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Novel and unexpected roles of butyrate and butyrate derivatives in the control of metabolism

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Abstract

The increasing incidence of obesity worldwide and its related cardio metabolic complications is an urgent public health problem. While weight gain results from a negative balance between the energy expenditure and calorie intake, recent research has demonstrated that several small organic molecules containing a four-carbon backbone can modulate this balance by favoring energy expenditure, and alleviating endoplasmic reticulum stress and oxidative stress. Such small molecules include the bacterially produced short chain fatty acid butyric acid, its chemically produced derivative 4-phenylbutyric acid (4PBA), the main ketone body D- β -hydroxybutyrate - synthesized by the liver - and the recently discovered myokine β -aminoisobutyric acid. Conversely, another butyrate-related molecule, α -hydroxybutyrate, has been found to be an early predictor of insulin resistance and glucose intolerance. In this minireview, we summarize recent advances in the understanding of the mechanism of action of these molecules, and discuss their use as therapeutics to improve metabolic homeostasis or their detection as early biomarkers of incipient insulin resistance.

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