Pennington Biomedical Research Center
NewsWire
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Contact Glen Duncan 225-268-9750

Genes reveal how much we will benefit from regular exercise

BATON ROUGE - Stretching from here to Ontario, London to Edinburgh, Horsholm, Copenhagen to Stockholm, Sweden, and from Jupiter, Florida to Ann Arbor, Michigan, an international team of researchers from 14 institutions has peered into the human genome and has found a way to predict who will benefit the most from exercise.

The team is led by Claude Bouchard, Ph.D., of the Pennington Biomedical Research Center (PBRC) and James Timmons, Ph.D., of the Royal Veterinary College, University of London and the Center for Healthy Ageing, University of Copenhagen. Their latest work builds on the current belief among researchers that one of the best predictors of health and longevity is our body's ability to take in and use oxygen during maximum exercise. The more blood our heart can pump and the more oxygen our muscles can use, the less our risk of early disease and death.

They say that's why aerobic exercise is so important. All the brisk walking, running, biking, swimming and endurance training we undertake as a society can increase our body's ability to take in and use oxygen. Scientists call the maximum volume of oxygen our bodies use during exercise "VO_2 max." The higher our VO_2 max, the more resistant we are to illness.

Bouchard and Timmons noticed a problem, however, and brought together a team to address it: although aerobic exercise can and does increase VO_2 max in some people, exercise doesn't work equally for everyone. Some people who exercise experience little or no increased VO_2 max. Aerobic exercise for those people may not help ward off heart disease and other potential ailments.

According to Bouchard, executive director of PBRC, using lifestyle changes to prevent common diseases - such as starting an exercise routine - would be better targeted if healthcare specialists knew ahead of time who would benefit. Bouchard and his colleagues have now moved closer to that goal. They have just published a comprehensive look at a group of genes that modulate the increase in VO_2 max due to aerobic exercise.

"We can now take a biological sample from a person and tell if he or she is likely to increase VO_2 max through aerobic exercise training," Timmons said, "This new approach will help physicians personalize exercise programs to reduce or fight cardiovascular diseases. However, if a patient is not likely to benefit much from aerobic exercise, the physician could turn to other type of exercise or alternative therapies. This would be one of the first examples of personalized, genomic-based medicine."

In Bouchard and Timmon's study, published online today by the *Journal of Applied Physiology* (http://jap.physiology.org/papbyrecent.shtml), they and their partner researchers combined the results of two exercise studies conducted in Europe with a very large study performed in the United States. Participants were asked to undergo rigorous aerobic training, yet nearly one in five

participants showed less than a 5-percent increase in VO_2 max, and nearly 30-percent showed no increase in insulin sensitivity (a risk factor for diabetes). The researchers first took muscle tissue samples before and after the exercise. Using new informatics procedures developed by one of their collaborators, Medical Prognosis Institute in Denmark, the team then identified a set of about 30 genes that predicted the increase in VO_2 max. The researchers then discovered a subset of 11 of these genes that also showed differences in DNA sequences among the participants. Participants with a favorable DNA sequence at these genes increased VO_2 max most, while participants with an alternate DNA sequence did not benefit as much or at all.

"When dealing with genetic data, you're dealing with reams of numbers, and it is extremely difficult to see significant changes or differences." said Steen Knudsen of the Medical Prognosis Institute, "We had to develop entirely new procedures to discover the difference in the samples and make sure those procedures were reliable and accurate."

This means individuals that fall into each category can be identified beforehand by their genotype. Those who are less likely to gain by exercise could be guided toward more productive disease prevention programs to reduce the risks of cardiovascular disease or diabetes.

"We know that low maximal oxygen consumption is a strong risk factor for premature illness and death, " Bouchard said, "so the tendency is for physicians and public health experts to automatically prescribe aerobic exercise to increase oxygen capacity. Our hope is that before too long, they will be able to target that prescription just to those who may stand a greater chance of benefitting, and prescribe more effective preventive or therapeutic measures to the others."

Tuomo Rankinen, Ph.D., is a leading scientist in the Human Genomics laboratory at PBRC and is also a member of the team. He said their findings are a great first step in using genotype to determine who is most likely to benefit from exercise. This study focused on predicting the benefits of exercise on cardiorespiratory fitness, a strong predictor of cardiovascular disease and diabetes, but future studies should develop the use of genotypes to predict in whom exercise can decrease blood pressure, blood sugar levels, adiposity (amount of body fat) and inflammation.

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Participating Institutions:

Human Genomics Laboratory, Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA

Lifestyle Research Group, The Royal Veterinary College, University of London, UK

Centre for Healthy Ageing, Department of Biomedical Sciences, University of Copenhagen, Denmark

Translational Biomedicine, Heriot-Watt University, Edinburgh, Scotland

Medical Prognosis Institute, Hørsholm, Denmark

Department of Physical Medicine and Rehabilitation, University of Michigan Medical School,
Ann Arbor, Michigan, USA

Department of Molecular and Integrative Physiology, University of Michigan Medical School,
Ann Arbor, Michigan, USA

Centre of Inflammation and Metabolism, Faculty of Health Sciences, University of Copenhagen, Denmark

Department of Laboratory Medicine, Division of Clinical Physiology, Karolinska University Hospital, Sweden

Department of Paediatrics and Medicine (Neurology and Rehabilitation), McMaster University Medical Centre, Hamilton, Ontario, Canada

Department of Human Movement Sciences, Nutrition and Toxicology Research Institute Maastricht (NUTRIM), Maastricht University Medical Centre, The Netherlands

Centre for Integrated Systems Biology Medicine, University Medical School, Nottingham, UK

Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

Molecular and Integrative Neurosciences Department, The Scripps Research Institute, Jupiter, Florida