

Nobel Day Festivities at Biomedicin

10th of December 2009



Traditionally on 10th December, the anniversary of Alfred Nobel's death, is awarded the Nobel Prize in Physiology or Medicine. Biomedicine show attention to this day by organizing own research activities and festivities

Invitation and Programme



Place:

HSP1 (Lecture hall 1, Prisma House)
Örebro University

Organizing and Hosted by:


Biomedicine
Division of Clinical Medicine
School of Health and Medical
Sciences, Örebro University

Program Committee:

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ÖREBRO UNIVERSITY
SCHOOL OF HEALTH
AND MEDICAL SCIENCES

Time	PROGRAMME Thursday, 10 of December 2009 Lecture hall HSP1	Speaker
15.30-16.00	Set up time for Posters: Place: Main entrance hall 2 nd floor, Prisma House	
16.00-16.05	 Welcome	Allan Sirsjö Nikolaos Venizelos
16.00-17.00	Nobel Days Lecture: Fast food based hyper-alimentation induces insulin resistance but elevates muscle mass and HDL cholesterol	Fredrik H. Nystrom MD, PhD, professor, <i>Department of Medical and Health Sciences, Faculty of Health Sciences, University Hospital of Linköping</i>
17.00-17.15	Coffee Break	
17.15-17.30 17.30-17.45 17.45-18.00 18.00-18.15	PhD presentations: ➤ Role and expression of CYP26 in the vasculatur. ➤ Prevalence of HTLV ½-infection in Sweden. ➤ Loss of mitochondrial solute carrier SLC25A43- a common event in HER2 positive breast cancer. ➤ Phenotypical and functional characteristic of T cells in microscopic colitis.	Ali Ateia Elmabsout Kerstin Malm Breezy Paul Ashok Kumar Kumawat
18.15-19.15	Poster presentations:	See Abstracts list
19.15-	Nobel Days Dinner, Foyer Hall 2nd Floor Prisma House	See Menu

LIST OF PARTICIPANTS

Name	
Kerstin Malm	Shahida Hussain
Johanna Sundin	Johanna Lönn
Christina Karlsson	Berolla Sahdo
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Ashok Kumar Kumawat	Sten Wigren
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Anna Göthlin-Eremo	Allan Sirsjö
Ali Elmabsout	Nikolaos Venizelos
Christer Larsson	Kristina Elgbratt

LIST OF ABSTRACTS

POSTER 1

Interleukin-1beta inhibits tyrosine transport in fibroblasts from schizophrenic patients and healthy controls

J. Johansson, R. Vumma, N. Venizelos

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Objective: A repeated finding in schizophrenic patients is an aberrant tyrosine transport, shown in fibroblast cell model by our group and others. Altered levels of the pro-inflammatory cytokine interleukin-1beta (IL-1 β) are indicated in schizophrenic patients and IL-1 β has shown to have inhibitory effect on amino acid transport systems. Based on these findings, the aims of this study were to examine the effect of IL-1 β on tyrosine uptake in fibroblasts of schizophrenic patients and healthy controls and to study any difference in tyrosine uptake between patients and controls.

Method: Fibroblast cells were incubated with different concentrations (0.01 ng/ml to 10 ng/ml) of IL-1 β for different time periods (1 hour to 24 hours) to optimise the effect of IL-1 β on tyrosine uptake. The optimised conditions were used to study the difference in tyrosine uptake between patients and controls. Fibroblast cell lines from schizophrenic patients (n=10) and healthy controls (n=10) were treated with 5 ng/ml of IL-1 β for 6 hours. Fibroblasts untreated with IL-1 β were used as controls in all studies. Uptake of ¹⁴C (U)-L-tyrosine was measured using the cluster tray method.

Results: IL-1 β significantly inhibited the tyrosine uptake in fibroblasts from patients with schizophrenia by 43 % (p < 0.001) and healthy controls by 42 % (p < 0.001). The inhibition of tyrosine uptake by IL-1 β was abolished in the presence of IL-1 β receptor antagonist. No difference in uptake levels between fibroblasts of schizophrenic patients and controls was found.

Conclusions: This study demonstrated that the pro-inflammatory cytokine IL-1 β have a strong inhibitory effect on tyrosine transport systems, which indicates that increased levels of IL-1 β in schizophrenic patients can be a factor of importance in the availability of tyrosine. As tyrosine is the precursor for the monoamines dopamine and noradrenaline and since the brain is the only organ for which amino acid transport is limited, a limited transport of tyrosine caused by IL- β could lead to disturbances in dopamine and noradrenaline metabolism. Further studies are needed to elucidate the transport aberration and the significance of these findings.

