MedicalXpress

New clinical trial results show how personalized medicine will alter treatment of genetic disorders

December 27 2007

One of the nation's pre-eminent genetic researchers, Eric Hoffman, PhD, of Children's Research Institute at Children's National Medical Center, predicts that in relatively short order, medicine's next innovation--individualized molecular therapies--will have the unprecedented ability to treat muscular dystrophies, and other disorders.

In the latest edition of the *New England Journal of Medicine*, Dr. Hoffman posits that the results of a small clinical trial involving a new treatment for Duchenne muscular dystrophy provides a proof-of-principle for personalized molecular medicine.

Practical implementation of the 'exon-skipping' approach described in the co-published report of vanDeutekom et al. will require advances in systemic administration of large amounts of customized DNA-like drugs, and proof that long-term delivery is not toxic. However, these advances are likely to come in short order, with the oversight and regulations of the FDA critical for appropriate labeling and marketing of such personalized molecular target drugs.

Though this particular treatment remains in its early stages, within the foreseeable future the now-standard Phase I, II, and III pathway to drug approvals may need to be re-evaluated.

How can DNA-like drugs specific to a single patient's mutation go

through the existing approval process" Are the current standards of rodent and monkey toxicity studies relevant and appropriate for DNA-like drugs, when the animals do not have the same DNA target (or off-target) sequences as humans" These and other questions are certain to pose exciting challenges to both the approval and marketing processes of drugs.

The study featured in the latest edition of The New England Journal of Medicine, involves application of a nucleic acid drug called PRO051. It shows some success at restoring the expression of the specific protein--dystrophin, that is linked to healthy muscle tissue. This approach was shown to reactivate dystrophin protein production in small areas of muscle tissue at the injection site of muscular dystrophy patients.

"Dozens of specific sequences will be required for effectively treating the majority of patients with Duchenne muscular dystrophy," writes Dr. Hoffman. "But in order to realize the promise of personalized molecular medicine in muscular dystrophies and, ultimately, other disorders, it will be important to re-evaluate current measures of toxicity, efficacy, and marketing that ensure both safety for the patient, as well as rapid development and distribution of life-saving drugs."

Dr. Hoffman envisions that some parts of the approval process may be developed for DNA-like molecular medicine as a 'class' of drugs, rather than individual testing of hundreds of different sequences.

"The patients and their families are crossing their fingers that the drug’s overall chemistry can be shown to be safe," he says.

Source: Children's National Medical Center