Obesity, diabetes mellitus, and cancer

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The interaction of genomic variation with the micro- and macro-environment is believed to result in the phenotype, including disease manifestation. It is ironic that the genomic variation that has evolutionarily sustained populations exposed to long periods of famine and has been selected for is now interacting with ‘modern’ environments and may no longer result in a survival advantage. *Au contraire*, this genomic variation likely predisposes to obesity and type 2 diabetes mellitus (T2DM), and over recent years has been shown to take on a new bedfellow: cancer.

In adults, obesity is defined as a body mass index (BMI) >30. A recent study demonstrated that the widely applied BMI formula ($\text{BMI} = \text{weight in pounds}/(\text{height in inches})^2 \times 703$; $\text{BMI} = \text{weight in kilograms}/(\text{height in meters})^2$), which was developed by Lambert Adolphe Jacques Quetelet (1796–1874), underestimates the prevalence of obesity, especially when compared to a direct measurement of percentage body fat by dual-energy X-ray absorptiometry! (Shah & Braverman 2012). An adjusted, more appropriate definition for obesity of BMI >24 in females and >28 in males was, therefore, proposed (Shah & Braverman 2012).

Worldwide, ~475 million people are obese. The National Health and Nutrition Examination Survey (NHANES), which tracks the prevalence of obesity in the United States over time, shows a significant increase in obesity with prevalence rates currently exceeding 30% in a majority of states in most sex and age groups (Finucane *et al.* 2011, Ogden *et al.* 2012).

‘Falstaff: You make fat rascals, Mistress Doll.

Doll Tearsheet: I make them?! Gluttony and diseases make them; I make them not.’

William Shakespeare, *2 Henry IV* 2.4.37

Obesity leads to significant morbidity, premature mortality, and impaired quality of life; together with all preventive attempts, it consumes more than 10% of the health care budget in the western world (Whitlock *et al.* 2009, Congressional Budget Office 2010). Obesity is associated with an increased incidence of T2DM, cardiovascular disease (hypertension, heart disease, and stroke), sleep apnea, respiratory diseases, nonalcoholic fatty liver disease, and an increased risk of disability (Malnick & Knobler 2006).

The NHANES data also show a greater than fourfold increase in the T2DM prevalence over the past 30 years (Danaei *et al.* 2011). Obesity has a strong association with insulin resistance, hyperinsulinemia, and glucose intolerance and may eventually lead to T2DM (Reaven 2011). Among adults with T2DM, severe obesity is now present in one out of every five adults. In a recent meta-analysis, the relative risk of developing T2DM for obese persons, compared with those with normal weight, was sevenfold (Abdullah *et al.* 2010). It is generally accepted that the increased prevalence of T2DM is in large part due to the increased prevalence of obesity. T2DM has also been associated with premature

mortality from several cancers, infectious diseases, and degenerative disorders (Seshasai *et al.* 2011, Florez & Castillo-Florez 2012). This issue of *Endocrine-Related Cancer* is dedicated to the global problem of obesity, T2DM, and the management of these two diseases, as well as their relationships with an increased cancer risk.

To set the stage, Manami Inoue and Shoichiro Tsugane discuss the epidemiological evidence for the relation between insulin resistance and cancer (Inoue & Tsugane 2012). YunFeng Cui and Dana Andersen follow by discussing the complex relationship between T2DM and type 3c DM and pancreatic cancer (Cui & Andersen 2012). Dara Cohen and Derek LeRoith focus on the role of insulin and the insulin-like growth factor (IGF) in the association between obesity, T2DM, and the risk of cancer and cancer-related mortality (Cohen & LeRoith 2012). Mathis Grossmann and Gary Wittert discuss the current epidemiological and mechanistic evidence regarding the interactions between metabolic conditions, sex steroids, and prostate cancer risk and management (Grossman & Wittert 2012). Aimee Varewijck and Joseph Janssen discuss the potential clinical relevance and potential mechanisms behind the activation of the insulin receptor and IGF1 receptor by insulin analogues, and how this activation may be linked to mitogenesis (Varewijck & Janssen 2012). Roman Vangoitsenhoven, Chantal Mathieu, and Bart van der Schueren discuss the benefits and potentially cancer-promoting risks of using the new incretin-based therapies, dipeptidyl peptidase-4 inhibitors, and glucagon-like peptide 1 receptor agonists for the treatment of T2DM (Vangoitsenhoven *et al.* 2012).

We hope the readership will enjoy this series of authoritative reviews on this complex and continually unfolding interplay of obesity, diabetes, and cancer.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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