real problem, alternative computation paths are not independent — for example, in factoring, if a number is divisible by 6 then it will certainly be divisible by 3. Thus one cannot be sure that there is not a much faster way of solving the problem than by blind search: either of these problems might turn out to be more like finding a needle in a department store than finding one in a haystack.

Unable to answer their biggest questions, complexity theorists have retreated to proving two lesser kinds of theorems: oracle results and completeness results. Oracle results concern the power of computers that can ask questions of a black box without being allowed to look inside it. The f functions considered above are an example of an oracle. Because Deutsch and Jozsa's proof does not allow the computer to 'open the box' and examine the instructions for calculating f, it is not an absolute proof that quantum computers are more powerful than classical ones, merely a proof that they are more powerful if certain kinds of f functions exist — functions that are balanced or unanimous, but whose instructions cannot easily be analysed to determine which. Gilles Brassard of Montréal and Andre Berthiaume[3], now at Oxford, as well as Bernstein and Vazirani[2] have proved a number of oracle results based on Deutsch and Jozsa's construction, which characterize in considerable detail the power of oracle-assisted quantum computers relative to their oracle-assisted classical analogues. The bravest of these results is a family of oracle problems which are easy for quantum computers but not for classical ones, even when the latter are allowed to make errors.

The other approach, the completeness approach, eschews oracles and is based instead on finding problems that, although not known to be hard, can be proved to be at least as hard as any other problem in a given class. Thus, in classical complexity theory, the travelling-salesman problem is called NP-complete because all other problems in the class NP can be reduced to it. It may similarly be possible to characterize the power of quantum computation by finding problems that are provably at least as hard as any problem in a given quantum complexity class. □

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CANCER

Fusion potential for vaccines

Joyce Taylor-Papadimitriou and Frances Balkwill

THE development of cancers that express tumour-specific or tumour-associated antigens implies that immune mechanisms have not been effective in rejecting the tumour. Cancer treatments aimed at mobilizing host immunity must therefore not only identify tumour antigens but improve the efficacy of antigen presentation. Recognition of the importance of local cytokine action in increasing antigen presentation has led Tao and Levy (page 755 of this issue[1]) to construct a novel and effective vaccine: the vaccine is a fusion protein which combines a well-characterized tumour-specific antigen and a cytokine that stimulates accessory-cell function. The antigen concerned is an antibody corresponding to the specific idiotype expressed on a murine B-cell lymphoma, and the cytokine is murine granulocyte–macrophage colony-stimulating factor (GM-CSF).

The fusion protein has cytokine activity, elicits a strong antibody response, and protects mice from subsequent challenge with tumour cells bearing the specific antigen. Moreover, tumours arising in immunized animals still express the idiotype and there is no evidence of outgrowth of an antigen-negative subclone of the original tumour. Co-administration of the antigen and cytokine, or a fusion protein containing species-specific human GM-CSF, are both ineffective. The fusion of the immunogen with a general carrier protein also generates less effective immunity. These results could have important implications for the design of cancer vaccines, because the administration of a genetically engineered protein offers many advantages over other formulations involving cells or viruses, or both.

How applicable, though, might this approach be to other tumours, particularly human cancers? Obviously, in human clonal B-cell lymphomas, a new vaccine would be required for each patient, but other more widely expressed antigens are currently being developed as immunogens[2,3]. These will have to be tested as fusion proteins with several cytokines. The generality of the immune-stimulating effect of GM-CSF needs to be examined. This cytokine may not be effective with all antigen–target cell combinations, and evaluation of various cytokines may be necessary to optimize presentation of a particular antigen; a fusion protein of interleukin-2 and a viral antigen, for instance, also seems to be strongly immunogenic[4]. Interestingly, a study of irradiated murine tumour cells, which had been transduced with retroviruses encoding ten different cytokines or immunomodulators, showed that cells expressing murine GM-CSF were the most effective at stimulating long-lasting and specific immunity[5].

Another concern is that the fusion protein described by Tao and Levy is tetrameric, comprising two functional GM-CSF molecules, which presumably allows crosslinking of the receptors and generation of a strong functional signal in the effector cells. It is not certain whether the approach would always be as effective using single-chain antigens, or cytokines such as tumour necrosis factor or interferon-γ which are biologically functional as tetramers or dimers.

In the principal human cancers, a similar vaccine could presumably be used as a prophylactic treatment, particularly in patients in remission or those at high risk of developing cancer. There are, however, few data to suggest that vaccination will act against an existing tumour, particularly when the tumour may generate an immunosuppressive microenvironment[6]. Tao and Levy's system would provide a good model for investigating this, and the relative merits of other cytokines as fusion partners.

The use of a tumour vaccine to prevent or delay the onset of malignant disease is one of the ultimate goals of cancer research, but the toxicity of vaccination in a healthy individual is a possible worry, particularly if a cytokine is involved. So it is encouraging to read in the paper[1] that effective immunity was generated with doses as low as 5 nanograms of GM-CSF, well below the doses that stimulate normal or malignant haemopoiesis and are obviously toxic in humans[7].

The data presented by Tao and Levy open up intriguing possibilities. The applicability of the system to other murine tumour antigens, to human cancer, or indeed to pathogenic organisms, will no doubt now be the subject of a flurry of further papers. □

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