Quorum Sensing Peptides in Muscle Wasting: Insights from iAM373

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Introduction

Sarcopenia is a prevalent and clinically relevant condition, yet the development of predictive biomarkers and effective pharmacological interventions remains limited. Bacterial quorum sensing peptides (QSPs) have recently emerged as bioactive molecules with diverse functions, including potential roles as biomarkers and therapeutic agents in muscle wasting. However, their presence in humans and pharmacodynamic properties are poorly understood.

Methods

In a cohort of 193 older adults, we used LC-MS/MS to determine the plasma concentrations of five QSPs, previously reported to have cellular and/or preclinical effects on muscle wasting: iAM373, CSP-7, PlnA, LamD, and CSP-21 [10.1016/j.bbadis.2019.165646; 10.1016/j.bbadis.2024.167094; 10.1002/ctm2.1053]. Concentrations were estimated using maximum likelihood methods for censored data. To further explore iAM373, we investigated its cell-penetrating properties in C2C12 myoblasts using fluorescence microscopy. Mechanistic insights were obtained through assays assessing cellular redox status and related pathways.

Results

All five QSPs were detected in human plasma at concentrations within the pico- to nanomolar range, with estimated mean values ranging between 0.1 and 10 pM. iAM373 exhibited the highest prevalence (12% above LOD). *In vitro*, iAM373 penetrated C2C12 cells and significantly altered the redox balance, suggesting at least a direct intracellular mode of action.

Conclusion

This study demonstrates for the first time that multiple QSPs are present in the circulation of older adults, with iAM373 emerging as the most prevalent. Its ability to enter muscle cells and disrupt redox homeostasis highlights iAM373 as a promising biomarker and effector in sarcopenia pathophysiology.

Keywords

Peptides, quorum sensing, sarcopenia, iAM373

Disclosures

The authors declared no competing interests.