

Abstract

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Severe diabetes, age-dependent loss of adipose tissue, and mild growth deficiency in mice lacking Akt2/PKB beta.

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BACKGROUND: The serine/threonine kinase Akt/PKB plays key roles in the regulation of cell growth, survival, and metabolism. It remains unclear, however, whether the functions of individual Akt/PKB isoforms are distinct.

OBJECTIVE AND METHODS: To investigate the function of Akt2/PKBbeta, mice lacking this isoform were generated.

RESULTS: Both male and female Akt2/PKBbeta-null mice exhibit mild growth deficiency and an age-dependent loss of adipose tissue or lipoatrophy, with all observed adipose depots dramatically reduced by 22 weeks of age. Akt2/PKBbeta-deficient mice are insulin resistant with elevated plasma triglycerides. In addition, Akt2/PKBbeta-deficient mice exhibit fed and fasting hyperglycemia, hyperinsulinemia, glucose intolerance, and impaired muscle glucose uptake. In males, insulin resistance progresses to a severe form of diabetes accompanied by pancreatic beta cell failure. In contrast, female Akt2/PKBbeta-deficient mice remain mildly hyperglycemic and hyperinsulinemic until at least one year of age.

CONCLUSION: Thus, Akt2/PKBbeta-deficient mice exhibit growth deficiency similar to that reported previously for mice lacking Akt1/PKBalpha, indicating that both Akt2/PKBbeta and Akt1/PKBalpha participate in the regulation of growth. The marked hyperglycemia and loss of pancreatic beta cells and adipose tissue in Akt2/PKBbeta-deficient mice suggest that Akt2/PKBbeta plays critical roles in glucose metabolism and the development or maintenance of proper adipose tissue and islet mass for which other Akt/PKB isoforms are unable to fully compensate.

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