L'acide valproique stoppe la perte de vision chez les patients souffrant de rétinite pigmentaire 11/2010

Les chercheurs de l'école de Médecine de l'université du Massachusetts croient qu'ils ont trouvé un nouveau traitement pour soigner la rétinite pigmentaire, une maladie neurodégénérative de la rétine qui finalement conduit à la cécité.

Une des plus communes maladies dégénératives de la rétine, la rétinite pigmentaire est causée par la mort des cellules photoréceptrices. Elle affecte une personne sur 4.000. Cette affection se manifeste typiquement chez les adultes jeunes et est d'abord marquée par une perte de la vision nocturne ou par une diminution de la vision périphérique. Dans la plupart des cas la progression de la maladie se fait vers la cécité aux environs de 40 ans.

L'article du Dr Shalesh Kaushal, MD, PhD, professeur d'ophtalmologie à l'université du Massachusetts et de ses collaborateurs, a été publié le 20 juillet 2010 dans l'édition en ligne du British Journal of Ophthalmology. Cet article montre une nouvelle potentialité thérapeutique à l'utilisation de l'acide valproïque dans le traitement de la rétinite pigmentaire. Le traitement pourrait avoir des avantages énormes chez les patients souffrant de cette maladie. L'acide valproïque a été approuvé par l'organisme américain de contrôle des médicaments, la FDA pour traiter l'épilepsie, les migraines et les désordres bipolaires. Dans beaucoup de cas son utilisation chez les patients souffrant de rétinite pigmentaire a eu comme conséquence une amélioration du champ de vision.

Ces résultats en conjonction avec les résultats antérieurs in vitro suggèrent que l'acide valproïque pourrait être un traitement efficace de la perte des cellules photo réceptrices associée avec la rétinite pigmentaire.

Jusqu'ici la découverte d'un traitement pour la rétinite pigmentaire a été compliquée par le fait que plus de 40 gènes différents sont reliés à la maladie, rendant ainsi beaucoup d'interventions impraticables ou impossibles ; en conséquence la maladie demeure en grande partie non traitée chez les patients actuels. La plupart des thérapeutiques actuellement à l'étude sont centrées sur les supplémentations nutritionnelles, les supplémentations de vitamines A, sur la réduction de la lumière ou sur la thérapie génique.

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Contact: Jim Fessenden
james.fessenden@umassmed.edu
508-856-2000
University of Massachusetts Medical School

Valproic acid shown to halt vision loss in patients with retinitis pigmentosa

UMass Medical School coordinating a $2.1 million 3-year clinical trial

WORCESTER, MASS. — Researchers at the University of Massachusetts Medical School (UMMS) believe they may have found a new treatment for retinitis pigmentosa (RP), a severe neurodegenerative disease of the retina that ultimately results in blindness. One of the more common retinal degenerative diseases, RP is caused by the death of photoreceptor cells and affects 1 in 4,000 people in the United States. RP typically manifests in young adulthood as night blindness or a loss of peripheral vision and in many cases progresses to legal blindness by age 40.

In the July 20 online edition of the *British Journal of Ophthalmology*, Shalesh Kaushal, MD, PhD, chair of ophthalmology and associate professor of ophthalmology and cell biology at UMMS, and his team, describe a potential new therapeutic link between valproic acid and RP, which could have tremendous benefits for patients suffering from the disease. In a retrospective study, valproic acid—approved by the FDA to reduce seizures, treat migraines and manage bipolar disorder—appeared to have an effect in halting vision loss in patients with RP and in many cases resulted in an improved field of vision. Results from this study, in conjunction with prior in vitro data, suggest valproic acid may be an effective treatment for photoreceptor loss associated with RP.

UMass Medical School will be the coordinating site for a $2.1 million, three-year clinical trial funded by the Foundation Fighting Blindness/National Neurovision Research Institute quantifying the potential of valproic acid as a treatment for RP. The clinical trials will build upon Kaushal's work in the retrospective study in which patients were treated off-label with doses of valproic acid ranging from 500mg to 750mg per day over the course of two to six months. Treated at a time when patients normally experience rapid vision loss as a result of RP, five of the seven patients in the study experienced improvement in their field of vision.

"Inflammation and cell death are key components of RP," said Kaushal. "It appears the valproic acid protects photoreceptor cells from this. If our observations can be further substantiated by randomized clinical trials then low dose valproic acid could have tremendous potential to help the thousands of people suffering from RP."

To date, discovery of a treatment for RP has been complicated by the fact that more than 40 different genes have been linked to the disease, making many interventions impractical or impossible; as a result, the disease remains largely untreated for an estimated 100,000 patients in the U.S. Most RP therapies currently being investigated focus on nutritional supplementation, vitamin A supplementation, light reduction or gene therapy.

Dr. Kaushal and colleagues, having previously demonstrated the use of the small molecule, retinoid, as a pharmacological agent capable of increasing the yield of properly folded RP rhodopsins, began screening other small molecules for similar attributes. Because of its already known qualities as a potent inhibitor of the inflammatory response pathway and cell

death, valproic acid was believed to have a unique profile making it a potential candidate as a retinal disease treatment.

"Traditionally, moving a new scientific discovery from the bench to the patient requires a significant investment of time and resources," said Kaushal. "Repurposing drugs already approved by the FDA and which have been shown to be safe, such as valproic acid, is an economical and time-efficient way to quickly bring new treatments to patients."

"The Foundation Fighting Blindness is delighted to be moving Dr. Kaushal's outstanding work with valproic acid into our clinical trial network, because the drug has the potential to preserve vision for thousands of people affected by retinal diseases," said Steve Bramer, Ph.D., chief drug development officer, National Neurovision Research Institute, a clinical support arm of the Foundation Fighting Blindness. "It's an exciting research collaboration for us, because of the drug's potential, and the knowledge and expertise Dr. Kaushal and the University of Massachusetts Medical School bring to the clinical study."

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About the University of Massachusetts Medical School

The University of Massachusetts Medical School, one of the fastest growing academic health centers in the country, has built a reputation as a world-class research institution, consistently producing noteworthy advances in clinical and basic research. The Medical School attracts more than $240 million in research funding annually, 80 percent of which comes from federal funding sources. The mission of the Medical School is to advance the health and well-being of the people of the commonwealth and the world through pioneering education, research, public service and health care delivery with its clinical partner, UMass Memorial Health Care. For more information, visit www.umassmed.edu.