A review on use of computational biology in testing of skeletal muscle function in COPD patients

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Abstract

Computer biology and bioinformatics are interdisciplinary fields that develop and apply computational methods to analyse large amounts of biological data, such as genetic sequences, cell populations, or protein samples, in order to make new predictions or find novel biology. Analytical approaches, mathematical modelling, and simulation are among the computational methods employed.

Chronic Obstructive Pulmonary Disease (COPD) is a lung inflammatory disease that causes persistent airflow restriction. These individuals frequently have extensive systemic consequences, such as skeletal muscle dysfunction, which severely restrict their life expectancy. Despite extensive research, the molecular basis of muscle deterioration in COPD remains a matter of contention. We used a network biology approach to investigate the link between the molecular and physiological responses of muscles to training and systemic inflammatory mediators in this study. Failure to coordinately activate expression of various tissue remodelling and bioenergetics pathways is a distinctive feature of COPD diseased muscles, according to our model. Our findings also point to a relationship between this phenomena and aberrant expression of a number of histone modifiers, which we discovered associated with oxygen utilisation. These findings highlighted the intriguing hypothesis that cell hypoxia is a crucial contributor in COPD patients' skeletal muscle.

Keywords: Computational biology, skeletal muscle function testing, COPD.

INTRODUCTION

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Computing biology is the study of biological, ecological, behavioural, and social systems through the development and implementation of data analytical and theoretical methods, mathematical modelling, and computational simulation techniques. The field is broadly defined, encompassing foundations in biology, applied mathematics, statistics, biochemistry, chemistry, biophysics, molecular biology, genetics, genomics, computer science, ecology, and evolution, but it is most commonly thought of as the intersection of computer science, biology, and big data.

Chronic Obstructive Pulmonary Disease (COPD) is a lung inflammatory disease that causes persistent airflow restriction. These individuals frequently have extensive systemic consequences, such as skeletal muscle dysfunction, which severely restrict their life expectancy. Despite extensive research, the molecular basis of muscle deterioration in COPD remains a matter of contention. We used a network biology approach to investigate the link between the molecular and physiological responses of muscles to training and systemic inflammatory mediators in this study. Failure to coordinately activate expression of various tissue remodelling and bioenergetics pathways is a distinctive feature of COPD diseased muscles, according to our model. Our findings also point to a relationship between this phenomena and aberrant expression of a number of histone modifiers, which
we discovered associated with oxygen utilisation. These findings highlighted the intriguing hypothesis that cell hypoxia is a crucial contributor in COPD patients' skeletal muscle deterioration.(1)

Systemic co-morbidities that impact prognosis afflict a high percentage of individuals with chronic obstructive pulmonary disease (COPD), with muscle loss being particularly devastating. Despite much research, the aetiology of this critical extrapulmonary manifestation remains unknown. The extent to which systemic inflammatory mediators may play a role in this disorder is a fundamental topic that has yet to be answered.(2)

We investigated whether long-term exercise training deteriorates muscle redox status in COPD patients. Muscle and blood protein oxidation levels were correlated in COPD patients. Training improved physiological parameters and blood protein nitration in patients. High-intensity exercise training did not impair muscle oxidative stress in COPD patients.(3)

To improve our understanding of complex biological systems such as illnesses, we must put all available data into context and use it to find relationships, patterns, and rules that may be used to construct prediction hypotheses. Life science has evolved into a data-rich field, with data on the behaviour of millions of things such as genes, chemical compounds, diseases, cell types, and organs stored in a variety of databases and/or dispersed throughout the literature.(4)

Existing knowledge, such as genotype-phenotype relationships or signal transduction pathways, must be semantically integrated and dynamically organised into structured networks linked to clinical and experimental data.

There are a variety of ways to this problem, but none has proven to be completely adequate thus far.(4)

After exercise, IL-6, IB, TNF-α, IL-1, superoxide dismutase, thioredoxin, heme oxygenase 1, and heat shock protein-70 were raised in muscle in healthy participants, whereas only IL-6 mRNA was upregulated in COPD patients. When compared to control subjects, exercise-induced antiapoptotic Bcl2 mRNA levels were lower in COPD patients. Patients with COPD had increased basal muscle protein oxidation than control subjects, but this decreased after activity. There were no exercise-induced alterations in NF-B DNA-binding activity in either group's muscle or PBMCs. NF-B-regulated genes encoding inflammatory cytokines, antioxidants, stress proteins, and survival factors have a reduced response to exercise in Nuclear factor (NF)-kB activation and oxidative stress are physiologic responses of skeletal muscle to exercise but may be impaired in patients with COPD. Therefore, we investigated NF-κB activity and expression of NF-κB-regulated genes in muscle of patients with COPD and control subjects before and after exercise(5).Methods nQuadriceps specimens were obtained before, immediately after, and 2 h after a submaximal cycle ergometry test from seven patients with COPD (50.6 ± 5.7 SEM FEV1 of patients with COPD) and seven age-matched control subjects. NF-κB DNA-binding activity in muscle and peripheral blood mononuclear cells (PBMCs) was determined using electrophoretic mobility shift assay and enzyme-linked immunosorbent assay, respectively. mRNA expression and protein carbonylation were measured by

