Docket #: S21-391

Capped peptides are novel secreted peptides with signaling activity

The maintenance of lean muscle mass is fundamental for healthy metabolism and healthy aging. Lower muscle mass across large human cohorts has been strongly associated with higher incidence of obesity, worsened diabetes and metabolic disease, frailty in the elderly, and even increased mortality. A class of peptide ligands that regulate muscle mass are growth hormone (GH) secretagogues. These peptide agonists act in the pituitary to increase GH secretion, leading to downstream activation of insulin-like growth factor (IGF1) and IGF1-mediated anabolic pathways. GH secretagogues have attracted considerable therapeutic potential as anti-frailty and anti-cachexic agents, while also being explored for growth retardation, gastrointestinal dysfunction, and cardiometabolic disease.

Inventors at Stanford have devised a genomic prediction algorithm to identify candidate pyroglutamyl amidated peptides that might be hidden within existing genomic sequences. By applying this algorithm to the mouse and human genomes, they have identified candidate peptides sequences with both N- and C-terminal posttranslational modifications that are 100% conserved between the two species. A subset of the synthetic peptides corresponding to these predicted sequences exhibit robust GH secretagogue activity in vitro. The inventors showed robust detection of these peptides in mouse plasma, establishing their endogenous presence. Furthermore, they have obtained evidence for a receptor-based mechanism of action that is independent of the classical GHS receptor and GHRH receptor pathways. The identified peptides might be useful for the treatment of disorders, including cachexia, growth retardation, frailty, and gastrointestinal dysfunction, via the anabolic activation of the GH/IGF1.

Applications

- -A drug for patients for increasing muscle mass and preventing frailty, cachexia, or growth retardation.
- -Cellular and molecular research techniques
- -Cell signaling
- -Algorithm to identify peptides for metabolic pathways

Advantages

- -Computational platform enables identification of peptides that activate the GH/IGF1 axis independent of any of the known upstream pathways
- -Predicted sequences are validated in vitro
- -can be used to detect peptides from unknown pathways

Publications

- Amanda L. Wiggenhorn, Hind Z. Abuzaid, Laetitia Coassolo, Veronica L. Li, Julia T. Tanzo, Wei Wei, Xuchao Lyu, Katrin J. Svensson, Jonathan Z. Long. "A class of secreted mammalian peptides with potential to expand cell-cell communication." *bioRxiv*. 2023.06.02.543503.
- Wei, W., Riley, N. M., Lyu, X., Shen, X., Guo, J., Raun, S. H., ... & Long, J. Z. (2023). " Organism-wide, cell-type-specific secretome mapping of exercise training in mice". Cell Metabolism.
- Tanzo, Julia T., Veronica L. Li, Amanda L. Wiggenhorn, Maria Dolores Moya-Garzon, Wei Wei, Xuchao Lyu, Wentao Dong et al. " CYP4F2 is a human-specific determinant of circulating N-acyl amino acid levels". Journal of Biological Chemistry (2023): 104764.

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