POSTER 2

Prevalence of HTLV 1/2-infection in Sweden

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³*Department of Virology, Swedish Institute for Infectious Disease Control, Stockholm, Sweden*

Background and objective: Prevalence data on HTLV-1/2 in Sweden have not been updated since 1995 when mandatory screening of new blood donors was introduced. The seroprevalence among blood donors at that time was 0.2/10000. A few years earlier, a high prevalence of HTLV-2 was found in intravenous drug users (ivdus) in Stockholm, Sweden (3.4%). In 2003 mandatory screening of couples preparing for in vitro

fertilization (IVF) was initiated in Sweden. The objective of this study was to update information on seroprevalence of HTLV in these groups.

Methods: Serum samples from pregnant women in Örebro county, during the years 1995, 1998, 2000 and 2003 (n=11 997) were investigated for HTLV-1/2 antibodies. We also included 355 samples from anti-HCV positive individuals, representing a risk group for blood borne infections outside the greater urban areas. Serum samples from intravenous drug users in Stockholm, were also collected and analysed (n= 1079). Data from the mandatory HTLV-1/2 screening (2003-2006) on patients attending clinics for in-vitro fertilization were compiled, as well as data from new blood donors.

Results: Among 11 997 tested pregnant women, no anti-HTLV-1/2 positive individual was found. Eight of the 40 000 investigated IVF-patients were anti-HTLV-1/2 positive (2 HTLV-1, 1 HTLV-2, 5 untyped; seroprevalence 2.3 per 10 000). Of the anti-HCV – positive individuals (n=355) one sample was HTLV-1 – positive (28.2 per 10 000). During the years 1995-2007, 18 HTLV-positive new blood donors were found (16 HTLV-1, 2 HTLV-2), out of approximately 550 000 individuals tested (0.3 per 10 000). 37 of 1079 tested ivdus were screening reactive. Typing shows that a majority of these are HTLV-2.

Conclusion: The seroprevalence among Swedish IVF patients is ten times higher than among blood donors. This is comparable to a European seroprevalence study among pregnant women made in 2003, in seven countries. However, it cannot be ruled out that the IVF group includes individuals with a higher risk of acquiring STIs including HTLV, than the general population. Among known risk group persons, the seroprevalence was substantially higher than the other groups studied. HTLV-2 appears to still be prevalent among Swedish ivdus.

POSTER 3

Reduced expression of mitochondrial solute carrier SLC25A43 helps breast cancer cells escape apoptosis.

Marika Gabrielson, (PhD-student)

Hälsoakademin, Breast Cancer Research Group, Klinisk Forsknings Centrum,USÖ

During the past decade, the role of mitochondria as a key regulator of cell survival and apoptosis has become clearer. Alongside, the involvement of an altered energy metabolism in mitochondria of developing malignant cells is currently being argued as an addition to the list of cancer hallmarks. The solute carrier protein family 25 (SLC25) has 46 known members, and is involved in the transportation of molecules across the mitochondrial membrane. The transported molecules, such as ADP/ATP and CoA are crucial regulators of various essential functions within the cell. Little is known about SLC25A43. Here we present novel information revealing the involvement of SLC25 member A43 in regulating survival of normal and breast cancer cells *In Vitro*. We show that the SLC25A43 gene is expressed at a 14-fold lower concentration in the breast cancer BT474 cell line compared to normal MCF10A epithelial breast cells. In both cell types, the SLC25A43 gene expression increases over time corresponding to the proliferation rate of the cells. siRNA targeting SLC25A43 in MCF10A and BT474 cells resulted in a 91% and 82% mRNA reduction respectively. Inhibition of the gene also induced extensive necrosis in MCF10A cells, whereas no significant necrosis was observed in the cancer cells. We show here, for the first time, that the mitochondrial solute carrier gene SLC25A43 is involved in the growth and survival of normal breast epithelial cells. An extensively reduced expression of the gene in breast cancer cells BT474 along with continued growth upon gene silencing, indicates an alteration of the mitochondrial functions in the carcinogenic cells. Further investigations have to be conducted in order to identify the specific mechanisms regulated by SLC25A43, both in normal and cancer cells.

