

Regulation of AgRP hunger stimulating neurons by microRNAs

Brain controlled appetite disorders such as anorexia nervosa, bulimia nervosa or binge eating disorder, are becoming one of the major psychiatric problems of our society, especially affecting the young generation. Dysregulation of neuronal circuits controlling physiological hunger lies at the basis of these diseases. On the other hand, unprecedented availability of cheap carbohydrate- and fat-rich food disrupts brain reward systems leading to obesity. The majority of obese patients additionally develop cardiovascular disease and type 2 diabetes mellitus, collectively referred to as the metabolic syndrome. Such condition ultimately may result in cancer development and reduces life expectancy.

Most of the brain centers responsible for the control of hunger/satiety balance are located within the hypothalamus. Agouti-related protein (AgRP) neurons are crucial for feeding behavior since they strongly stimulate hunger in animals. Regulation of activity of AgRP neurons, especially on the protein level, is not fully understood. Recently, we have shown that microRNAs (small non-coding regulatory RNAs) in the arcuate nucleus of the hypothalamus may strongly influence the activity of AgRP neurons, mainly by dysregulation of protein translation, which ultimately leads to an obesity phenotype in mice. In the proposed project, we would like to study orexigenic AgRP neurons confronted with a loss of microRNAs.

We expect that the obtained results will 1) provide a basic knowledge about the function of AgRP neurons, especially regarding the expression of neuropeptides and crucial proteins and 2) promise to allow for development of targeted therapies of brain controlled appetite disorders in the future.