# Metabolic Programming of Obesity

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Obesity incidence is growing all over the world and has become one of the main public health challenges. In particular, the increasing number of affected children is alarming as for the first time it is expected a decrease in life expectancy due to cardiovascular diseases, diabetes and other medical problems associated with obesity. Increased availability of palatable energy dense food and a sedentary life style are often considered underlying the obesity pandemic. Such a consideration, although true, should be extended, because environmental factors not only in adulthood but particularly in early life may have long-term consequences and be important in establishing the risk to disease, a concept that has been referred to as programming or *metabolic programming*. The programmed differences in the susceptibility to obesity can be deduced from both epidemiological studies in humans and intervention studies in animal models where the interaction between components of food or other environmental factors with our chromosomes, may lead to an "*imprinting*" or “metabolic programming” of metabolic pathways and processes in individuals that may confer a different susceptibility to suffer abnormalities in adulthood. It involves the concept that a stimulus or insult operating at a critical or sensitive period of development (the specific window of sensitivity) could result in a long-standing or life-long effect on the structure and/or function of the organism. *Epigenetics* refers to these stable alterations in gene expression that do not involve sequence changes of the DNA itself while conferring stable maintenance of a particular gene expression pattern through mitotic cell division. We will concentrate in a few nutritional factors or influences. Interestingly, there is very solid epidemiological evidence in humans suggesting that breastfeeding compared with infant formula confers protection against obesity (and related alterations) later in life and, 15 years a go, we found that leptin (a protein that is present in breast milk but no available in infant formulae) can be responsible or is one of the important factors accounting for the beneficial effects of breastfeeding. The involved mechanisms and related findings are under study. In related models we have observed that the effects of a moderate caloric restriction (20-30% less energy intake) in the mother’s differentially affects the predisposition of the progeny to develop obesity when adulthood, the difference depending on the physiological state: the restriction being favourable during lactation and negative when the restriction occurs during the first half of pregnancy. All these findings open a new area of research on both the use of leptin in the design of more appropriate infant formula, the identification of potential factors influencing leptin levels in maternal milk, or the effects of reduced/increased exposure to other nutrients, which appear aspects of great relevance due to the increased prevalence of obesity and its associated health complications