POSTER 4

CYP26B1 plays a major role in the regulation of all-*trans* retinoic acid metabolism in human aortic smooth muscle cells (AOSMCs).

Ali Ateia Elmabsout¹, Pauline Ajok Ocaya¹, Peder Stefan Olofsson², Hans Törmä³, Andreas Carl Gidlöf² and Allan Sirsjö¹

¹Division of Biomedicine, Department of Clinical medicine, Örebro University, Örebro, Sweden, ²Center for Molecular Medicine, Department of Anesthesiology and Intensive Care Medicine, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden, ³Department of Medical Sciences/Dermatology, Uppsala University, Uppsala, Sweden.

Aim: The cytochrome P450 enzymes of the CYP26 family are involved in the catabolism of the biologically active retinoid, all-*trans*-retinoic acid (atRA). Since it would be possible that an increased local CYP26 activity may reduce the effects of retinoids in vascular injury, we investigated the role of CYP26 in the regulation of atRA levels in human aortic smooth muscle cells (AOSMCs).

Methods: The expression of CYP26 was investigated in cultured AOSMC using real time PCR. The metabolism of atRA was analyzed by HPLC and R115866 or siRNA was used to suppress cyp26 activity/expression

Results: We found that AOSMCs expressed CYP26B1 constitutively and atRA exposure augmented CYP26B1 mRNA levels. Silencing of CYP26B1 gene expression or reduction of CYP26B1 enzymatic activity by using the inhibitor R115866 increased atRA mediated signalling and resulted in decreased cell proliferation. The CYP26 inhibitor also induced expression of atRA-responsive genes. Therefore, atRA-induced CYP26 expression accelerates atRA inactivation in AOSMCs, giving rise to an atRA-CYP26 feed-back loop. Inhibition of this loop with a CYP26 inhibitor increases retinoid signalling.

Conclusion: The results indicate that CYP26 inhibitors may be a therapeutic alternative to exogenous retinoid administration.

POSTER 5

STAPHYLOCOCCUS AUREUS TOXINER AKTIVERAR INFLAMMASOMEN I HUMANA NEUTROFILA GRANULOCYTER

Berolla Sahdo¹, Bo Söderquist² och Eva Särndahl¹

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Staphylococcus aureus är en välkänd patogen som kan orsaka allt från banala till livshotande blodförgiftning eller inflammation i hjärtats klaffar. Vi vet inte varför vissa personer drabbas av svåra infektioner med hög dödlighet, medan andra uppvisar lindriga sjukdomssymptom. En kombination av bakteriens sjukdomsframkallande faktorer och varje individs unika immunförsvar är det man idag tror avgör sjukdomens svårighetsgrad. En förståelse av kroppens mekanismer under en infektion är därför nödvändig för att i framtiden kunna hindra svåra bakteriella infektioner i synnerhet med det ökade hotet från antibiotika resistent bakterier. Kunskapen om den inflammatoriska processen vid infektioner har ökat genom upptäckten av intracellulära receptorer, Nod-like-receptors (NLR), som vid aktivering av bl a komponenter från bakterier bildar multi-proteinkomplex som kallas inflammasomer. Inflammasomen

aktiverar caspase-1 som i sin tur klyver prointerleukin-1 β (proIL-1 β) till sin aktiva form. IL-1 β är kroppens mest potenta pro-inflammatoriska cytokin och ger upphov till feber och leukocytos.

Staphylococcus aureus producerar ett stort antal toxiner och enzymer som tros vara orsaken till det breda spektrum av olika infektioner denna bakterie orsakar. Denna studie undersöker två olika toxiner (α -toxin och PVL-toxin). α -toxin och PVL bildar porer i cellerna, men man vet inte vilka mekanismer som ligger bakom ett påverkat inflammatoriskt svar.

Aktivt caspase-1 detekteras i humana neutrofila granulocyter med hjälp av FLICA som är en fluorescentmärkt inhibitor vilket analyseras via flödescytometri. Preliminära resultat visar att bakteriestammar som producerar stor mängd av α -toxin respektive PVL-toxin ger en aktivering av caspase-1. Dessa resultat indikerar att *S. aureus* aktiverar ett inflammatoriskt svar genom att de por-formande toxinerna aktiverar inflammasomer.

