a US citizen, and gone on to start a biotechnology company that would have made a product that revolutionized genome sequencing. The company would have employed at least 500 people, in part of Michigan that is desperate for jobs. He does eventually start just such a company, but it's in Shanghai.

Not every one of the foreign students who would have come to the USA, but didn't because the Big Science

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Program absorbed so much money, would have had such an impact, of course, but enough of them would have to result the creation of about 5,000 new jobs nationwide.

And somewhere in New Mexico (or maybe Toulouse, or Sienna, or Cape Town), a high school student who dreams of becoming a scientist is told that the summer internship he has been dreaming of landing in a university laboratory will not come to pass, because the funds for such internships were cut this year by the agency that normally provided them. It seems they had to find the money to start some Big Science Program - very flashy, exciting new stuff. 'Discovery-driven' research they called it, which sounds very glamorous and adventurous (and so much better than 'fishing expedition'). Deeply disappointed, the high school student takes a summer job in a brokerage house instead, and ends up going into finance as a career. A pity, because, 10 years later, he will invent the new financial instrument whose widespread use (and misuse) will tip the country into a deep recession, costing maybe 4 million jobs.

Somewhere in Washington, DC (or maybe London, or Brussels, or Tokyo), a science administrator is reviewing the Big Science Program. It has produced terabytes of data, but no important discoveries. Its initial funding period is coming to an end, and an external review panel has recommended that it be phased out. The decision that now must be made is whether to do that or continue it. The heads of the Big Science program argue not merely that it be continued, but expanded, to increase the likelihood of making a big discovery. They will then be able to employ 120 people - think what a good thing that would be. While not saying so explicitly, they imply that Congress might not be happy if the program were terminated, as that would suggest that its initial funding might have been a mistake. Congress, of course, never wastes money - only silly scientists do that. The science administrator also knows that his own prestige - and possible promotion - are tied to this program, which he originally backed. The decision is an easy one. He recommends renewal, with an increased budget. The head of his agency, afraid that to admit the program didn't work would give Congress a license to cut her budget, approves the recommendation. What she doesn't realize is that, in so doing, she has tipped over a rectangular tile with a line dividing its face into two square ends, each end being marked with a number of spots.

I am not categorically opposed to big science programs. Many of them have been very worthwhile, and have

produced results that have fueled a significant number of investigator-initiated, hypothesis-driven projects. But many others have not. The problem is not that some have failed (we should always have a respectable failure rate in science, otherwise we are not taking enough risks), it is that we never seem to be able to discontinue any of them, not even the ones that have failed or outlived their usefulness. They grow, morph into even bigger programs, or reproduce themselves, like some alien creature out of a 1950s B-movie. And because the total amount of money available for science is finite, their existence, and their growth, comes at a price, a price we never seem to consider until long after they spring to life - a life they, through their supporters, cling to with all the tenacity of an actual living organism.

The time to consider such consequences is before such projects start - before we are so invested in them, financially and emotionally, that we cannot extricate ourselves when we should. When administrators, urged on by a set of powerful scientists who see big programs as their ticket to fame and even more power, advocate big, 'discovery-driven' programs in the halls of Congress and the offices of funding agencies, is there anyone to ask who profits from such an activity, and whether that profit is worth the cost? Is there anyone who will remind us, in our eagerness for the new, the flashy, the easily sold, that there is a price to be paid for everything, and it may be a much bigger price than we can see from where we stand? Who will ask, and who will listen to, the question that must be asked whenever we are tempted to follow the siren song of big science: if we do this, what will we *not* be able to do as a consequence?

For want of a nail the shoe was lost.

For want of a shoe the horse was lost.

For want of a horse the rider was lost.

For want of a rider the battle was lost.

For want of a battle the kingdom was lost.

And the dominoes tumble.

Published: 30 November 2011

doi:10.1186/gb-2011-12-11-134

Cite this article as: Petsko GA: Dominoes. *Genome Biology* 2011, **12**:134.