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Paris, June 15th, 2017

Dear Esther Schnapp,

We would like to submit for publication into *EMBO Reports* as a Scientific report, a manuscript entitled "Egr1 deficiency induces browning of inguinal subcutaneous white adipose tissue in mice". This manuscript has been posted to bioRxiv the 14th June 2017, doi:10.1101/150003.

Adipose tissue plays a central role in fat storage, metabolic control and thermoregulation. Excess food intake and poor energy expenditure leads to obesity. The identification of thermogenic beige adipocytes within white adipose tissue depots has attracted growing interest on their ability to increase energy expenditure and counteract obesity. In this manuscript, we identified the zinc finger transcription factor EGR1 as a negative regulator of the beige fat differentiation program. Loss of *Egr1* induces spontaneous beigeing/browning of white adipose tissue in mice, without external stimulation such as cold stimulation or fasting. EGR1 directly represses white fat browning via the recruitment to the *Ucp1* promoter. Conversely, EGR1 gain-of-function experiments reduce the beige differentiation ability of mouse mesenchymal stem cells. Global profiling of subcutaneous inguinal white adipose tissue in postnatal *Egr1*$^{-/-}$ mice identifies the molecular signature of white adipose tissue browning downstream of Egr1 deletion. This signature includes a concomitant upregulation of numerous beige differentiation markers and downregulation of extracellular matrix genes. These results identify *Egr1* deletion as a putative therapeutic target to prevent obesity. We believe that these data constitute a significant progress in the adipose tissue research field and is of strong interest to the broad readership of *EMBO Reports*.

Yours sincerely,

Emmanuelle Havis, Ph.D.
Delphine Duprez, Ph.D.