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Molecular mechanisms regulating skeletal muscle homeostasis: effects of V1a AVP receptor over-expression.

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The mantainance a working skeletal musculature is conferred by its remarkable capacity to regenerate after mechanical or pathological injury. Most muscle pathologies are characterized by the progressive loss of muscle tissue due to chronic degeneration combined with the inability of the regeneration machinery to replace damaged myofibers. In particular, cachexia or muscle wasting is characterized by a dramatic loss of adipose and muscle mass associated with a compromised muscle regenerative ability. Arg-vasopressin (AVP) is a potent myogenesis promoting factor and activates both the calcineurin and CaMK pathways, whose combined activation leads to the formation of transcription factor complexes *in vitro*. The local over-expression of V1a AVP receptor (V1aR) in injured muscle results in enhanced regeneration. V1aR over-expressing muscle exhibits: early activation of satellite cells and regeneration markers, accelerated differentiation, increased cell population expressing hematopoietic stem cell markers and its conversion to the myogenic lineage.
Here we investigated the role of V1aR over-expression in animals undergoing cachexia as a result of muscle over-expression of a specific cytokine (TNF-α). In these conditions, the local V1aR over-expression counteracts the negative effects of cachexia on muscle, as demonstrated by morphological and biochemical analysis. In particular, the presence of V1aR results in increased Pax-7, myogenin and myosin expression levels both in wild type and in cachectic muscles.
The positive effects of V1aR on muscle homeostasis are due to the promotion of the calcinuerin-IL-4 pathway and to the inhibition of atrophic genes expression mediated by FOXO phosphorilation.
This study highlights a novel *in vivo* role for the AVP-dependent pathways which may represent a potential gene therapy approach for many diseases affecting muscle homeostasis.

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