POSTER 6

Wwox expression in breast cancer tissue from patients treated with or without tamoxifen

Anna Göthlin-Eremo, Pia Palmebäck Wegman, Sten Wingren

Hälsoakademin, Breast Cancer Research Group, Klinisk Forsknings Centrum,USÖ

Background: A positive estrogen (ER) and progesterone (PgR) status is regarded as a good indicator for outcome of breast cancer considering that these tumors are candidates for endocrine therapy such as tamoxifen. Unfortunately close to 30 % fail to respond and 40 % of initial responders develop resistance towards tamoxifen. Reliable markers for treatment outcome are yet to be discovered which is of substantial clinical relevance given that resistant patients are in risk of relapse from disease. The gene coding for the WW domain-containing oxidoreductase protein (WWOX, FOR) is located at a genomic fragile site (FRA16D) where loss of heterozygosity and hypermethylation, resulting in WWOX inactivation, has been reported in several types of cancer. Wwox participates in cellular processes such as growth, apoptosis and tumor suppression (Del Mare et al 2009). Reduced or absent expression of Wwox is associated with tamoxifen resistance and ER status in breast cancer according to a study by Guler et al (2007). Also, Wwox seem to have an important, but still left to be fully elucidated, role in hormonally influenced tissue and can interact with several proteins of interest such as p53 and HER4.

Objective: In our study, we aimed to investigate the relationship between Wwox and outcome of breast cancer in breast tissue from patients randomized to treatment or no treatment with tamoxifen.

Method: We used immunohistochemistry on tissue micro arrays (TMA) from paraffin-embedded breast material from 912 cancer patients. The results were evaluated in a microscope.

Preliminary results: Patients treated with tamoxifen who had a moderate/high cytoplasmic staining of Wwox had a significantly ($p=0,01$) improved recurrence free survival compared to those with a weak or negative staining. For untreated patients there was no difference in outcome depending on grade of staining ($p=0,56$). Tamoxifen treated patients with Wwox signal in nuclei had a greatly improved survival ($p=0,002$) compared to patients without nuclear staining. In patients with no tamoxifen treatment, there was no difference in survival regarding nuclear staining of Wwox ($p=0,67$).

Conclusion: As suggested, Wwox seem to play a role in the cellular response to tamoxifen and possibly resistance mechanisms. Preliminary results show that higher Wwox expression is correlated to a better survival in tamoxifen treated breast cancer patients. Future studies will hopefully give more insights of the importance of Wwox in breast cancer.

POSTER 7

Phenotypical and functional characteristics of T cells in Microscopic Colitis

Ashok Kumar Kumawat

DEPARTMENT OF CLINICAL MEDICINE, SCHOOL OF HEALTH AND MEDICAL SCIENCES, ÖREBRO UNIVERSITY

Background

The intestinal immune system, which is the largest and most complex immune compartment of the entire body, plays a major role by responding to harmful pathogens while tolerating dietary antigens and beneficial bacteria. It employs several strategies to maintain its' homeostatic balance. Dysregulated immune responses in the intestine can lead to chronic inflammatory diseases such as inflammatory bowel disease (IBD), [comprising Crohn's disease (CD) and Ulcerative colitis (UC)], and microscopic colitis (MC). MC is a more recently discovered form of colonic inflammation previously regarded rare, but with an incidence roughly the same as for UC. The name originates from the fact that the colonic mucosa is macroscopically normal whereas microscopic examination of biopsies reveals distinct histopathology. MC comprises two conditions, collagenous colitis (CC) and lymphocytic colitis (LC). Both diseases present increased densities of lymphocytes and plasma cells in the mucosa, whereas CC also has a thickened subepithelial collagen band. MC tends to affect the middle-aged population, the peak incidence is around 60-65 yr of age and the majority of them are women, often associated with other autoimmune disorders such as celiac disease, thyroid disorder, diabetes and arthritis. The prevalence of MC is 4-5% in general population and 7-14% in the elderly population. MC is multifactorial and mostly unknown. The overall goal of this project is to investigate the role of immunoregulatory dysfunctions in the gastrointestinal mucosa in the etiology and pathogenesis of MC.

