Letter to the Editor

Increased Activity of the Oncogenic Fatty Acid Synthase and the Impaired Glucose Uptake in the Metabolic Syndrome

To the Editor: Ashbeck et al. (1) report that components of metabolic syndrome (MS) that capture impaired glucose uptake increase the odds of colorectal metachronous neoplasia. I would like to add the following comments to strengthen some issues of this theme. (a) Insulin resistance in obesity, specifically within adipose tissue, is thought to be caused by increased glucocorticoids (2). Furthermore, the metabolic consequences of visceral obesity, the hallmark of the MS, have been associated with amplification of glucocorticoids, due to increased activity of 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) in adipose tissue. Indeed, inhibitors of 11β-HSD1 have shown considerable potential in rodents and primates as insulin sensitizers and as agents that may aid weight loss (3). Consistent with these studies, converging evidence has also shown that increased 5α-reductase activity is associated with obesity and type 2 diabetes (2). In addition, treatment with insulin sensitizers decreases the expression of 5α-reductase enzymes in the liver of rodents (2). Taken together, this evidence indicates that the activities of both 11β-HSD1 and 5α-reductase increase in MS. (b) In the MS, the activities of both 5α-reductase enzymes are activated. As a result, there is increased conversion rate of testosterone to dihydrotestosterone, a more potent androgen. A consequence of increased 5α-reductase activity is activation of the sterol regulatory element binding protein pathway (4) and a downstream effect of sterol regulatory element binding protein pathway activation is abnormal activation of the oncogenic enzyme, fatty acid synthase (FAS). The expression of FAS is markedly increased in several human malignancies, and its overexpression in tumor tissues from patients with colon, breast, and prostate carcinomas, as well as melanoma and gastrointestinal stromal tumors, is associated with poor prognosis (5).

In summary, impaired glucose uptake due to the MS is related to increased activities of both 11β-HSD1 and 5α-reductase. These changes could lead to FAS activation and tumorigenesis. These data concur with the proposal of Ashbeck et al. (1), relating the impaired glucose uptake to the increased odds of metachronous neoplasia in colorectal tissue.

Salvador Vale
Departamento de Investigación, Laboratorios Trinidad, Mexico DF

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

References

Note: Personal Phone and Fax: 55-5593-3714.
Copyright © 2009 American Association for Cancer Research.
doi:10.1158/1055-9965.EPI-09-0418
Increased Activity of the Oncogenic Fatty Acid Synthase and the Impaired Glucose Uptake in the Metabolic Syndrome

Salvador Vale


Updated version

Access the most recent version of this article at:

http://cebp.aacrjournals.org/content/18/7/2151

Cited articles

This article cites 4 articles, 2 of which you can access for free at:

http://cebp.aacrjournals.org/content/18/7/2151.full#ref-list-1

E-mail alerts

Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions

To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions

To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.