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Role of Pax3 in the differentiation of human induced pluripotent stem cells into brown and white adipocytes

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Identification of molecular mechanisms involved in generation of different types of adipocytes is progressing substantially in mice. However, much less is known regarding characterization of brown and white adipocyte progenitors (APs) in humans, highlighting the need for an *in vitro* model of human adipocyte development. Here we report a procedure to selectively derive brown and white APs from human induced pluripotent stem cells. Molecular characterization of APs of both phenotypes revealed that *BMP4, Hox8, Hoxc9* and *HoxA5* genes were specifically expressed in white APs, whereas expression of *PRDM16*, *Dio2* and *Pax3* marked brown APs. We focused on Pax3 and we showed that expression of this transcription factor was enriched in human perirenal white adipose tissue samples expressing *UCP1* and in human classical brown fat. Finally, functional experiments indicated that Pax3 was a critical player of human AP fate as its ectopic expression led to convert white APs into brown-like APs. Together, these data support a model in which Pax3 is a new marker of human brown APs and a molecular mediator of their fate. The findings of the present study could lead to new anti-obesity therapies based on the recruitment of APs and constitute a platform for investigating *in vitro* developmental origins of human white and brown adipocytes.

Biography

Christian Dani completed his PhD in Molecular Biology in Montpellier University. Then, he conducted a 2-year program research on the biology of embryonic stem cells in Pr. A. Smith's laboratory (Edindurgh, Scotland). He is now Director of research at the French National Institute for Health and Medical Research (INSERM) and the Director the "Stem Cells and Differentiation" laboratory at the University of Nice-Sophia Antipolis. He is member of the editorial board of Stem Cells and of *American Journal of Stem Cells* journals

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