

New compound could reverse loss of muscle mass in cancer and other diseases

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A new antibody could dramatically boost strength and muscle mass in patients with cancer, chronic obstructive pulmonary disease (COPD), sporadic inclusion body myositis, and in elderly patients with sarcopenia according to research published ahead of print in the journal *Molecular and Cellular Biology*.

"Age-related loss of muscle mass is a major contributing factor to falls, broken bones, and the loss of mobility," says co-corresponding author David Glass of Novartis, Cambridge, MA, one of the compound's developers, along with first author Estelle Trifilieff, also of Novartis. "This study illustrates that we may have a powerful tool to prevent muscle wasting and promote growth."

The new compound (BYM338) acts to prevent muscle wasting by blocking a receptor that engages a cellular signaling system that exists to put the brakes on [muscle development](#) when appropriate. But sometimes those brakes are activated inappropriately, or are stuck on.

"Our goal was to release the brakes," says Glass.

A variety of signals can activate the receptor. Prior to development of BYM338, compounds developed to block these molecules were blunt instruments, either trapping all incoming signals (which stimulated [muscle growth](#) but also caused harmful side effects) or blocking just a single receptor activator (providing only tepid growth stimulation.) BYM338 was designed to be in the Goldilocks zone (just right.)

In the study the compound boosted [muscle mass](#) 25 to 50 percent and increased strength in animal models. Those gains were significantly superior to those of compounds that blocked a single receptor activator. Clinical trials are currently underway.

The conditions BYM338 is designed to treat are losses of [skeletal muscle](#) and fat, which are not reversed by simply eating more, and are known as cachexias when associated with certain chronic illnesses. Cancer cachexia develops in a majority of patients with advanced malignancy, and can interfere with the ability to undergo chemotherapy, says Glass. COPD afflicts an estimated 65 million people worldwide, and is predicted to become the third leading cause of death by 2020. As many as a quarter of COPD patients suffer from cachexia, which can worsen already dire respiratory difficulties.

Sarcopenia—age-related loss of muscle and physical function—afflicts 5-13% of 60-70 year olds, rising to 11-50% in individuals over 80 years old. These individuals become especially vulnerable to falling. Among older adults, falls are the leading cause of both fatal and non-fatal injuries, according to the Centers for Disease Control and Prevention.

Preliminary data on the antibody was promising enough to have it designated a breakthrough therapy by the US Food and Drug Administration for sporadic inclusion body myositis, a rare muscle wasting disease with no approved therapies.

"We need to be able to help people maintain productive and meaningful lives, and [muscle](#) function is a major part of the equation," says Glass. "It could be the difference between independent living and having to move into a nursing home."

More information: [www.asm.org/images/Communicati ...
2013/1213wasting.pdf](http://www.asm.org/images/Communicati...2013/1213wasting.pdf)

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