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LMNA p.R482W mutation related to FPLD2 alters SREBP1-A type lamin interactions in human fibroblasts and adipose stem cells

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SREBP1 (Sterol regulatory element binding protein 1), transcription factor that regulates hundreds of genes involved in lipid metabolism and adipocyte differentiation, is a direct partner of A-type lamins. We show that i) *in vitro*, the tail regions of prelamin A, lamin A and lamin C bind a polypeptide of SREBP1 and ii) within cells, interactions between wild-type A-type lamins and SREBP1 occur mainly at the nuclear periphery but also within the nucleoplasm. While A-type lamin R482W mutation is responsible for Dunnigan type familial partial lipodystrophy (FPLD2), we show that both overexpression of *LMNA* p.R482W in primary human preadipocytes and endogenous expression of A-type lamins p.R482W in FPLD2 patient fibroblasts, reduce A-type lamins-SREBP1 *in situ* interactions and upregulates a large number of SREBP1 target genes [1]. As this *LMNA* mutant was previously shown to inhibit adipogenic differentiation, we propose that deregulation of SREBP1 by mutated A-type lamins constitutes one underlying mechanism of the physiopathology of FPLD2.

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Reference

1. Vadrot N, Duband-Goulet I, Cabet E, Attanda W, Barateau A, Vicart P, *et al*: **The p.R482W substitution in A-type lamins deregulates SREBP1 activity in Dunnigan-type familial partial lipodystrophy.** *Human molecular genetics* 2015, **24(7)**:2096-109.

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