Title: Skeletal muscle cells differentiated from urine-derived stem cells as a functional tool to investigate new players in muscle contraction/relaxation

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Abstract:

Muscular diseases are characterized by a wide genetic diversity and the Ca^{2+}-signalling machinery is often perturbed. Its characterization is therefore pivotal and requires appropriate and personalized cellular models. Muscle biopsies are the best approach but are invasive for the patient. To circumvent this, interest is mounting in urine-derived stem cells that can be differentiated into skeletal muscle cells. Therefore, we isolated stem cells from urine (USC) samples and differentiated them into skeletal muscle cells (USC-SkMC). As expected, USCs and USC-SkMCs are characterized by a radically different pattern of expression of stem and skeletal muscle markers. Moreover, undifferentiated and differentiated cells differ in the expression of key proteins involved in Ca^{2+}-homeostasis and also displayed different Ca^{2+}-responses to external stimuli, confirming that during differentiation there was a transition from a non-excitable to an excitable phenotype. In USCs, the main mechanism of calcium entry is IP3 dependent, while in USC-SkMCs both store- and receptor-operated calcium entry are active. Furthermore, ryanodine receptors and the voltage-operated calcium channels are operative in USC-SkMCs, unlike in USCs. Lastly, differentiated cells demonstrated a great capability to contract in response to acetylcholine challenge. These data confirmed that skeletal muscle cells derived from USCs are an easily amenable tool to generate personalized cellular model to study Ca^{2+}-homeostasis, contraction/relaxation mechanism.

Taking advantage of this cellular model, we investigated the expression and role of bitter taste receptors (TAS2Rs) in skeletal muscle. Indeed, TAS2Rs have been discovered in extra-oral sites where they are involved in various physiological functions. We serendipitously observed the expression of the subtype TAS2R46 in human skeletal muscle section, then we moved to investigate its role in USC-SkMC model. We showed, for the first time, experimentally the presence and functionality of a type 2 bitter receptor in human skeletal muscle cells and demonstrated TAS2R46 role in mediating relaxation of acetylcholine pre-contracted myocytes. Given the tendentially protective role of the bitter receptors starting from the oral cavity and following also in the other ectopic sites, and

given its expression already at the myoblast level, we hypothesize that the bitter receptor can play an important role in the development, maintenance and in the protection of muscle tissue functions.

Biography:

Maria Talmon graduated in Cellular and Molecular Biology at University of Torino (Italy) and obtained the PhD in 2016 in in Biotechnology for Human Health at the University of Piemonte Oriental (UNIUPO, Novara, Italy) with a thesis entitled “Cell and gene therapy of Hemophilia A”. From 2016 to 2022 she worked as a senior post doc in the lab of pharmacology of Department of Health Sciences UNIUPO. In particular, she studied the calcium homeostasis downstream bitter taste receptors located in extra oral tissues, highlighting their bronchodilation and anti-inflammatory effect in the respiratory system. Since June 2023 she is a RT at the Department of Pharmaceutical Science, UNIUPO.

During her career she published 22 peer reviewed publications (H-index: 9, citations: 223, source Scopus) and received several awards: ● Best Oral Presentation Award at the VIII SYRP: S.I.Fit. Young Researchers Project meeting, 2019, Imola, Italy ●Young Investigator Award at the XXIII International Society of thrombosis and haemostasis (ISTH) congress, 2015, Toronto, Canada ●Young Investigator Award at the XXII International Society of thrombosis and haemostasis (ISTH) congress, 2013, Amsterdam, The Netherlands.

In 2020 she received a grant from “Roche per la Ricerca Indipendente” foundation for a project entitled “SNPs of bitter taste receptors as predictive marker of asthma in children".