

What is new in the world of Pharmaceuticals

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Flexible artificial blood cells could improve drug delivery, says US group

Artificial red blood cells (RBCs) that mimic "biologically optimized" characteristics could better nanotech drug delivery, say US scientists.

The team from the University of California modified spherical poly lactic-co-glycolic acid (PLGA) particles using an alcohol treatment until they formed the classic "dimpled" RBC shape. This was then used as a mould on which multiple layers of cross-linked proteins were built up creating, when the PLGA core was dissolved, a flexible shell capable of passing through tubes the size of blood capillaries.

The work is detailed in a paper entitled "Red blood cell-mimicking synthetic biomaterial particles," which was published in the Proceedings of the National Academy of Sciences (PNAS) recently. And, although work on use of the artificial RBCs for drug delivery is at a relatively early stage, the team has already used them to transmit iron-oxide nanoparticles, according to a report in an article in the MIT Technology Review.

The scientists are now looking at how the artificial RBCs perform in animal models to fully assess their potential in drug delivery. Last year a Frost & Sullivan report predicted that the nanotech drug delivery market will generate \$700-\$800bn by 2015, which makes it likely that the development of innovative technologies by academic groups will attract more and more drug industry attention over the next few years.

EU revives GMP for Excipients

The European Fine Chemicals Group (EFCG) has welcomed the addition of excipient GMP requirements to the draft amendments of the EU falsified medicines directive but warned that deeper analysis is needed to establish which products warrant further regulation. A directive to establish good manufacturing practices (GMP) for certain excipients was dropped by the European Commission (EC) last year following concerns about the inflexibility of the proposal. The issue is now back on the agenda after a draft opinion from the Committee on the Environment, Public Health and Food Safety (ENVI), the lead group for the anti-counterfeiting directive, proposed GMP requirements for excipients.

Some excipients are already appropriately regulated. To avoid overlap in legislation, and the subsequent burden on excipient manufacturers, a "deeper analysis" of the situation is required. This would identify which excipients need further legislation, such as those not covered by suitable food regulations. As per EFCG GMP legislation covering excipients should differ from active pharmaceutical ingredients (API) regulations, to ensure that legislation ensures patient safety without subjecting excipient manufacturers to unnecessary burdens.

InNexus developing topical psoriasis treatment

InNexus Biotechnology believes 2010 is the year for biotechs to differentiate and has begun this process by using its Transmab delivery technology in a product for treating psoriasis.

The treatment, called IXSCD11a, is an antibody fragment based on the Transmab technology, which is capable of penetrating cell membranes and dermal barriers. By using Transmab InNexus believes it can significantly improve cell penetration compared to other psoriasis treatments. Using this system the antibody fragment binds to a cell surface molecule involved in inflammation. Specifically, the fragment binds to CD11a which is part of the process that leads to psoriatic lesions.

The antibody fragment was developed by another company and shown to be effective but was dropped due to incidences of fatal brain infection. These were caused by systemic immuno-suppression and InNexus believes its treatment will avoid these problems. InNexus is formulating IXSCD11a for topical use, either as a lotion or in patches which would be applied to the affected areas.

Insect cells could cut vaccine production to 10 weeks

Vaccines could be produced in less than 10 weeks from first isolation of the RNA sequence by using insect cell derived influenza virus-like particles (VLPs), according to research which has implications for H1N1 and H5N1.

The threat of newly emerging pandemic influenza strains, and limitations of egg-based culture, has driven the need for rapid response manufacturing methods. Researchers from Austria believe they have

developed an approach that could satisfy this demand.

In a paper published online on 29th December 2009 in Biotechnology journal, the researchers detail why they believe insect cell derived VLPs "are a very fast, safe and effective alternative Vaccine approach".

Using two insect cell lines, namely Sf9 and BTI-TN5B1-4, the team was able to produce the first batch of VLPs 51 days after cloning work began. Accounting for an additional two weeks of gene synthesis, vaccine production of a new influenza subtype could start less than 10 weeks after isolating the RNA sequence.

