The following articles focus on the need for activity as a means of improving cellular energy that is created in the heart; the only place where electrolytes are created by specific mitochondria.

Details for the cytokines that created bioelectric energy that include IL-3 - IL-33, IL-6 - IL-32 and IL-2 - IL-33 are available for discussion with entities that focus on cardiovascular health.

The articles affixed to this one are provided for discussion purposes; i.e. the need for exercise to prevent cancers from forming in cells due to the lack of energy.

https://www.sciencedaily.com/releases/2017/09/170921185009.htm

Being active saves lives whether a gym workout, walking to work or washing the floor

Date:

September 21, 2017

Source:

McMaster University

Summary:

Any activity is good for people to meet the current guideline of 30 minutes of activity a day, or 150 minutes a week to raise the heart rate, new research indicates.

Physical activity of any kind can prevent heart disease and death, says a large international study involving more than 130,000 people from 17 countries published this week in *The Lancet*.

The Prospective Urban Rural Epidemiology (PURE) study, led by the Population Health Research Institute of McMaster University and Hamilton Health Sciences, shows any activity is good for people to meet the current guideline of 30 minutes of activity a day, or 150 minutes a week to raise the heart rate.

Although previous research, from high income countries, shows leisure time activity helps prevent heart disease and death, the PURE study also includes people from low and middle-income countries where people don't generally don't participant in leisure-time physical activity.

"By including low and middle-income countries in this study, we were able to determine the benefit of activities such as active commuting, having an active job or even doing housework," said principal investigator Dr. Scott Lear. He added that one in four people worldwide do not meet the current activity guideline and that number is nearly three of four in Canada.

Lear holds the Pfizer/Heart & Stroke Foundation Chair in Cardiovascular Prevention Research at St. Paul's Hospital in Vancouver and is a professor of Simon Fraser University's Faculty of Health Sciences.

The PURE study showed that by meeting the activity guidelines, the risk for death from any cause was reduced by 28%, while heart disease was reduced by 20%, and it didn't matter what type of physical activity the person did. The benefits also continued at very high levels with no indication of a ceiling effect; people getting more than 750 minutes of brisk walking per week had a 36% reduction in risk of death. However, less than 3% of participants achieved this level from leisure time activity while 38% of participants achieved this level from activities such as commuting, being active at work or doing household chores.

Lear said that in order to realize the full benefits of physical activity, it needs to be incorporated into daily life. "Going to the gym is great, but we only have so much time we can spend there. If we can walk to work, or at lunch time, that will help too."

"For low and middle income countries where having heart disease can cause a severe financial burden, physical activity represents a low-cost approach that can be done throughout the world with potential large impact," said Dr. Salim Yusuf, director of the Population Health Research Institute and the principal investigator of the overall PURE study.

"If everyone was active for at least 150 minutes per week, over seven years a total of 8% of deaths could be prevented," he added.

The PURE study was led by the Population Health Research Institute and conducted in over 70 sites in 17 countries. It is funded from more than 50 sources, including the Population Health Research Institute at McMaster University and Hamilton Health Sciences, the Heart and Stroke Foundation of Ontario, the Canadian Institutes of Health Research, and the Ontario SPOR Support Unit.

Story Source:

Materials provided by **McMaster University**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Scott A Lear, Weihong Hu, Sumathy Rangarajan, Danijela Gasevic, Darryl Leong, Romaina Iqbal, Amparo Casanova, Sumathi Swaminathan, R M Anjana, Rajesh Kumar, Annika Rosengren, Li Wei, Wang Yang, Wang Chuangshi, Liu Huaxing, Sanjeev Nair, Rafael Diaz, Hany Swidon, Rajeev Gupta, Noushin Mohammadifard, Patricio Lopez-Jaramillo, Aytekin Oguz, Katarzyna Zatonska, Pamela Seron, Alvaro Avezum, Paul Poirier, Koon Teo, Salim Yusuf. **The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study**. *The Lancet*, 2017; DOI: 10.1016/S0140-6736(17)31634-3

Refer to our comments in the following article for why exercise is needed beyond CV health.

https://medicalxpress.com/news/2017-09-cells-healthier-longer-life.html

Exercise can make cells healthier, promoting longer life, study finds

September 22, 2017 by Josh Barney

Whether it's running, walking, cycling, swimming or rowing, it's been well-known since ancient times that doing some form of aerobic exercise is essential to good health and well-being. You can lose weight, sleep better, fight stress and high blood pressure, improve your mood, plus strengthen bones and muscles.

"Whether muscle is healthy or not really determines whether the entire body is healthy or not," said Zhen Yan of the University of Virginia School of Medicine. "And exercise capacity, mainly determined by muscle size and function, is the best predictor of mortality in the general population."

