Alzheimer’s drug to enhance immune response to DNA vaccination

Professor Sir Mark Pepys at University College London has repurposed the drug CPHPC — developed as a potential treatment for Alzheimer’s disease — to improve DNA vaccination.

Successful vaccination induces a protective immune response against particular components of the target pathogen called immunogens. However, for some diseases, the immunogens are unknown, and for others, they are difficult and expensive to produce, transport and administer, for example, the influenza vaccine must be produced in millions of chicken eggs. One solution is DNA vaccination — whereby the DNA gene encoding the immunogen is injected rather than the immunogen itself. The DNA then enters the person’s cells, predominantly at the site of injection, and causes them to produce the immunogen locally within the body.

DNA vaccination works well and stimulates an excellent protective immunity against a variety of different infections, and even some cancers, in mice, horses, dogs, rabbits and pigs. However, in humans, other primates, cows and sheep share with humans the presence of SAP proteins which bind strongly to DNA. The team believe that the binding of DNA by SAP may be responsible for blocking the immune response by DNA, and therefore, removal of SAP may overcome this inhibition.

Serum amyloid P

Sir Mark Pepys and colleagues have previously discovered, in work funded by the MRC, that serum amyloid P (SAP) — a plasma protein — is the only normal plasma protein that binds strongly to DNA. They have now found that in each of the animal species in which DNA vaccination is effective, this protein is either absent, or binds only weakly to DNA. In contrast, non-human primates, cows and sheep share with humans the presence of SAP proteins which bind strongly to DNA. The team believe that the binding of DNA by SAP may be responsible for blocking the immune response by DNA, and therefore, removal of SAP may overcome this inhibition.

CPHPC

Sir Mark Pepys previously developed the drug CPHPC as a potential treatment for amyloidosis as it removes almost all SAP — present in the plaques and tangles of nerve fibres found in the brains of people with Alzheimer’s disease — from the blood in humans. Another research team have recently reported that the presence of SAP inhibits DNA vaccination in mice and that this effect is reversed by CPHPC.

Clinical trials

Sir Mark Pepys has now begun the first human clinical trial of DNA vaccination after SAP depletion. The DNA vaccine to be tested is a promising new vaccine against HIV-AIDS, developed and manufactured with previous MRC awards. The group will measure the immune responses to the vaccination in healthy adult men, comparing a group in whom SAP has been completely depleted at the time of DNA vaccination and a control group vaccinated without SAP depletion. Proof of the concept that SAP depletion can enhance immune responses to DNA vaccination in humans will open up this approach for the many other diseases for which effective vaccination does not yet exist and in which it could have therapeutic as well as prophylactic benefits.

End notes

1 MB Pepys et al. Serum amyloid P component is the major calcium-dependent specific DNA binding protein of the serum. Biochemical and Biophysical Research Communications Volume 148, Issue 1, 14 October 1987, Pages 308–313
