Editorial

The Coming of Age of DNA Vaccines

Conventional immunization approaches utilize live attenuated pathogens, inactivated organisms, recombinant proteins or polysaccharide antigens to induce protective immunity. Twenty years ago in a major breakthrough it was shown that immune responses could instead be elicited by injecting plasmid DNA encoding relevant vaccine antigens [1-3]. This heralded the start of DNA vaccination. DNA vaccines offer many potential advantages; including speed and simplicity of manufacture. Despite early hype, this technology has yet to yield approved human products although there are already a number of approved veterinary DNA vaccines suggesting human applications are only a matter of time [4]. It should be remembered that monoclonal antibodies took over 2 decades from initial discovery to final successful human application. By these standards DNA vaccine technology is still in its relatively infancy.

Hence this special edition on DNA vaccines is timely to examine the state of the art in DNA vaccine technology. It is hoped this collections of papers will help address the perennial question asked on all long journeys, "are we there yet?" These papers convey a sense of the tremendous distance that DNA vaccine technology has come over the 20 years since its initial discovery. In particular, issues of DNA vaccine safety have by and large been satisfactorily addressed, leaving vaccine efficacy as the only real remaining challenge [5].

Despite the passage of time there is still a sense of excitement that surrounds the DNA vaccine field. These papers convey a willingness of those in the field to press on to solve the remaining challenges to bring DNA vaccines to the human market. This augurs well for the eventual success of DNA vaccine technology. A variety of key topics are covered by this collection. The excellent review by Jim Williams describes the state of the art in DNA plasmid design. It highlights just how far plasmid design has been advanced and explores how plasmids can be fine tuned for maximal protein expression. Kwilas *et al.,* describe a novel delivery approach that uses a jet injector device to deliver the plasmid intramuscularly without the need for a needle. Interestingly this form of administration appears to also enhance plasmid expression and vaccine immunogenicity. Another area where there have been major advances is the area of DNA vaccine adjuvants. Capitani *et al.* demonstrate that plasmids encoding aggregation-promoting domains act as DNA vaccine adjuvants by triggering frustrated autophagy leading to caspase activation and apoptotic cell death. The induction of cell death is common to traditional vaccine adjuvants including alum and squalene oil emulsions [6], but poses safety risks as excess cell death may trigger unwanted side effects and even autoimmunity in susceptible individuals [7, 8]. No discussion of DNA vaccines would be complete without including electroporation as a method of enhancing plasmid expression. Davtyan *et al.* describe studies on electroporation settings to maximize delivery of an Alzheimer's disease DNA vaccine encoding a β-amyloid epitope. Electroporation remains a potent tool for maximizing DNA delivery but with the downsides of inconvenience, cost and discomfort. Finally, Lucyna Cova examines the history of hepatitis B DNA vaccine development, describing the many challenges encountered along the way. This is a story that could easily be repeated for the many other DNA vaccines under development.

I trust this collection of papers on current DNA vaccine research will convince the reader that the field of DNA vaccines is not dead, and in fact under the surface vigorous research and development efforts continue towards a key milestone which will be approval of the first human DNA vaccine. Considering the more than 20 years that monoclonal antibody technology had to spend in the wilderness before all their problems were solved and they became the pharmaceutical industry's biggest success story, DNA vaccines may yet have their time in the sun.

REFERENCES

[1] Wolff JA, Malone RW, Williams P, *et al.* Direct gene transfer into mouse muscle in vivo. Science 1990; 247:1465-8.

[2] Tang DC, DeVit M, Johnston SA. Genetic immunization is a simple method for eliciting an immune response. Nature 1992; 356:152-4.

[3] Ulmer JB, Donnelly JJ, Parker SE, *et al.* Heterologous protection against influenza by injection of DNA encoding a viral protein. Science 1993; 259:1745-9.

[4] Saade F, Petrovsky N. Technologies for enhanced efficacy of DNA vaccines. Expert Rev Vaccines 2012; 11:189-209.

[5] Li L, Saade F, Petrovsky N. The future of human DNA vaccines. J Biotechnol 2012; 162:171-82.

[6] Petrovsky N, Aguilar JC. Vaccine adjuvants: current state and future trends. Immunol Cell Biol 2004; 82:488-96.

[7] Petrovsky N. Freeing vaccine adjuvants from dangerous immunological dogma. Expert Rev Vaccines 2008; 7:7-10.

[8] Petrovsky N, Heinzel S, Honda Y, Lyons AB. New-Age Vaccine Adjuvants: Friend or Foe? Biopharm Int 2007; 20:24-33.

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