Introduction

Therapeutic vaccines: Realities of today and hopes for tomorrow

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Vaccines are prophylactic in the sense that they are administered to healthy individuals to prevent a disease. Nevertheless, there is a growing trend to use vaccines to alleviate the suffering of those already with disease. Great effort is being devoted to developing therapeutic vaccines against tumors, AIDS, hepatitis B, tuberculosis, malaria, and possibly against the bacteria that cause gastric ulcers. Copolymer 1 (glatiramer acetate), used today as a therapeutic vaccine against multiple sclerosis, is a good example of a beneficial treatment for this autoimmune disease, based on its similarity to the myelin basic protein, one of the putative causes of multiple sclerosis. This finding could lead to therapeutic vaccines against other autoimmune diseases such as myasthenia gravis, systemic lupus erythematosus, and rheumatoid arthritis. Furthermore, current studies raise hope for vaccines against prion diseases, bovine spongiform encephalitis, and Creutzfeldt–Jakob disease. Passive antibodies against a peptide derived from β-amyloid plaques might be able to degrade plaques and be used as a therapeutic vaccine against Alzheimer's disease.

Preventive vaccines carry immunologic specificity for individual infective disease agents and provoke an immune response against them. It is a hope, if not a dream, that aside from copolymer 1, therapeutic vaccines of substantive importance will be achieved. Conventional preventive vaccines against infectious diseases have been highly effective at reducing drastically the incidence and morbidity of many life-threatening plagues such as smallpox and viral poliomyelitis. Preexposure vaccination is essential for most infectious diseases caused by viruses or bacteria. A single exception is the rabies vaccine, developed by Pasteur more than 100 years ago, which is administered only after exposure to the virus. In this disease, the virus is shown to progress from the distal site through the peripheral viruses to reach the brain. The mechanism for vaccine efficacy is believed to be that of induction of antibody that suppresses viral migration through the nerve axons.

The effort to develop therapeutic vaccines against persistent viral infections has had a renaissance in recent times, especially for therapeusis of HIV infection, which causes AIDS. Such vaccines have not yet materialized. The greatest chance for success would be for very early intervention postinfection to end progression to clinical disease. This still remains a vision without current scientific rationale.

Vaccines are for healthy people, to prevent them from getting sick. So perhaps the expression "therapeutic vaccine" is an oxymoron. The purpose of adding antigen to an already infected person may be tantamount to "carrying coal to Newcastle." It fits in with the concepts of certain medical practices in which the spurious notion that "like cures like" is applied. There is much research in the area of persistent infectious diseases, such as AIDS, hepatitis, and tuberculosis, work on cancer vaccines, and work on vaccines against autoimmune diseases, allergy, even against Alzheimer's disease, Huntington's disease, and mad cow disease. While of noble purpose, the effort seems doomed unless new and applicable immunologic principles can be discovered.

One such example is that of breaking immune tolerance in cancer through application of antigen bound to heat shock proteins that gain uptake through the CD91 receptor by dendritic cells where both cytotoxic T cells and T helper cell responses are evoked. Another lies in breaking the chain of continuing infection of new cells with HIV virus by substances that block viral entry into the cell. Another lies in the nonimmunologic intervention through specific gene (viral) silencing by RNAi interference through use of short interfering RNA.

It has been the purpose of this Colloquium to discuss immunotherapeusis in the hope for better understanding and cross-fertilization of ideas. This was undertaken in the spirit of the Arthur Sackler Colloquia, with declared purpose to provide a way to focus on interdisciplinary topics that ordinarily are not discussed at conventional meetings. This Colloquium has encompassed vaccinology, immunology, neurobiology, microbiology, autoimmunity, virology, cancer research, diabetes, allergy, and cognitive diseases and, hopefully, has served the useful purpose for which it was conceived.

With a few exceptions, the lectures given at the Arthur M. Sackler Colloquium on "Therapeutic Vaccines: Realities of Today and Hopes for Tomorrow" are presented here in PNAS. They include articles on cancer, autoimmune diseases, infectious diseases, persistent viral infections, allergy, cognitive diseases, organ transplantation, prion pathogenesis, Alzheimer's disease, and polyglutamine diseases such as Huntington's disease.

It is difficult to believe that a therapeutic vaccine will be as efficient as a prophylactic vaccine. Yet these efforts are being pursued, and most have little justification unless something new has been added to the present understanding of immune function. Nevertheless, there are so many efforts to develop therapeutic vaccines, that there must be hope that within the next decade some will be crowned with success.

The papers that were presented highlighted common efforts being made in therapeusis of disease while stressing the many differences between different diseases. It is reasonable to hope that such a background of information may lead to new understanding and new approaches to replace the current tide of "more of the same."

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This paper serves as an introduction to the following papers, which result from the Arthur M. Sackler Colloquium of the National Academy of Sciences, "Therapeutic Vaccines: Realities of Today and Hopes for Tomorrow," held April 1–3, 2004, at the National Academy of Sciences in Washington, DC.

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