### Opening Lecture

**Endocrine and secretory function of adipose tissue**

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For many years energy storage in the form of triacylglycerols was seen as the main role of adipose tissue, apart from providing mechanical and thermal isolation. Adipose tissue is now recognized as a major endocrine and secretory organ being involved in a wide range of metabolic and physiological processes. Fatty acids, which are quantitatively the largest adipose tissue secretory product (particularly at periods of negative energy balance) play a dual role: a) as energy substrates, and b) as regulators of genes expression that are involved in lipid, carbohydrate and protein metabolism, as well as regulators of cell growth and differentiation. In addition to fatty acids, some other lipid compounds are stored (cholesterol, retinol) and synthesized (prostaglandins, kortisol, estrogens, androgens, endocannabinoids) in adipose tissue. Furthermore, NO synthase has been found also in rat white adipose tissue, indicating that adipocytes are a potential source of NO. The discovery of leptin was a major event in our understanding of the role of adipose tissue as a secretory organ. Adipose tissue is recognized as an organ synthesizing and releasing approximately 60 diverse proteins and factors named adipokines, which are involved in the regulation of a range of processes as: appetite and energy balance, carbohydrate and lipid metabolism, insulin sensitivity, angiogenesis, immunity, inflammation and acute phase response, blood pressure, reproduction, bone development, and haemostasis. Some of adipokines may contribute to the development of vascular disease and cancer progression in obese patients. Adiponectin in addition to its anti-inflammatory action has been proposed as an antiatherogenic and antidiabetic protein. Recently it has been suggested that human adipose tissue is a source of multipotent stem cells.

### Parnas Lecture

**L-Asparaginases, their friends and relations**

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L-Asparaginases hydrolyze L-asparagine to L-aspartate and ammonia. However, due to posttranslational modifications of asparagine (glycosylation, isomerization to β-aspartyl residues), specialized enzymes are required for the hydrolysis of the β-amide bond in the general scheme of asparagine metabolism. In *E. coli*, there are two classic L-asparaginases. The homotetrameric periplasmic enzyme (EcAII), but not the homodimeric EcAI found in the cytoplasm, is a potent antileukemic agent. In plants, L-asparaginases are essential for nitrogen circulation. There are two types of plant asparaginases, with or without potassium dependence. *E. coli* expresses a protein (EcAIII) with intriguing sequence similarity to the plant enzymes. It is structurally unrelated to the classic bacterial enzymes but belongs to the family of N-terminal nucleophile (Ntn) hydrolases. We have shown that EcAIII and its yellow lupine homolog (LIA) are more active as isoaspartyl amionopeptidases. This dual activity is important in seeds for the removal of toxic β-aspartyl protein aberrations and for quick release of nitrogen during germination. The crystal structures of LIA and EcAIII show (αβ)2 heterotetramers composed of α and β subunits generated on autoproteolytic activation, which liberates a Thr nucleophile. A sodium-binding loop with conserved main-chain coordination is necessary for proper positioning of all the components of the active site. Despite sequence homology and structural similarity to human and bacterial aspartylglucosaminidases, LIA and EcAIII are unable to hydrolyze glycosylated asparagine. Unexpectedly, the structure of the plant-type enzymes bears resemblance to threonine aspartase (taspase), which hydrolyzes the α-peptide bonds of two Asp-Gly peptides of MLL, a protein implicated in some human leukemias.