Finicky flights of fancy

With the curtains drawn on the recent Olympic Games held in Atlanta, a question that seems to haunt the mind of many a physiologist is how far the Olympic motto can actually be stretched. How high, how swift and how strong can today's athlete become? Ehsan Masood wonders (in a briefing in *Nature*, vol. 382, 4th July 1996) how far this 'record-breaking' could last. Roger Woledge, professor of physiology from the University College, London believes that where the performance of the human body is concerned, there is certainly a limit. After all, the human race cannot be likened to an in-bred racehorse. A recent study conducted at University of California compared the metabolic rates of 37 species including human beings. In most cases, the ratio of the metabolic rates (that actually indicate the energy level) between subjects in the sleep phase and the active phase did not exceed 7:1. Even when unlimited food was provided to the subjects, this rate did not vary significantly. In retrospect, while improved training, sports equipment, clothing and nutrition may indeed enhance an athlete's performance, no one can really go on and on. There seems to be a well-meaning dot that punctuates every hundred metre dash.

'Y' are we so hungry?

Mechanisms that balance the food intake and the energy expenditure can determine whether an individual is fat or thin. A couple of years ago Jeffrey Friedman, from the Howard Hughes Medical Institute, identified the 'obese gene' from mice, whose protein product actually regulates this balance. The counterpart of this gene in the humans codes for a protein called 'leptin' that can suppress the appetite of an individual and increase the metabolic rate. Later, Millenium Pharmaceuticals succeeded in identifying the corresponding receptor situated on the cell membrane that binds to the leptin molecules. The protein entering the cell in this manner would then proceed to execute a particular metabolic function. Any aberration either in the obese gene or in the gene coding for its receptor protein is said to result in obesity. Even while Millenium Pharmaceuticals is involved in the formidable task of designing drugs to control obesity, the attention has now been diverted to a neuropeptide that seems to possess a master control of the feeding habits of an individual.

A few years ago, peptide hormones were in the news because of the crucial functions they are able to execute in the human body. PYY, one such hormone that is secreted by the pancreatic cells, has a unique amide attached to its C-terminal tyrosine group. This was later found to bear an uncanny resemblance to the Neuropeptide Y (NPY) that is widely distributed in the limbic regions of the brain. Earlier results have indicated that NPY binds to specific receptors of the 'Y' class. This class of receptors (Y1, Y2, and Y3) is found in mammals and can bind to such peptides with varying affinities resulting in the triggering of a biochemical signalling pathway.

Evidence so far indicates that the signal triggered by the NPY-receptor binding regulates the feeding habits of the individual. Attempts at identifying the receptor have finally yielded results, according to a recent report in *Nature* (Gerald *et al.*, vol. 382, 11th July 1996) The total mRNA (which acts as an intermediate in the DNA-to-protein transition) isolated from the hypothalamus of a rat was converted into a complementary DNA (cDNA) library using conventional methods in genetic engineering. The cDNA molecules were later introduced into an expression cloning system, where conditions allow for the DNA to be decoded into its corresponding protein. When the protein products were exposed to labelled NPY molecules, the protein that bound chemically to the labelled protein was fished out and its properties studied. This protein (that is actually the receptor) is said to bear scant resemblance (as judged by its amino acid sequence analysis) to the older receptor molecules, and has been duly named the 'Y5' receptor. In humans, the Y1 receptor identified earlier also bound to the NPY peptide. So in what way is the new Y5 receptor (that has also been identified in humans) related to Y1? For some unknown reason, the genes coding for the Y1 and the Y5 receptors map to the same locus of the same chromosome but in the opposite orientation.

Using the rat as the model system, an elaborate study of the Y5 receptor was conducted starting with the localization of this receptor in various tissues of the brain. Evidence now points out that through an intricate circuitry created by the receptor location in the brain, NPY may also regulate the emotional aspect of feeding behaviour. Y5 is clearly the best candidate for studying and understanding the physiology and psychology of feeding behaviour and that includes several feeding disorders.

The 'not so sweet news'

Aspartame is a high intensity artificial sweetener which is being marketed under various brand names like 'Equal', 'Nutrasweet' and 'Spoonful'. A recent report in the Journal of Diabetic Association of India' (Vol. 35) cautions the indiscriminate use of this sweetener that can lead to as many as 90 different documented symptoms including headaches, visual problems, and even heart palpitations. Aspartame, (which is L-Aspartyl Phenylalanine Methyl Ester) can breakdown in the body into amino acids and methanol. As there is no ethanol in Aspartame to counter the ill-effects of Methanol, it can lead to several of these undesirable side-effects. The FDA, however, claims that a daily dose up to 50 mg/kg body weight is safe.