A molecular and cellular analysis of the mechanisms coordinating growth arrest and myogenesis in muscle stem cells

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During tissue formation, the equilibrium between cell proliferation and cell differentiation is maintained by timely and tightly controlling growth arrest. Muscle differentiation is a coordinated process of tissue-specific gene expression and irreversible cell cycle exit. Growth arrest in myogenic cells is mediated by the cyclin-dependent kinases inhibitors (CDKIs) p21cip1 and p57kip2; nevertheless, the molecular link between cell cycle exit and myogenic cell differentiation is currently unknown. It was shown recently that during development the skeletal muscle progenitor cells require a direct interaction with the differentiating myoblasts via the Notch signaling pathway in order to maintain their pool and a novel molecular and cellular mechanism regulating tissue growth was described. Moreover, microarray data underline the differential expression of cell cycle transcripts as well as of the Notch signaling pathway between embryonic and adult stages. The knowledge of cell cycle exiting regulation and myogenesis during both development and adult will now be expanded, combining mouse molecular genetics with ex vivo studies. Mutant mice for CDKIs have been obtained and a novel conditional allele of p57kip2 that expresses the LacZ reporter was generated. Analysis of the latter is expected to shed light in the function of p57kip2 in adult myogenesis, using both in vivo strategies (Cre/LoxP analysis during muscle post-natal growth, homeostasis and regeneration) and single myofiber cultures. Aim is to examine the molecular and cellular mechanisms of growth arrest in muscle stem cells, with specific focus upon factors and signals involved in cell cycle exit, including the role of Notch signaling.

Biography

D Mademtzoglou has completed her BSc at the Faculty of Biology of the Aristotle University of Thessaloniki, where she conducted her Dissertation and further participated in a research project which focused on toxicology and lead to five publications. She completed her MSc in 2011 at the Faculty of Medicine of the University of Thessaly. She is currently conducting a bi-nationally supervised Doctoral Thesis in MyoGrad, an international graduate program for muscle sciences.

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