But why? Yan might have some answers. He and colleagues at UVA are peering inside the cell to understand, at a molecular level, why that workout – like it or not – is so vital to the body. They found that one important benefit involves the cellular power plant – the mitochondria – which creates the fuel so the body can function properly.

Exercise Stresses Mitochondria

Yan and colleagues have completed a study in mice that, for the first time, shows that just one bout of moderate-to-intense exercise acts as a "stress test" on mitochondria in muscles. They discovered that this "stress test" induced by aerobic exercise triggers a process called mitophagy, where the muscle disposes of the damaged or dysfunctional mitochondria, making the muscle healthier. Yan compares exercise-induced mitophagy to a state vehicle inspection that removes damaged cars from the streets.

"Aerobic exercise removes damaged mitochondria in skeletal muscle," Yan said. "If you do it repeatedly, you keep removing the damaged ones. You have a better muscle with better mitochondrial quality. We clean up the clunkers, now the city, the cell, is full of healthy, functional cars."

How Exercise Removes Mitochondria 'Clunkers'

For this study, Yan and colleagues assessed the skeletal muscle of a mouse model where they had added a mitochondrial reporter gene called "pMitoTimer." The mitochondria fluoresce green when they are healthy and turn red when damaged and broken down by the cell's waste-disposal system, the lysosomes.

MCFIP - Verifiable explanations for the “removal” of dysfunctional mitochondria using lysosomes is included as an attachment to this article.

The mice ran on a small treadmill for 90 minutes and Yan's team observed mitochondrial stress (signs of "state inspection") and some mitophagy (towing of the clunkers) at six hours after exercise. Yan explained that exercise in these mice also stimulated a kinase called AMPK, which in turn switched on another kinase, Ulk1. These chemical reactions appear to be important in control of the removal of

dysfunctional mitochondria. MCFIP - The document affixed to this one explains the epigenetic signaling that regulates mitophagy. Any cellular mechanism that requires transfer from the surface of a cell into the cytoplasm and that to perform its role must have bioelectric support from astrocytes that produce the energy. The connection between exercise and CV activity and CV activity and the energy to produce activity to maintain mitochondrial health becomes one of merely connecting dots to form a process.
Note: As part of discussions for cellular health, our explanations can include the cellular role of AMPK.

"When its turned on, Ulk1 activates other components in the cell to execute the removal of dysfunctional mitochondria," Yan said. "It's analogous to a 911 call where a tow truck removes the clunkers. However, we still do not know how these activities are coordinated." MCFIP - To avoid complexity, we have opted to set aside explanations for ULK1 - ULK3.

Some Mice Didn't Benefit From Exercise
Yan's lab also deleted the Ulk1 gene in mouse skeletal muscle and found that, without the gene, the removal of damaged or dysfunctional mitochondria is dramatically inhibited, suggesting a new role for the Ulk1 gene in exercise and mitophagy.

"Mice that were unable to do mitophagy did not have the benefit of exercise," explained study co-author Joshua Drake, a postdoctoral fellow in the Yan lab. "Even though, from an exercise standpoint, they still were able to run just as far as normal mice, they didn't benefit metabolically with training."

Drake pointed out that some people with type 2 diabetes don't respond to exercise, which is a growing clinical problem. He hopes that continued research in the Yan lab will lead to new discoveries to help these non-responders.

The findings have been published online by the scientific journal *Nature Communications*.
Explore further: **Calorie reduction + exercise = better muscle function in older adults**
More information: Rhianna C. Laker et al. Ampk phosphorylation of Ulk1 is required for targeting of mitochondria to lysosomes in exercise-induced mitophagy, *Nature Communications* (2017). **DOI: 10.1038/s41467-017-00520-9**

Journal reference: Nature Communications

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The following are byproducts of IL-3 that can be verified as an enzyme that is transported into the cytoplasm by GPCR activity that will

disassemble dysfunctional mitochondria in an autophagy-like manner using a lysosome.

Check point inhibitor drugs for PD-1 and PDL-1 are inhibiting the mechanism. The functional designation for the “marker” is CTLA4.

Mitophagy Signaling

Based on the identification of mitophagy on various cell types during research initiatives, a variety of designations were assigned to this universal mechanism. Examples of these trefoils include:

- TNNT1 – 3
- TIMP4 – 6
- KLF4 – 6
- SMAD4 – 6
- ME1 - 3
- PD-1 – PD-L1 – PD-L2

While these alternative designations are not listed in the GeneCard database (www.GeneCard.org) our modeling tool for identification of elemental constituents can be used by biologically astute individuals to independently validate this assertion.