

ERRgamma Preserves Brown Fat Innate Thermogenic Activity.

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Authors: Maryam Ahmadian, Sihao Liu, Shannon M Reilly, Nasun Hah, Weiwei Fan, Eiji Yoshihara, Pooja Jha, C Daniel De Magalhaes Filho, Sandra Jacinto, Andrew V Gomez, Yang Dai, Ruth T Yu, Christopher Liddle, Annette R Atkins, Johan Auwerx, Alan R Saltiel, Michael Downes, Ronald M Evans

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Public Summary:

Brown adipose tissue (BAT) adaptively transfers energy from glucose and fat into heat by inducing a gene network that uncouples mitochondrial electron transport. However, the innate transcription factors that enable the rapid adaptive response of BAT are unclear. Here, we identify estrogen-related receptor gamma (ERRgamma) as a critical factor for maintaining BAT identity. ERRgamma is selectively expressed in BAT versus WAT, in which, in the absence of PGC1alpha, it drives a signature transcriptional network of thermogenic and oxidative genes in the basal (i.e., thermoneutral) state. Mice lacking ERRgamma in adipose tissue (ERRgammaKO mice) display marked downregulation of BAT-selective genes that leads to a pronounced whitening of BAT. Consistent with the transcriptional changes, the thermogenic capacity of ERRgammaKO mice is severely blunted, such that they fail to survive an acute cold challenge. These findings reveal a role for ERRgamma as a critical thermoneutral maintenance factor required to prime BAT for thermogenesis.

Scientific Abstract:

Brown adipose tissue (BAT) adaptively transfers energy from glucose and fat into heat by inducing a gene network that uncouples mitochondrial electron transport. However, the innate transcription factors that enable the rapid adaptive response of BAT are unclear. Here, we identify estrogen-related receptor gamma (ERRgamma) as a critical factor for maintaining BAT identity. ERRgamma is selectively expressed in BAT versus WAT, in which, in the absence of PGC1alpha, it drives a signature transcriptional network of thermogenic and oxidative genes in the basal (i.e., thermoneutral) state. Mice lacking ERRgamma in adipose tissue (ERRgammaKO mice) display marked downregulation of BAT-selective genes that leads to a pronounced whitening of BAT. Consistent with the transcriptional changes, the thermogenic capacity of ERRgammaKO mice is severely blunted, such that they fail to survive an acute cold challenge. These findings reveal a role for ERRgamma as a critical thermoneutral maintenance factor required to prime BAT for thermogenesis.

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