

Exercise pill is no replacement for exercise

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Recently, researchers at the Salk Institute for Biological Studies, a research organization focused on biology and its relation to health, published a study in the journal *Cell* on the results of a substance that increased exercise endurance without daily exertion when tested in mice. Media reports have described this substance as an "exercise pill," potentially eliminating the need for exercise.

Frank Booth, a University of Missouri expert on inactivity, says the "exercise pill" study did not test all of the commonly known benefits of exercise and taking the pill cannot be considered a replacement for exercise.

In the *Cell* paper "Exercise Mimetics" the researchers demonstrated that AMPK-PPARd pathways, which is a cellular messenger system, can be targeted by orally active drugs to enhance training adaptation or even to increase endurance without exercise. However, Booth cautions that some of the commonly known benefits of exercise were not tested in the *Cell* paper including:

- -- Decreased resting and submaximal exercise heart rate
- -- Increased heart stroke volume at all exercise work loads
- -- Increased maximal exercise cardiac output
- -- Lower blood pressure and arterial stiffness
- -- Increased aerobic capacity

A complete list of the 26 benefits not tested in the paper is included below.



The prevention of the increased risk of chronic disease produced by lifelong physical inactivity also was not tested in the *Cell* paper. According to Katzmarzyk & Janssen (Can J Appl Physiol 29:90, 2004), human physical activity decreases the risk of:

- -- Coronary artery disease (decreases risk by 45 percent)
- -- Stroke (decreases risk by 60 percent)
- -- Hypertension (decreases risk by 30 percent)
- -- Colon cancer (decreases risk by 41 percent)
- -- Breast cancer (decreases risk by 30 percent)
- -- Type 2 diabetes (decreases risk by 50 percent)
- -- Osteoporosis (decreases risk by 59 percent)

Until targeting AMPK-PPARd pathways by drugs is shown to have all the above listed exercise benefits in humans, it is premature to use the term "exercise mimetics" from the very limited observations of the *Cell* paper, Booth said. Booth's expectation, based upon his more than 40 years of research experience in exercise and physical inactivity adaptations, is that the drugs in the *Cell* paper will only partially imitate exercise. In order for any "exercise pill" to counter physical inactivity, the pill must be polygenic, or control many genes at once; therefore the Cell drugs are not likely to provide all of the benefits of comprehensive physical activity. In Booth's opinion, the drugs used in the *Cell* paper were not conclusively proven to mimic exercise, contrary to media reports.

Booth has more than 40 years of research experience in physiological, biochemical, molecular and genetic adaptations that occur during exercise. He is a professor in the MU College of Veterinary Medicine and the MU School of Medicine and a research investigator in the Dalton Cardiovascular Research Center. He is a member of the editorial boards of Journal of Applied Physiology, American Journal of Physiology: Cell Physiology, Physiological Genomics and



CardioMetabolic Syndrome.

Commonly known benefits of exercise not tested in the *Cell* paper were:

- -- Decreased resting and submaximal exercise heart rate
- -- Increased heart stroke volume at all exercise work loads
- -- Increased maximal exercise cardiac output
- -- Lower blood pressure and arterial stiffness
- -- Increased aerobic capacity
- -- Increased strength and cross-sectional area of skeletal muscle
- -- Delayed loss of muscle mass and strength with aging and physical frailty
- -- Improved balance and coordination
- -- Improved flexibility
- -- Reduced osteoporosis
- -- Reduced joint stress and back pain
- -- Decreased gallstone disease
- -- Improved endothelial function
- -- Decreased incidence of myocardial ischemia
- -- Less myocardial damage from ischemia
- -- Decreased oxidative stress
- -- Decreased inflammation
- -- Improved immune function
- -- Decreased liver steatosis and fatty liver disease
- -- Improved insulin sensitivity and reduced risk of type 2 diabetes
- -- Less likelihood of depression, anxiety, stress and poor psychological well-being
- -- Ameliorating hyperlipidemia: lower total cholesterol, higher HDL, and decreased blood triglycerides
- -- Improved cognitive function in the elderly
- -- Increased blood flow and neurogenesis in the dentate gyrus of the hypothalamus
- -- Prevention of the loss of brain volume in the elderly



-- Delay in decline of physiological reserve in organ systems with aging

Source: University of Missouri-Columbia

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