Caveolar Kv1.3 targeting for proper insulin signaling in adipocytes

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The voltage dependent potassium channel Kv1.3 participates in the peripheral insulin sensibility. Because the genetic ablation of Kv1.3 triggers a lean phenotype this protein has been suggested as a pharmacological target for obesity and the associated Type II diabetes. However, this role is under intense debate because the Kv1.3 expression in the adipose tissue raises controversy. We demonstrated that Kv1.3 mRNA, protein and activity are expressed in white adipose tissue from humans and rodents. Moreover, other channels such as Kv1.1, Kv1.2, Kv1.4 and Kv1.5 from the same Shaker family are also present. Although the Kv phenotype during adipogenesis and upon insulin stimulation is remodeled, Kv1.3 is still participating in the insulin-dependent regulation of glucose uptake in mature adipocytes. Adipocyte differentiation increases the expression of Kv1.3 which targets to caveolae by molecular interactions with caveolin 1. By using a caveolin 1 deficient 3T3-L1 adipocyte cell line we demonstrated that the localizacion of Kv1.3 in caveolar raft structures is important for a proper insulin signaling. Insulin phosphorylates the channel being at the onset of the insulin-dependent signaling. However, when Kv1.3 is spatially out of these lipid microdomains exhibited an impaired phosphorylation. Our data bring light to the putative role of Kv1.3 in the weight gain and insulin-dependent responses and points to this channel as a putative target for obesity and related disorders.

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