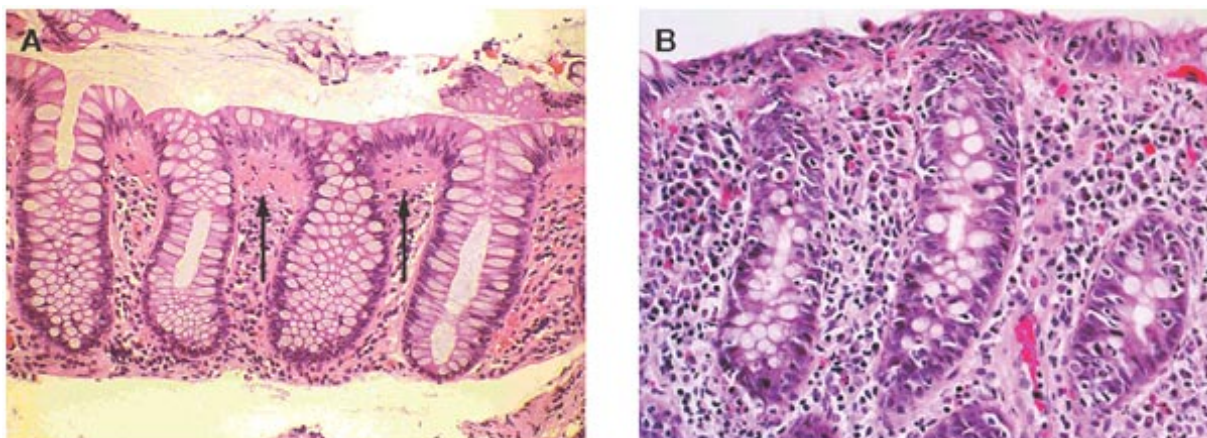


Figure 1. Microscopic colitis.

Nielsen O H *et al.* (2008), *Nat Clin Pract Gastroenterol Hepatol*

(A) Photomicrograph of colonic mucosa with collagenous colitis. A thickened layer of collagen is formed beneath the surface epithelium (arrows). Tenascin is incorporated into the collagen, which can be used to distinguish this layer from the normal basement membrane (hematoxylin and eosin stain, magnification $\times 200$). (B) Photomicrograph of lymphocytic colitis showing the inflamed colonic mucosa infiltrated with considerable numbers of cytotoxic lymphocytes in the epithelium. In this case, more than 40% of the cells in the epithelial layer are lymphocytes. The leukocytes infiltrating the lamina propria include a mixture of lymphocytes, plasma cells, macrophages, eosinophilic granulocytes, and, occasionally neutrophils (hematoxylin and eosin stain, magnification $\times 200$).

Material

Biopsies from MC and IBD patients as well as from healthy individuals are being provided by colleagues at the Dept of Gastroenterology, Örebro University Hospital, Örebro. As IBD is well characterized at the pathophysiological level, these patients will be used as positive controls.

Research Plan

We are performing a detailed flow cytometric characterization of the intraepithelial lymphocytes (IELs) and lamina propria lymphocytes (LPLs) isolated from mucosal biopsies from MC and IBD patients.

We will also perform an initial screening of a large number of immune related genes using gene PCR array analysis on the biopsies. Following the phenotypic delineation, the isolated lymphocytes will be activated with monoclonal antibodies (anti-CD3, 2, 28) and will be investigated for cytokine production using the Luminex or ELISA.

Based on the flow cytometric and RT-PCR results, we will perform immunohistochemistry of key markers on mucosal biopsies collected from MC patients. With these studies we hope to shed further light on pathophysiology of MC. Significantly, new avenues for immune based differential diagnosis and treatment of MC will be opened.

POSTER 8

STEROID HORMONE RECEPTORS IN NON-SMALL CELL LUNG CARCINOMAS

Christina Karlsson¹, Oswaldo Fernandes² & Mats G Karlsson^{1,3}.

School of Health and Medical Sciences¹, Örebro University and Depts of Thoracic surgery² and Pathology³, Örebro University Hospital, Sweden.

Background

Steroid hormone receptors have been studied in non-small cell lung carcinomas (NSCLC) in the perspective of gender-associated differences in tumour types and prognosis. During recent years receptor subtypes for both oestrogen (ER α /ER β) and progesterone (PRA/PRB) have been identified and conflicting results concerning their expression have been reported.

Methods

A consecutive material of 270 NSCLC surgically treated at Örebro University hospital between 1990 and 1995 has been studied. The tumours consisted of 126 squamous cell carcinomas (SCC), 140 adenocarcinomas (ADCA), 3 adenosquamous carcinomas and one large cell carcinoma. 172 of the patients were males and 98 females. Immunohistochemistry was performed, including heat epitope antigen retrieval, with monoclonal antibodies to ER α , ER β , PRA and PRB using Envision® visualization procedure. Nuclear positivity was scored positive when > 10% of tumours cells were stained.

