Overall research theme:

Renal and cardiovascular regulation of salt and water balance in the normal condition, during development, and under pathological salt and water retaining conditions.

Latest update:

July 19, 2002

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Characteristics of the research group:

The group is characterised by using many different techniques to answer the questions. Basic techniques include isolation of RNA and DNA, cDNA cloning, sequencing, RT-PCR, Northern and Southern blotting, Rnase protection assays, Western, immunostainings, RIA, ELISA, electrophysiology, in vitro microperfusion, fluorescence measurements on living cells, servo-mechanisms for controlling body contents of water, salt and blood pressure. The models used include cell lines, primary cultures, fresh microdissected tissue, sampled human tissue, chronic animal models in metabolic cages, conscious dogs, rat, guinea pig and sheep fetal models, and finally the group do investigations on healthy volunteers and on patients.

Running projects: Titles and abstracts:

Renin-producing cells: differentiation and mechanisms of secretion

Renin is a hormone which is synthetized, stored and released from juxtaglomerular cells in the renal blood vessels. Renin is the main determinant of the activity of the Renin-Angiotensin-Aldosterone system, which is involved in the regulation of the blood pressure, the salt and water and the renal function. Renin is released when the organism lacks salt and when the blood pressure falls. Renin is probably involved in the pathogenesis of hypertension. By acute stimulation renin is released from pre-existing JG cells but during chronic stimulation new JG cells are recruited. We study the mechanisms that are involved in the acute cellular control of renin secretion, and the chronic processes involved in the transformation from vascular smooth muscle cell to renin-producing cell in the afferent arteriole.

Mechanisms of contraction in the renal afferent arterioles

The arterial blood pressure is regulated in an interaction between circulating vasoactive substances, salt excretion and the central nervous system. The kidney plays a central role in this regulation, both through release of renin (see above) and as the organ for controlled salt excretion. The renal afferent arterioles are central for regulation of renal blood flow and glomerular filtration, and changes in the

function and structure seems to play an important role in the pathophysiology of hypertension. We are currently studying the function, interaction and intracellular signalling pathways of different hormones and ion channels. Current investigations focus on voltage-dependent calcium channels, steroid hormones and nitric oxide.

Renal mechanisms of salt retention during liver cirrhosis and nephrotic syndrom
In certain conditions, such as liver cirrhosis, nephrotic syndrome and heart failure, a number of salt-retaining mechanisms are activated. We study the mechanisms involved in the activation of sodium retaining factors (renin-angiotensin-aldosterone system, prostaglandins, relevant ion channels) and mechanisms that decrease the effect of sodium excretory factors (ANP, NO). We use a combination of molecular techniques and functional studies on animalsl in vivo and in vitro. In addition we perform pharmacological intervention studies on humans.

The pathogenesis of development of hypertension after fetal growth restriction.
Epidemiological studies in humans have demonstrated a correlation between low birth weight and development of high blood pressure and diabetes mellitus. In this project we want to use a combination of molecular, morphological and functional investigations to elucidate the mechanisms that lead to increased blood pressure in adult animals after experimentally induced fetal growth restriction in the fetal stage in rat and guinea pig. The kidney development seem to be central for the effect of growth restriction on high blood pressure and we therefore focus on the development of the kidney and and cardiovascular system after birth with special emphasis on insulin-like growth factor (IGF), insulin-binding proteins and the renin-angiotensin-aldosterone system.

Boye Jensen and Peter Bie are sending separate descriptions. The publications do not include Peter Bies publications

Recent publications related to the projects described above:

1. UG Friis, BL Jensen, JK Aas and O Skøtt. Direct demonstration of exo- and endocytosis in single mouse juxtaglomerular cells ***Circ Res***, 84: 929-939, 1999
2. BL Jensen, B Mann, O Skøtt, A Kurtz.Differential regulation of renal prostaglandin receptor mRNA by dietary salt intake. ***Kidney Int*** 56: 528-537, 1999
3. Han VK, Carter AM, Chandarana S, Tanswell B, Thompson K. Ontogeny of expression of insulin-like growth factor (IGF) and IGF binding protein mRNAs in the guinea-pig placenta and uterus. ***Placenta***;20:361-377, 1999
4. Han VK, Carter AM. Spatial and temporal patterns of expression of messenger RNA for insulin-like growth factors and their binding proteins in the placenta of man and laboratory animals. ***Placenta*** 21:289-305, 2000
5. D Andreasen, BL Jensen, PB Hansen, T-H Kwon, S Nielsen, O Skøtt. The α_{1G} subunit of a voltage-dependent Ca^{2+} channel is localized to distal nephron and collecting tubules of the rat kidney ***Am J Physiol Renal Physiol*** 279: F997-F1005, 2000
6. PB Hansen, BL Jensen, D Andreasen, UG Friis, O Skøtt Vascular smooth muscle cells express the α_{1A} subunit of a P/Q-type voltage-dependent calcium channels and it is functionally important in renal afferent arterioles. ***Circ Res*** 87: 896–902, 2000
7. Praetorius J, Andreasen D, Jensen BL, Ainsworth MA, Friis UG, Johansen T. NHE1, NHE2, and NHE3 contribute to regulation of intracellular pH in murine duodenal epithelial cells. ***Am J Physiol Gastrointest Liver Physiol***. ;278:G197-G206. 2000
8. Hofbauer KH, Jensen BL, Kurtz A, Sandner P. Tissue hypoxygenation activates the adrenomedullin system in vivo. ***Am J Physiol Regul Integr Comp Physiol***. 278:R513-R519. 2000
9. Mann B, Hartner A, Jensen BL, Kammerl M, Kramer BK, Kurtz A. Furosemide stimulates macula densa cyclooxygenase-2 expression in rats. ***Kidney Int.*** 59:62-68. 2001
10. Mann B, Hartner A, Jensen BL, Hilgers KF, Hocherl K, Kramer BK, Kurtz A. Acute upregulation of COX-2 by renal artery stenosis. ***Am J Physiol Renal Physiol***.;280:F119-F125. 2001

11. Han VK, Carter AM. Control of growth and development of the feto-placental unit. ***Curr Opin Pharmacol***. 1:632-640, 2001
12. BL Jensen, J Stubbe, PB Hansen, D Andreasen, O Skøtt: Expression of Prostaglandin E_2 EP2 and EP4 receptors in the rat kidney. ***Am J Physiology Renal Physiol*** 280: F1001-F1009, 2001
13. PB Hansen, BL Jensen, D Andreasen, O Skøtt. Differential expression of T and L--type voltage-dependent calcium channels in renal resistance vessels ***Circ Res.*** 89: 630-638, 2001
14. R Brown, A Ollerstam, B Johansson, O Skøtt, S Gebré-Medhin, B Fredholm, AEG Persson. Abolished tubuloglomerular feedback and increased plasma renin in adenosine A1 receptor deficient mice ***Am J Physiol Regul Integr Comp Physiol*** 281:R1362-R1367, 2001
15. UG Friis, BL Jensen, S Sethi, D Andreasen, PB Hansen, O Skøtt Control of renin secretion from rat juxtaglomerular cells by cyclic AMP-specific phosphodiesterases ***Circ Res***. 90: 996-1003, 2002
16. HC Thiesson, O Skøtt, B Jespersen, OB Schaffalitzky de Muckadell. Inhibition of nitric oxide synthase with L-NMMA does not improve renal function in decompensated liver cirrhosis. ***Am J Gastroenterology*** (in press)