real-time polymerase chain reaction and Western blot,

respectively results in control subjects, IL-6, lκBα, tumor necrosis factor-α, IL-1β, superoxide dismutase, thioredoxin, heme oxygenase 1, and heat shock protein-70 were upregulated in muscle after exercise, whereas in patients with COPD only IL-6 mRNA was increased. Exercise-induced antiapoptotic Bcl2 mRNA levels were attenuated in patients with COPD compared with control subjects. Basal muscle protein oxidation was higher in patients with COPD than in control subjects, but attenuated in response to exercise. No exercise-induced changes in NF-κB DNA-binding activity in muscle and PBMCs of either group were detected. Conclusions Skeletal muscle of patients with COPD is characterized by an impaired response to exercise of NF-κB-regulated genes encoding inflammatory cytokines, antioxidants, stress proteins, and survival factors in COPD patients' skeletal muscle. (5)

Patients with chronic obstructive pulmonary disease (COPD) have a wide range of clinical symptoms and disease progression patterns. Muscle dysfunction/wasting and co-morbidity patterns are two significant criteria that can be used to distinguish COPD subtypes. COPD heterogeneity, we predicted, is caused in part by complicated interactions between several genes and pathways. We investigated the prospect of identifying such pathways using a Systems Medicine approach, as well as developing predictive computational models that may be employed in clinical practice.(6-15)
Skeletal muscle dysfunction and its underlying pathology are well-known in late chronic obstructive pulmonary disease (COPD), but they have received little attention in patients with mild-to-moderate airflow obstruction. We anticipated that in the skeletal muscle of patients with mild- to-moderate COPD, a loss of oxidative phenotype (oxphen) is related with lower endurance.(16-30)

Skeletal muscle dysfunction is a defining feature of severe chronic obstructive pulmonary disease (COPD), and it plays a substantial role in reduced exercise capacity and poor quality of life. The two principal myopathological abnormalities known in individuals with advanced COPD are peripheral skeletal muscle wasting and a loss of oxidative phenotype (oxphen), both of which are associated with decreased muscular strength and endurance, respectively. It's worth noting that research on skeletal muscle failure and its underlying pathology in COPD has been done.(31-40)

An integrated network inference approach was used to explore muscle loss as a systemic consequence in COPD patients. This research has resulted in a model that describes the link between systemic inflammatory mediators and muscle molecular and physiological responses to exercise. For the first time, this model has demonstrated that oxygen- dependent changes in epigenetic modifier expression, rather than chronic inflammation, are directly associated to muscle failure.(8)

Lung functions in individuals with chronic obstructive pulmonary disease (COPD) have a limited correlation with exercise capacity and do not predict individual patient exercise responses. As a result, most recent research has focused on muscle function impairments, which are known to exist in COPD patients. Muscle mass, strength, and endurance are all diminished in COPD, as is resting and exercise muscle metabolism. As a result, lactic acidosis occurs at lower intensities of exercise, resulting in increased ventilatory demand and the start of muscle exhaustion earlier. In COPD patients, biochemical and morphological alterations in the vastus lateralis muscle were observed, indicating that a peripheral muscle shifts from oxidative to glycolytic metabolism.(9)

The underlying inflammatory response in obstructive lung illnesses causes airway remodelling, airflow limitation, and increased ventilation-perfusion (V/Q) mismatch, resulting in decreased lung function. COPD is defined by chronic and irreversible airflow obstruction, whereas asthma is characterized by variable airflow obstruction and airway hyper-responsiveness of the airway smooth muscle.(10) Their usefulness in computational biology stems from the capacity to derive predictive models without relying on strong assumptions about underlying mechanisms, which are often unclear or inadequately characterized. As an example, the most accurate prediction of gene expression levels is currently performed utilizing a broad variety of epigenetic variables and sparse linear models or random forests; how the selected features determine transcript levels is still a hot topic of research. Machine learning algorithms are used to make predictions in genomics, proteomics, metabolomics, and sensitivity to chemicals.(11)

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