Results

ER α expression was focally present in 4 adenocarcinomas.

ER β was present in 63 tumours. ER β expression was more frequent in SCC, 29%, then in adenocarcinomas, 19%, $p=0.04$ (Pearson χ^2 -test).

The differences between histological types could be seen in the male group ($p=0.03$) while it failed to reach statistical significance amongst women. Overall, female tumours were ER β positive in 28% whilst male tumours in 21%, (ns, χ^2 -test). There was no difference concerning mean age between ER β groups in either gender.

None of the tumours expressed PRA or PRB.

Discussion

Taking our and previously published data into consideration, discrepancies in ER α expressions seems to be antibody dependent. Our data supports that only a very small fraction of NSCLC expresses ER α . The absence of PR expression is in concordance with the absence of functional ER α signalling.

ER β expression occurs frequently with a slight predominance in SCC compared to ADCA, without influence of gender. Whether ER β mediated effects occurs in NSCLC remains to be studied.

POSTER 9

Loss of mitochondrial solute carrier SLC25A43- a common event in HER2 positive breast cancer

Breezy Malakkaran,

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Mitochondria have been traditionally considered as the “Powerhouse” of the cell. In 1926, Otto Warburg observed that cancer cells depend on aerobic glycolysis instead of oxidative phosphorylation for ATP and suggested aberrant mitochondria as a key factor in carcinogenesis. Since then this role of mitochondria is being explored.

Deletion of SLC25A43 (a mitochondrial solute carrier), was discovered in 80% (20 of 25) of HER 2 positive breast cancer (BCA) cases by whole genome SNP array (Affymetrix GeneChip Human Mapping 250K[®] Nsp1). LOH (loss of heterozygosity) analysis using ABI 3130xl Genetic Analyzer revealed that 45% (5 of 11) harboured allelic imbalance (AI). Similar result was also found in a larger cohort of HER2 positive BCA (51%, 14/27), HER2 negative BCA (13%, 3 of 22), cervical cancer (46%, 12 of 26) and lung cancer (23%, 3 of 13). Mutation analysis on all 6 exons of SLC25A43 gene by SSCP (Single-strand Conformation Polymorphism) and Sanger chain termination DNA sequencing, revealed a single mutation in exon 1 in one of the cases.

The mitochondrial solute carriers (SLC) are almost always localized in the inner mitochondrial membrane and provide a link between cytosol and mitochondria. SLC 25A43 belongs to SLC 25 family of 46 members that carry molecules like ATP/ADP, aminoacids, other metabolic intermediates and uncoupling proteins (UCP). Energy intermediates ultimately run the electron transport chain (ETC) and produce ATP, while UCP decouple ETC and release energy in the form of heat instead. Since SLC25A16, the closest kin of SLC25A43 (29% aminoacid homology with SLC25A43) carry CoA, we believe that SLC25A43 is also involved in carrying energy intermediates. LOH in this gene would therefore lead to impaired oxidative phosphorylation and thus will force the cell to rely on aerobic glycolysis for its energy needs. This dependence on aerobic glycolysis for energy instead of oxidative phosphorylation is one of the early events in cancer. Thus, these preliminary results suggest that dysfunctional SLC25A43 by LOH or mutation could be an early event in a tumor cell's switch from oxidative phosphorylation to aerobic glycolysis.

POSTER 10

Hepatocyte growth factor: En biokemisk markör vid krans-kärlsförträngning och parodontit?

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¹ PEAS Institut AB, Linköping, ² Avd. f. Klinisk Medicin, Örebro Universitet, ³ Avd. f. Läke-medelsforskning, Linköpings Universitet, ⁴ Centrum för Oral Rehabilitering, Linköping, ⁵ Avd. f. Klinisk Fysiologi, Kalmar Länssjukhus, ⁶ Avd. f. Cardiologi, Linköpings Universitetssjukhus.

Bakgrund

Ett flertal studier visar en ökad prevalens av krans-kärlsjukdom hos patienter med parodontit. Hepatocyte growth factor (HGF) är en endogen, antiinflammatorisk och angiogenetisk faktor som är viktig vid läkning. Höga HGF-nivåer har associerats med hjärt-kärlsjukdom, och även parodontit. Trots höga HGF-nivåer kan

den biologiska aktiviteten vara reducerad, möjligen på grund av proteasaktivitet från parodontala bakterier (t.ex. *Porphyromonas gingivalis*) och/eller av världens immunförsvar.

