

New insights into the early steps of adipocyte generation unveiled by transcriptomics

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Although adipocyte terminal differentiation has been extensively studied, the early steps of adipocyte development and the embryonic origin of this lineage remain largely unknown.

To uncover the developmental pathways and genes involved in the commitment of stem cells to the adipocyte lineage we used retinoid-treated mouse embryonic stem cells (mESCs) as main model. Retinoic acid receptor b (RAR β) activation is both sufficient and necessary to induce mESC adipogenesis provided that the glycogen synthase kinase 3 (GSK3) remains active. The induction of mESC differentiation upon single or combined treatment with RAR β agonist and GSK3 inhibitors therefore provided a selective set of screening conditions to perform a large-scale gene expression profiling of adipogenesis in mESCs. We found this process to be coupled to blood vessel and neural development. This observation led us to show that adipocytes could be generated by the neural crest (NC) in vitro, as well as in vivo during mouse development.

In parallel, we showed that out of 30 microarray candidate genes, most were expressed in mouse adipose tissue and embryonic mesenchyme. We proceeded to study the role in adipocyte development of one such candidate gene, the pre-B-cell leukaemia transcription factor 1 (PBX1), using both mESCs and human Multipotent Adipose-Derived Stem cells. Our data suggests that PBX1 regulates adipocyte development at multiple levels, promoting the generation of NC-derived adipocyte progenitors (AP) during embryogenesis. Whereas in postnatal life, PBX1 favors APs proliferation and prevents their commitment to the adipocyte lineage most likely by regulating the biosynthesis of PPAR γ endogenous ligand(s).

Biography

Before his PhD, Miguel Caetano Monteiro managed research projects on thyroid cancer, immunology and cell cycle. In 2010, he completed his PhD from the University of Nice Sophia-Antipolis, sponsored by the competitive European Marie Curie program and did a short postdoc at the CNRS UMR6543 unit. He was part of the FP6 consortium "Functional Genomics in Embryonic Stem Cells" (FunGenES) and has published 7 papers in international peer-review journals. Given his interest in business he completed an MBA at EDHEC business school (Nice, France) in 2011 and is currently seeking challenging positions in the Life Sciences industry.