Endocrinology and Metabolism

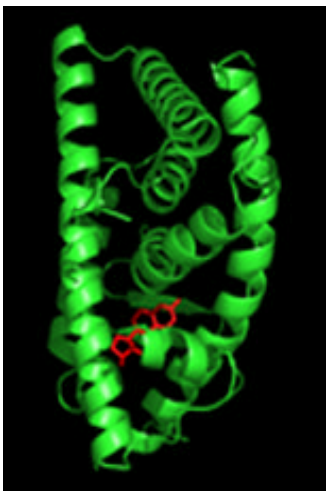
The physiological homeostasis of the individual is under influence by endogenous and exogenous factors. By controlling the interaction between various tissues, hormones govern most aspects of life. Hormonal and dietary factors act against the individual's specific genetic background, and may initiate and promote the development and progression of important clinical disease entities such as obesity, diabetes, dyslipidemia and hypertension, as well as dementia and malignancy.

At Karolinska Institutet there is a strong and longstanding interest in this research field. The studies of many research groups represent a broad level of competence in both basic and clinical aspects, and there is a particular emphasis on translational research. Researchers in the Network for Endocrinology and Metabolism collaborate in projects utilizing state-of-the-art techniques ranging from structural and molecular biology over in vitro and in vivo experiments to epidemiology and clinical trials. There is also a graduate curriculum with emphasis to integrate the knowledge from laboratory studies with clinical problems and drug development.

Several groups have highly competitive research programs relating to the control of energy generation and distribution, both at the subcellular level and in the whole organism. Regulation of hormone release, signalling pathways for hormones and nuclear receptors controlling intermediary metabolism, developmental and adaptive regulation of cellular organelles, and integrative physiology and pathophysiology of fluxes of important metabolites represent strong areas of research. The availability of well characterized patient series including biobanks as well as excellent competence in medical genetics makes the focus on human disease and its treatment particularly attractive.

Examples of important projects in this field include:

Endocrine function of adipose tissue
The endocrine and autocrine regulation of known and novel secretory proteins in adipocytes is studied, and their importance for adipocyte lipolysis in normal and pathological conditions (such as obesity, insulin resistance, diabetes and polycystic ovary syndrome) is explored. Genes associated with obesity are investigated by combining adipose tissue microarray with DNA studies in large case-control and family cohorts.



Estrogen receptor
Our understanding of estrogen signalling has undergone dramatic changes following the discovery of the second estrogen receptor (ERß). In many cases the actions of ERa and ERß oppose each other (yin/yang principle); for instance, ERa often stimulates proliferation whereas ERß is antiproliferative. Details of these mechanisms are currently being dissected in breast, prostate and colon tissues where estrogen signalling seems to play important roles in carcinogenesis. This research is particularly relevant since synthetic ERß agonists have been shown to kill human cancer cells from some of these tissues and to reduce the size of animal model tumors in these organs.

The molecular structure of ERß

Hormonal and genetic influence on cholesterol metabolism
The effects of hormones (growth hormone, thyroid hormone and sex steroids) on hepatic cholesterol and bile acid metabolism are studied using human and animal models. Based on advanced metabolic phenotype characterization, new forms of monogenic hyperlipidemias are identified by genome-wide screening of families. Novel forms of therapy based on stimulating reverse cholesterol transport are developed and tested in animals and humans.

Mechanisms of insulin secretion from isolated pancreatic beta-cells
Molecular mechanisms of regulation of insulin release from exocrine pancreatic beta-cells are studied with the aim to understand the etiology of type 2 diabetes. Techniques are developed to characterize the role of individual ion channels in relation to cell surface receptors and the exocytotic process for insulin.

Mitochondrial mutations and their influence on the ageing process
Mouse models are developed to study mitochondrial dysfunction and regulation of mtDNA expression and to evaluate their role in the ageing process. Biochemical mechanisms of mammalian mtDNA replication and potential mitochondrial side effects of nucleoside analogues are studied.

For more information on the Endocrinology projects, please contact:

Professor Bo Angelin, Department of Medicine, Clinical Department of Endocrinology, Metabolism & Diabetes,
Phone +46 8 585 823 44, +46 70 484 0115, or mail: bo.angelin@ki.se