In earlier work published in The New England Journal of Medicine it is claimed it could produce a H5N1 vaccine within 12 weeks of an outbreak. This used African green monkey kidney cells and the Austrian researchers draw parallels between mammalian and insect cell culture.

Both techniques offer fast production but notably the systems differ in the way they perform complex glycosylation. However, there have been no reports that this negatively impacts on the immunogenicity of products manufactured using either method.

In tests on mice the Austrian researchers claim the VLPs they produced from both insect cell lines induced high titers of neutralising antibodies, leading them to believe that the vaccine could be effective.

Although both cell lines quickly produced effective VLPs the researchers believe BTI-TN5B1-4 has advantages over Sf9, in part because it decreases protein and baculovirus background. This reduces DNA contamination in BTI-TN5B1-4. Furthermore, cells derived from BTI-TN5B1-4 are used in the production of GlaxoSmithKline's Cervarix [human papillomavirus (HPV) bivalent (types 16 and 18) vaccine, recombinant]. Cervarix has been approved by the European Medicines Agency (EMA) and US Food and Drug Administration (FDA), establishing a regulatory precedent for therapeutics made using BTI-TN5B1-4.

Environmental sustainability should be built into GMP; MPA

Environmental certification of production facilities should be introduced to GMP legislation and sustainability risk assessments linked to marketing

authorisations, according to a Medical Product Agency report.

Swedish research indicated that emissions from the manufacture of drugs and active pharmaceutical ingredients (API) in India could seriously affect human and animal health. This led to the Swedish government commissioning its Medical Products Agency (MPA) to investigate how to strengthen environmental requirements. The MPA has now published its findings in a report.

As a first priority the MPA proposes that good manufacturing practice (GMP) legislation is expanded to include a requirement for the environmental certification of drug and API production facilities. Changes to national legislation would have limited impact, according to the MPA, and consequently the agency is pushing for a harmonised policy to cover the European Union (EU). To drive this forward the MPA has been in discussions with the relevant people in the EU. Enforcing the revised legislation would require resources but Unger believes the potential for long-term harm means "it will be more expensive to ignore" the issue. These costs could ultimately be felt by governments and pharmaceutical companies. The MPA also proposes that an environmental risk assessment is included in the application for the marketing approval of a drug. This would give the EU the power to deny a marketing approval based on the risk of negative environmental effects.

NAFDAC launches mobile anti-counterfeiting service

Biofem Pharmaceuticals and NAFDAC have launched an anti-counterfeiting pilot project in Nigeria, using a mobile authentication service (MAS) to validate if a medicine is genuine. Counterfeit products have had a significant impact on Nigeria, with diethylene glycol substitution being linked to the deaths of 84 children last year, leading to increasing efforts to tackle the problem.

The Nigerian National Agency for Food and Drug Administration (NAFDAC) has been particularly vocal in its opposition to counterfeit drugs and has now partnered with Biofem to launch a technological solution.

Using technology from Spoxil, Biofem and NAFDAC have launched the MAS pilot programme. Packaging of drugs included in the programme will include a scratch card with six labels, each of which hides a code.

Patients should send these codes for free by SMS text message to 38353. Shortly after sending the message, often within one minute according to NAFDAC, the patient will receive a reply stating if the medicine is genuine or fake. Currently the scratch cards are only included with packs of Glucophage (metformin) but NAFDAC is working with the Pharmaceutical Industry and health stakeholders to expand the service. The goal is to implement MAS for all drugs at risk of counterfeiting.

Patients seeking to authenticate their Glucophage will also receive a tip for managing diabetes with each validation message. This is intended to keep patients informed of "the latest discoveries in diabetes care management".

The system runs on Spoxil's MAS technology. This is based on asymmetric encryption, which also underpins bank transfers and e-commerce. Consequently, NAFDAC is confident that if users send their message to the correct number they will receive a genuine reply.

