GENE THERAPY AND GENETIC VACCINATION: TWO HALLMARKS OF GENETIC MEDICINE.

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The remarkable progress in the isolation and characterisation of new genes as well as in the understanding of gene function in health and disease has now led to direct application of genes in what is called genetic medicine. Two approaches of using genes, rather than their protein products, in the treatment or prophylaxis of disease are intensively explored.
Gene therapy consists in delivering, either by ex vivo genetic modification of body cells or by direct in vivo delivery, genes whose expression will allow to exert a therapeutic effect in the patient. Gene therapy is being evaluated under the form of gene replacement therapy in patients who suffer from the lack of a functional protein. It is also used to battle cancer through genetic modification of cancer or immune cells.
Genetic vaccines are currently being explored as a promising new way of vaccination. In this approach, gene expression cassettes encoding antigens are administered intramuscularly, and the subsequent in vivo expression of the antigens induces specific immune responses leading eventually to protection against pathogens.
In both these types of genetic medicine, vector development and gene delivery methods are key issues since they will determine the efficacy, safety, and long-term outcome of genetic medication.
Discussion

Brown: The guinea pig model is the gold standard for protection in the HSV field. I did not see any of those data. Has that been done?

Dalemans: Yes, by other groups as well as ours and we have seen efficacy towards HSV infection. There is a need for improvement because if you then need to use the gold standard for the HSV model which is an adjuvented protein these do perform better. If you go to a bigger animal it is clear that you have to add something more.

Brown: Some of the DNA infection protocols require a membrane disturbing agent.

Dalemans: We did not check this. It is a very controversial way of doing it. It has been shown that if you pre-treat the muscle with de-stabilising agents, or which lyses the muscle, and then inject the DNA, you have a much better transfection and expression efficiency due to the regeneration of the muscle. It is also claimed that this gives a better immune response. Others claim it does not work.

Onions: We have been doing a number of DNA vaccinations of domestic animal species. One of these is a Nef IV model for HIV and we see a consistent pattern with the DNA vaccination using a defective single cycle vector. It is put in as DNA in parallel experiments with virus as a vector. We see a consistent qualitative change in the immune response between the envelope and the gag proteins with a shift in response towards the gag proteins in the DNA vaccinates as opposed to the ones given the whole vector. Do you see similar changes?

Dalemans: We have not been comparing DNA and live vectors in HIV or in any other field. A shift in immunological response has been seen by others in multiple DNA vaccinations. It shifts from a cellular response to a CH2, or antibody type response. This is dependent on the antigen being very prominent for the envelope, much less so for the gag.