Report from the lecture presented by Jeffrey Friedman

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Dr Jeffrey M. Friedman of The Rockefeller University started out by discussing regulation of energy (food) intake in humans. The worldwide trend towards increased body weight might be interpreted as if energy balance in humans was under rather imprecise regulation. He made a compelling argument by comparing the normal situation in which we eat when we are hungry and cease to do so when satisfied to that of using the declaration of energy content for the particular type of food that we choose as a way to regulate caloric intake. His conclusion was that using such declarations is by far a less accurate method to maintain constant body weight over time as compared with relaying on our normal appetite-based energy intake regulation. Leptin was then introduced as the molecule that relay information regarding the size of energy stores (size of adipose tissue) to the central nervous system and thus constituting a crucial link in the network that regulate human energy balance. Initial experiments aimed to identify such factors were performed by Dr Douglas L. Coleman at The Jackson Laboratory, USA in which he used the parabiosis (union of two organisms sharing blood circulation) technique to pinpoint the defects in two mouse mutants with severe obesity *ob/ob* (*ob*, *obese*) and *db/db* (*db*, *diabetes*). Dr Coleman concluded that in *ob/ob* mice a circulating factor is missing and that the *db/db* strain lacks the corresponding receptor. To some extent based on these findings Dr Friedman set out to clone the gene mutated in ob/ob mice. This was a heroic undertaking since at the time DNA sequencing and mapping techniques were still very rudimentary as compared to the ones available today. Still the project was successful and in a Nature paper 1994 Dr Freidman and coworkers at The Rockefeller University described the identity of the elusive factor and named it Leptin. Subsequent work from Cambridge University demonstrated the importance of Leptin in humans by identifying individuals (children) with mutations in their Leptin gene. These children displayed severe obesity, increased food intake and delayed puberty. These symptoms subsided upon Leptin administration. In the final part of the presentation Dr Friedman discussed the role of Leptin signaling in hypothalamic neurons and how Leptin, as a

messenger from the periphery, convey information to central neuronal circuits regulating food intake.

In the discussion that followed the role of Leptin in treating conditions characterized by failure to produce appropriate amount of adipose tissue (e.g. lipodystrophy) was discussed. It was concluded that Leptin administration reverses many of the symptoms seen in such patients e.g. lipid accumulation in the liver.

For further information (Dr Friedman's homepage):
http://www.rockefeller.edu/labheads/friedman/friedman-lab.php