To accommodate patients without mobile phones NAFDAC has made it free to send the confirmatory text message. This allows users to borrow a mobile phone from someone else, for instance the pharmacist.

US patent for NexBio sialic acid targeting flu drug tech

US biotechnology firm NexBio has received a patent for "pioneering" host cell-targeting influenza drugs that can cut the risk of viral mutation and the emergence of drug resistant strains.

Vaccines such as Sanofi Pasteur's Fluzone and neuraminidase inhibitors like Roche's Tamiflu and GlaxoSmithKline's (GSK) Relenza aim to prevent influenza infection by targeting the virus directly via specific molecular interactions. This approach, while effective, is prone to the development of resistant strains as mutations during viral replication will inevitably produce viruses that such therapeutic agents cannot attach to, which are known as "escape mutants". In contrast, NexBio's technology blocks infection and development of resistant strains by cleaving the invariant sialic acid molecules on epithelial cells in the respiratory tract that the virus would otherwise use as a point of attachment and entry.

Access' oral insulin shows preclinical promise

Access Pharmaceuticals' insulin diabetes treatment has shown promise in preclinical trials, achieving over 80 per cent oral bioavailability, leading the company to target proof-of-concept studies in humans. Developing alternate routes of administration for large molecules is a potentially lucrative business for pharmaceutical companies, with patients keen to be free of the need for daily or weekly injections. This is particularly true for diabetics and consequently Access has applied its cobalamin drug delivery technology to delivering insulin. Cobalamin is a vitamin B-12 analog which is used to coat an insulin-containing nanoparticle formulation. Following oral administration cobalamin binds to intrinsic factor in the gut leading to the absorption of the nanoparticle formulation. By using this method Access claims to have recorded 80 per cent of the bioavailability achieved by subcutaneous injection. This result has been validated by two companies that Access is collaborating

with on the development of oral insulin. Having gained this data Access is now pursuing options with other companies to try to initiate a proof-of-concept in man study.

Collaborations have been a key aspect of Access' development of cobalamin. In addition to the agreements it already has in place the company is in discussions with pharmaceutical companies to apply the technology to other drug candidates.

The candidates Access has applied the technology to include an ovarian cancer treatment, currently in Phase II, and human growth hormone, which is being moved towards clinical trials. Future collaborations could see cobalamin used to deliver small molecules, monoclonal antibodies or siRNA. Access believes the technology may be particularly beneficial as an intracellular delivering technology for siRNA as demand for B12 increases in many disease states.

Nanotech safety bill introduced to US Senate

Nanotechnology safety legislation designed to address potential health and safety risks posed by the technology has been introduced to the US Senate.

Researchers have shown nanotechnology has applications in drug delivery, as well as an array of other fields, but the technology's rise has led to concerns about its impact on humans and the environment.

To address these issues US Senators Mark Pryor and Benjamin Cardin have introduced the Nanotechnology Safety Act of 2010. This would amend the Federal Food, Drug and Cosmetic Act to establish a nanotechnology programme at the US Food and Drug Administration (FDA). If approved, the programme would assess the health and safety implications of nanotechnology in everyday products and develop best practices for companies using the technology. To support this programme the legislation authorises funding of \$25m (€17.6m) a year from 2011 to 2015. The FDA would use this funding to perform nanotechnology toxicology studies, develop analytical tools to quantify nanomaterials in complex matrices and create procedures for characterising the technology in regulated products. Senator Mark Pryor believes the National Center for Toxicological Research (NCTR) in Jefferson, Arkansas, US and the FDA headquarters in White Oak, Maryland already have the infrastructure to perform the work. He described the NCTR "as an ideal candidate for leading our nation's nanotechnology health and safety studies", adding that "the high-tech infrastructure" at White Oak is also important. The FDA has already created a Nanotechnology Core Facility in Jefferson and is devoting some resources to understanding the technology. However, Pryor believes ring-fencing funds for the research and giving the FDA the necessary authority is required.

Reference: www.PharmaTechnologist.com