



DIAGNOSTICS AND THERAPEUTICS OF QUORUM SENSING MOLECULES IN MUSCLE WASTING.

Introduction

Muscle wasting is an important clinical syndrome because of its increasing prevalence and its causal association with mortality, fall risk and quality of life. It can be acute (e.g. critical illness myopathy), subacute (e.g. cancer cachexia) or chronic (e.g. sarcopenia) in onset. Although exercise, nutrition and hormonal therapies are currently recognized to have some beneficial effects on muscle wasting diseases, these interventions either require large efforts for relatively small health gains or have an unfavorable benefit/risk profile. Recently, the gut microbiome has been suggested to have a causal role in the pathophysiology of muscle wasting diseases. However, the causal mediators in this gut-muscle axis are unknown.

Technology

Quorum sensing molecules (QSM) are characteristic bacterial products, constitutively produced by living bacteria. The bacteria generally exhibit an increased production of QSMs in “stress” conditions. Interestingly, our research group found that some of these QSM selectively affect muscle cells in the context of muscle wasting, both in vitro as well as in vivo in preclinical models. Moreover, potential antagonists of these QSM could be identified. The present invention could thus open a new diagnostic and therapeutic dimension in fighting muscle wasting diseases.

Applications

Diagnostics for analyzing the presence of QSMs in a human or animal sample to assess the presence of QSMs that influence muscle wasting syndrome (QSM as biomarkers).

Probiotics, producing neutral or good QSM for treating patients, for replacing in the gut the strains that have QSMs shown to negatively influence aspects of health.

Agonists or antagonists of QSM's, for prophylactic or curative purposes to reduce muscle wasting.

Advantages

- QSMs (profiling): additional and novel diagnostic biomarker for these diseases.
- QSM have well-defined chemical structure (↔ e.g. protein mixtures), facilitating product development
- Potential QSM (derived) drugs and/or probiotics are expected to be of a low toxicity in ‘weakened’ population.
- First therapeutics influencing one of the muscle disease-causes (contrary to currently available therapies such as vit.D, testosterone, life-style), can be personalized and targeted.

State of development

We investigated the effects of 75 different quorum sensing molecules as microbial communicators on C2C12 muscle cells (rodent cell line). Thirty QSM showed effects, from which 5 strong hits were identified. Effects were observed mainly on muscle cell viability and inflammation, and to a lesser extent on mitochondrial changes, differentiation and protein degradation. In confirmatory in-vitro experiments, the 5 strong hits were also shown to affect human muscle cell lines.



Our first in-vivo experiments with the 5 strong hits on *C. elegans* and in mice models corroborate the in-vitro effects of QSM on muscle. More elaborated in-vivo experiments are currently on-going.

Partnership

We are looking for an industrial partner for collaborative research and development of diagnostic tests and/or therapeutic products (probiotics, ATMP, small/peptide/...pharmaceuticals).

Intellectual property

European priority patent application EP19207716.2: "DIAGNOSTICS AND USE OF QUORUM SENSING MOLECULES IN MUSCLE WASTING"; filing date: 7 November 2019

Figure

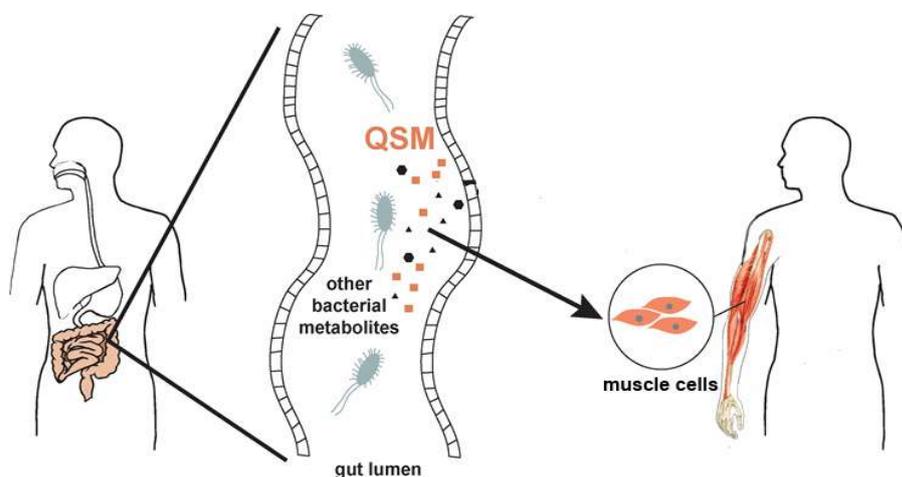


Figure 1. Our invention consists of gut bacterial QSM acting on muscle in the context of muscle wasting diseases. This invention has potential applications in diagnostics (QSM biomarkers) and therapeutics ((ant)agonists, probiotics).

References

Quorum sensing molecules as a novel microbial factor impacting muscle cells.
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Keywords

Quorum sensing, muscle wasting, myopathy, cancer, cachexia, sarcopenia, diagnostic, therapeutic, probiotic

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