

Signaling Network of the Novel Genes Specifically Expressed at the Early Stage of Adipocyte Differentiation

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Adipocyte differentiation is known to be regulated by a complex array of genes known as master regulators. Several lines of evidence revealed that PPAR, C/EBP family and SREBP-1 function as master regulators of adipocyte differentiation. However, their expression is observed from the mid phase to log phase of adipogenesis and the factors initiating differentiation at the earliest phase are poorly isolated and characterized. Using a PCR-subtraction method, we previously isolated 102 genes, which are expressed in the early stage of adipocyte differentiation. Of these, 46 clones had no significant similarity with genes of known function listed in DNA databases. Three of these genes named *fad24* (factor for adipocyte differentiation 24), *fad104* and *fad158* seem to be a novel gene, since there is no significantly similar gene listed in databases. The knocked down and overexpression experiments revealed that all these three genes have the ability to regulate adipocyte differentiation positively, especially at an early stage. It is reported that the clonal expansion is required at the earliest step of the adipocyte differentiation for entering the next step in 3T3-L1 cells. Some genes described above have a functional role on the clonal expansion, and also on the signaling through PPAR. Especially, FAD24 interacts with HBO1, a histone acetyltransferase and positive regulator of DNA replication initiation. We also found that FAD24 is involved in the regulation of DNA replication by recruiting HBO1 to origins of DNA replication and is required for the clonal expansion during adipocyte differentiation. The signaling network of these novel genes and other known key factors is discussed.