Androgen-receptor in skeletal muscle biopsies and cells

Sorrentino Carmela*[1] Gentile Giulia*[1], D'Angiolo Rosa[1], Barra Carmela[1], De Stefano Ferdinando[1], Licitra Fabrizio[1], Sabbatino Emilia[1], Tutino Viviana[1], Moretti Antimo[2], Giovannelli Pia[1], Iolascon Giovanni [2], Migliaccio Antimo[1], Castoria Gabriella[1] and Di Donato Marzia°[1].

- *Co-first authors
- ° corresponding author: marzia.didonato@unicampania.it

[1] Dept of Precision Medicine, University of Campania "L.Vanvitelli"
[2] Multidisciplinary Department of Medical-Surgical and Dental Specialties

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Aging is characterized by the loss of skeletal muscle mass, likely caused by a decrease in sex steroid hormone levels. Androgens increase, indeed, the muscle size through the androgen receptor (AR), which activates both genomic and non-genomic pathways to trigger various biological responses. Non-genomic androgen effects occur through the upstream interaction of AR with effectors or scaffolds, including the Src tyrosine kinase or filamin A. As a consequence, activation of several downstream effectors (paxillin, FAK, MAPK, Akt) follows. Such events induce cell proliferation and survival, motility and invasion as well as metabolic changes.

The activation status of signalling hubs linking the AR non-genomic circuit with cytoskeleton organization has been analyzed by Western blot of lysate proteins from human skeletal muscle biopsies (obtained by young or old females) and C2C12 skeletal muscle cells. Phosphorylation of both Ser-2152 filamin A and Tyr-118 paxillin is stronger in biopsies from old females, as compared with those observed in young females. Conversely, AR is weakly expressed in samples from old females, as compared with young females. Consistent with these findings, C2C12 cells express abundant amounts of AR that seems involved in the androgen-triggered rapid activation of several signalling effectors (e.g. MAPK, Akt, Src, FAK).

Taken together, our findings suggest that derangement of androgen/AR axis occurs in skeletal muscle of old females, thus allowing to excessive metabolic functions and loss of skeletal muscle. Further investigation in cultured cells and mouse models might help us in targeting the skeletal muscle AR axis with new compounds, such as new selective androgen receptor modulators or small drugs specifically interfering in the non-genomic androgen actions, to restore the muscle functions and improve the clinical outcome of age-related frailty and sarcopenia.