

## Report and Abstracts of the 19<sup>th</sup> Meeting of the Interuniversity Institute of Myology: Assisi, October 20-23, 2022

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### Abstract

After two years of conferences on a virtual platform due to the Covid-19 pandemic, finally, the 19th annual meeting of the Interuniversity Institute of Myology (IIM) has returned to the heart of central Italy, in Assisi, an important cultural hub, which boasts a wide range of historic buildings and museums. This event brought together scientists from around the world providing a valuable opportunity to discuss scientific issues in the field of myology. Traditionally, the meeting particularly encourages the participation of young trainees, and the panel discussions were moderated by leading international scientists, making this a special event where young researchers had the opportunity to talk to prestigious scientists in a friendly and informal environment. Furthermore, the IIM young researchers' winners for the best oral and poster presentations, became part of the IIM Young Committee, involved in the scientific organization of sessions and roundtables and for the invitation of a main speaker for the IIM 2023 meeting. The four keynote speakers for the IIM Conference 2022 presented new insights into the role of multinucleation during muscle growth and disease, the long-range distribution of giant mRNAs in skeletal muscle, human skeletal muscle remodelling from type 2 diabetic patients and the genome integrity and cell identity in adult muscle stem cells. The congress hosted young PhD students and trainees and included 6 research sessions, two poster sessions, round tables and socio-cultural events, promoting science outreach and interdisciplinary works that are advancing new directions in the field of myology. All other attendees had the opportunity to showcase their work through poster presentations. The IIM meeting 2022 was also part of an advanced training event, which included dedicated round tables and a training session of Advanced Myology on the morning of 23 October, reserved for students under 35 enrolled in the training school, receiving a certificate of attendance. This course proposed lectures and roundtable discussions coordinated by internationally outstanding speakers on muscle metabolism, pathophysiological regeneration and emerging therapeutic approaches for muscle degenerations. As in past editions, all participants shared their results, opinions, and perspectives in understanding developmental and adult myogenesis with novel insights into muscle biology in pathophysiological conditions. We report here the abstracts of the meeting that describe the basic, translational, and clinical research and certainly contribute to the vast field of myology in an innovative and original way.

**Key Words:** Muscle development; adult myogenesis; metabolism; epigenetics; omics; metabolism; 3D cell models; organoids; extracellular vesicles: homeostasis; neuromuscular features; Duchenne muscular dystrophy; cachexia; sarcopenia; muscle stem cells; clinical studies; personalized medicine.

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The 19<sup>th</sup> annual meeting of the Interuniversity Institute of Myology (IIM), founded in 2004 by several Italian universities, was held from 20 to 23 October 2022. Due

to the greatly improved COVID-19 pandemic situation, the meeting was held in Assisi in the Umbria region of central Italy. The desire to meet in person in the official headquarters of the last IIM meetings attracted many

participants, which were 118 scientists coming from different countries, including Italy, Belgium, France, Denmark, USA and Brazil. This year we had four main talks and 33 talks selected from the submitted contributions and 42 posters were the basis for a lively scientific debate, mainly aimed at promoting the active participation of the young participants, as typical of all IIM meetings. Keynote speakers were Doug Millay (Department of Pediatrics, University of Cincinnati Cincinnati, OH, USA); Scott Q. Harper (Nationwide Children's Hospital, Ohio State University College of Medicine Columbus, OH, USA); Jean Farup (Dept of Biomedicine, Aarhus University Aarhus, Denmark); Chiara Mozzetta (Institute of Molecular Biology and Pathology, National Research Council of Italy, Rome, Italy). The 4th edition of the Advanced Training Course in Advanced Myology within the IIM meeting was organized through a collaboration with the University of Perugia, Italy. During the training course, fourteen participants under the age of 35 attended lectures and round tables with the international speakers, in addition to be exposed to the fully immersion the IIM meeting itself. This year, the panel discussions were on skeletal muscle aging (discussants: Doug Millay, Sestina Falcone, and Antonio Musarò) and environment (discussants: Jean Farup and Scott Q. Harper). To further stimulate the involvement of the young participants, one of the keynote speakers and the theme of the roundtables were selected by the IIM Young Committee, composed by trainees who won prizes in past editions of the IIM meeting. Also in this IIM edition, Gloria Antonini, Parent Project Italy, brought the voice of patients affected by Duchenne and Becker Muscular Dystrophies. The industry was represented by Barbara Canonico who spoke about the world of extracellular vesicles<sup>1</sup> and their cargos, a technical talk promoted by Prodotti Gianni. Both Parent Project and Prodotti Gianni sponsored the meeting. The scientific topics of the presentations in an interdisciplinary fashion covered several aspects of the skeletal muscle biology including, muscle genetics and epigenetics, stem cells and regenerative medicine, muscle and exercise, signaling and metabolism, clinical studies and therapeutic approaches to muscle diseases. The first keynote lecture was given by Douglas P. Millay, Professor at Department of Pediatrics, University of Cincinnati, USA. The title of his talk was: Mechanisms of myoblast fusion and role of multinucleation during muscle development, growth, and disease. He presented the latest study of his team about the biochemical activities of the myogenic fusogens, deciphering the role of multinucleation for myofiber growth and adaptations. These results include the recent results on myomerger fusogenic activity that requires its two ectodomain helices, responsible for the membrane-stressing activity during the final step of myoblast fusion spatially and temporally regulated<sup>2</sup>. The second keynote lecturer, Dr. Harper's primary research focus at Nationwide Children's has been developing gene therapies to treat

