Age-reversal effects of 'young blood' molecule GDF-11 called into question

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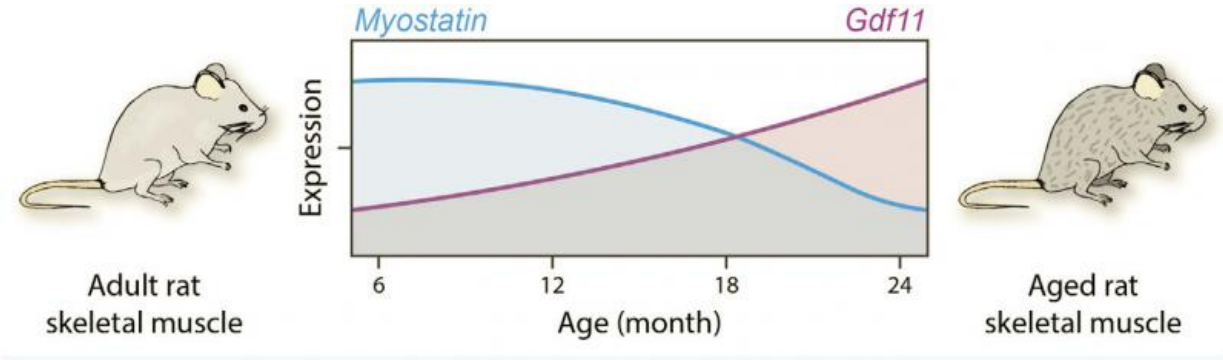

While myostatin expression decreases from 6 to 24 months in skeletal muscle rat, GDF-11 expression increases during this period. Credit: Rudnicki et al./*Cell Metabolism* 2015

The leading theory for why the blood of younger mice rejuvenates the muscles of older mice is now in contest. The vampiric exchange of young blood and old blood has long been reported to have anti-aging effects, but it was in 2013 when Harvard University researchers first linked GDF-11, a molecule that circulates in the blood, to this effect.

Now, an analysis that set out to see how GDF-11 works in the muscles published May 19 in *Cell Metabolism* found just the opposite. The investigators showed first that GDF-11 was not specifically measured; the methods that were previously used were not specific for GDF-11,

but also measured another molecule it closely resembles, called myostatin, which is well known to inhibit muscle growth.

The new study, led by David Glass at the Novartis Institutes for BioMedical Research, in collaboration with Massachusetts General Hospital and the University of California, San Francisco, used tests to more accurately measure GDF-11 (short for Growth Differentiation Factor 11) in the blood of animals and humans and found that it showed hints of increasing with age, and clearly did not decrease with age. They also show that regularly injecting mice with pure GDF-11 causes muscle repair to worsen, resembling effects seen in older age.

"This is a carefully conducted study that is certain to generate a vigorous discussion about what role GDF-11 plays, if any, in aging muscle," says Se-Jin Lee, an expert on growth/differentiation factors and molecular biologist at Johns Hopkins University who did not participate in the research.

"I think that these new results definitely raise questions as to whether GDF-11 was really being exclusively detected in the prior paper," Lee adds. "Clearly, these discrepancies will need to be resolved with additional studies, especially given the enormous effort being undertaken in the pharmaceutical community to target the myostatin pathway to treat muscle loss."

Giving GDF-11 at doses previously used in aged animals did not improve regeneration, as previously claimed. When younger animals were treated with GDF-11, regeneration was worsened. The authors developed a test that could detect GDF-11 levels specifically and suggest that, for humans, testing for high levels of GDF-11 could potentially make them eligible for medicines that block GDF-11 activity.

"Clearly, like the mythical fountain of youth, GDF11 is not the long

sought rejuvenation factor," write Caroline Brun and Michael A. Rudnicki of the Ottawa Hospital Research Institute in a preview to the Cell Metabolism paper. They say, given these new findings, "the suggested 'rejuvenating' activity of GDF11 in the heart and brain should also be re-examined - since the underlying premise of those other two manuscripts, that GDF11 decreases with age, is contradicted by [the new] manuscript."

More information: *Cell Metabolism*, Egerman et al.: "GDF11 increases with age and inhibits skeletal muscle regeneration" DOI: dx.doi.org/10.1016/j.cmet.2015.05.010

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