neuromuscular and neurological disorders. Scott Harper is Professor of Pediatrics at the Ohio State University College of Medicine, USA and serves as chief scientific adviser at Armatus Bio, a gene therapy startup company in Columbus, Ohio. He was invited by the IIM Young Committee and his talk was entitled: Development of DUX4 inhibition therapies for Facioscapulohumeral muscular dystrophy (FSHD). He presented recent data from his lab on a meticulous screening to identify a subset of serine/threonine phosphomimetic mutants and an arginine methylation null mutant which protected cells against double homeobox 4 protein (DUX4) -mediated toxicity in FSHD patients<sup>3</sup>. In follow-up studies, they demonstrated the therapeutic promise of targeting DUX4 post-translational modifications that could protect against DUX4-induced cell death in FSHD myoblasts. The third Keynote lecture was presented by Jean Farup, assistant professor at Dept of Public Health Aarhus University, Denmark. In his talk entitled "Human skeletal muscle fibro-adipogenic progenitors in degeneration and regeneration", he focused on the human muscle microenvironment and the role of fibro-adipogenic progenitors (FAPs) in skeletal muscle homeostasis. His work highlighted the important role of FAP subsets in human skeletal muscle during chronic muscle degeneration, focusing on the crosstalk between FAPs and macrophages in regulating immune cell infiltration and local tissue inflammation. Indeed, type 2 diabetes mellitus (T2DM) is associated with impaired skeletal muscle function and FAPsCD90<sup>+</sup> hyperproliferative population and production of extracellular matrix. In general, FAP levels return to the baseline upon resolution of the muscle injury and FAPCD90<sup>+</sup> proliferation was reduced by in vitro treatment with metformin.<sup>4</sup> These data provided new insight into the dynamics and multiple roles of FAPs in human T2DM skeletal muscle. The fourth keynote lecture was given by Chiara Mozzetta, a group leader at Institute of Molecular Biology and Pathology (IBPM) of the National Research Council of Italy, located at University Sapienza of Rome, Italy. The title of her talk was Role of peripheral heterochromatin in the maintenance of fibro-adipogenic progenitors' genome integrity and cell identity and she gave an overview on the heterochromatic lamina modulation during cell division. She showed that PR domain containing 16 (Prdm16) mediates FAP developmental capacities through the lamina-associated domain organization and heterochromatin sequestration at the nuclear periphery. Prdm16 cooperates with the H3K9 methyltransferases G9a/GLP to mediate tethering and silencing of myogenic genes, thus repressing the myogenic fate in FAPs<sup>5</sup>. This information could be relevant for FAP reprogramming during muscle regeneration in dystrophic muscles paving the way of possible therapeutic approach. Also in this edition, the voice of patients affected by Duchenne and Becker Muscular Dystrophy (DMD and BMD) was brought by Gloria Antonini, from the Parent Project

association that it is indeed a social promotion association (aps) founded in Italy in 1996 (after the USA and the Netherlands) and currently is in touch with over 800 families of DMD and BMD patients. This relatively young aps economically supports research and dissemination of the multidisciplinary approaches to treat patients that so far doubled the life expectancy of DMD patients improving overall the quality of life. A technical talk promoted by the sponsor Prodotti Gianni introduced the world of extracellular vesicles, highlighting recent results and troubleshooting in emerging technologies. Among the submitted abstracts, 33 talks were selected covering all the topics of the meeting, ranging from basic muscle function and repair to the effects of exercise, molecular mechanisms, and possible therapeutic approaches to muscle degeneration. The speakers came from Italy, Belgium, France and Brazil. The quality of the interventions was very high creating intense discussions among the participants of all ages. Overall, 42 posters were discussed with good interactions between presenter and attendees. At the end of the meeting, prizes were awarded to young researchers (less than 35 years old) based on the evaluation of groups of scientists selected by the IIM scientific board. For the best talks the prizes were awarded to David Osamwonuyi Amadsun and Laura Yedigaryan, while Federica Esposito won the prize for best poster and the one for the best active participation was awarded to Sara Roccabianca. Finally, on 22/10/2022, during the 19th annual IIM conference, the elections for the renewal of the Director and the scientific council were held and all conference participants had the right to vote. Sorci Guglielmo, Musarò Antonio, Falcone Sestina, Latella Lucia, Penna Fabio, Mocciaro Emanuele, Urciuolo Anna, Palacios Daniela, Riuzzi Francesca were elected by secret ballot. The scientific council has elected Doctor Guglielmo Sorci director of the IIM for the three-year period 2022-2025. Subsequently, pursuant to Art. 5 of the Statute, Alessandra Sacco, Davide Gabellini, Maurilio Sampaolesi, and Stefania Fulle joined the IIM Scientific Council as associate members. After the pandemic period, the 19th IIM Meeting managed once again highlighted the participation of young researchers, bringing together many mythologists, with interests from basic science to preclinical and clinical studies formulation of new hypotheses and new international collaborations. Without a doubt, the young researchers of IIM meeting, the young clinicians of Padua Muscle Days (PMD, a meeting more oriented towards advanced translational myology) and the young authors of articles printed electronically in the European Journal of Translational Myology (EJTM) shape the future of research in myology. Here, the abstracts of the 19th IIM meeting show the relevant research contribution of this community of myologists in anticipation of the 20th IIM Congress, scheduled for October 12-15, 2023, to be held in Assisi, Italy.

### List of acronyms

IMM - Interuniversity Institute of Myology  
 PMDs - Padua Muscle Days  
 COVID-19 - Disease caused by SARS\_CoV-2  
 DMD - Duchenne muscular dystrophy  
 E-C coupling - excitation-contraction coupling  
 FSHD - Facioscapulohumeral muscular dystrophy  
 T2DM - type 2 diabetes mellitus

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