Projektet syftar till att analysera serumkoncentration och biologisk aktivitet av HGF hos patienter med kranskärslssjukdom, samt studera koppling till parodontalt status och närvaro av *P. gingivalis* i tandficka.

Metod

Serumprover från 46 patienter med kranskärlsförträngning analyserades före samt vid 4 tillfällen upp till 12 månader efter enbart angiografi eller efter ingrepp (ballongvidgning eller bypass-operation). Parodontalt status undersöktes och klassificerades i 3 grupper och förekomst av *P. gingivalis* i tandficka detekterades med PCR.

Serumnivåer av HGF mättes med ELISA och biologisk aktivitet analyserades med SPR (Biacore). Serum från 53 friska givare användes som kontroll.

Resultat

Den biologiska aktiviteten hos HGF var lägre hos kranskärslsjuka jämfört med friska ($p=0.038$), och minskade ytterligare 24 timmar efter ingrepp.

Aktiviteten var som högst efter 1 månad ($p=0.003$ vs. 24 tim, $p=0.015$ vs. 12 mån), och minskade till nästan samma nivå som förprovet efter 12 månader.

HGF-nivåerna var konstant högre hos patienterna vid alla provtagningstillfällen jämfört med friska ($p<0.0001$).

Patienter positiva för *P. gingivalis* och patienter med grav parodontit visade något minskad HGF-aktivitet, men inga skillnader i koncentration.

Sammanfattning

Höga cirkulerande HGF-nivåer hos patienter med kranskärslssjukdom är en markör för arterotrombotiska händelser. Vi har påvisat höga men oförändrade HGF-nivåer upp till ett år efter ingrepp. Däremot medföljde den inflammatoriska reaktionen hos patienterna en nedsatt biologisk aktivitet av HGF som nådde högsta nivå 1 månad efter ingrepp men sjönk tillbaka till grundnivån efter 12 månader. Detta kan vara av betydelse vid kärlnybildning och återhämtningförmåga.

Studier pågår för att vidare undersöka detta fynd samt koppling till parodontit och betydelsen av *P. gingivalis* vid utveckling av hjärt-kärlsjukdom.

POSTER 11

Microbe-Gut Interaction in Microscopic Colitis and Post-Infectious Irritable Bowel Syndrome (IBS)

Johanna Sundin

DEPT OF MEDICINE, SCHOOL OF HEALTH AND MEDICAL SCIENCES, ÖREBRO UNIVERSITY

Patients with microscopic colitis or post-infectious IBS (approximately 25% of all IBS affected) have on a histological level, a subtle to mild inflammation in mucosa. However, it is thought that it is not only the presence of pathogenic microbes that lead to illnesses, but there is also unknown changes in the colon that are necessary for disease progression and phenotype. Pathophysiology as well as individual susceptibility is unclear.

The intestinal microbiota together with nutrients in the intestinal lumen determine both the quantitative and qualitative composition of the gut and the interaction with the intestinal mucosa. This system is very dynamic, as food antigens and the natural intestinal flora must be tolerated by the immune system but at the same time be ready to react to invading pathogens. If the regulation of these immune responses is dysfunctional, this can lead to chronic inflammation in the gastrointestinal tract. The immune functions of the mucosa are closely linked to afferent sensory signals in a two-way signalling between the gut and the brain.

Earlier evidence indicates that psychological stress may be related to an increased severity of immune and inflammatory responses as well as being a major part of the origin and development of IBS and microscopic colitis.

For these reasons this project aims to systematically describe the pathophysiological link between the environment in the colons lumen (mainly inhabited by bacteria), immune response and activation of the enteric nervous system (ENS) in patients with microscopic colitis and post-infectious IBS.

Research on three cohorts, one with IBS patient, one with microscopic colitis patients and the last with healthy controls will achieve this. Biopsies and blood samples will be collected from the participants. Evaluation of the composition, function and microbial stability will be achieved by an array method (HIT-Chip Technology) where the normal flora in the gut is used to determine differences in bacterial strains between the cohorts. Characterization of the mucosal lymphocytes will be accomplished by isolation of T lymphocytes from mucosa that will be analyzed by flow cytometry. Relative mRNA variations between samples will be measured by microarrays. Analyse of cytokine production will be realized by the Luminex™ system. We will evaluate visceral sensitivity/perception on patients that will answer questions about complaints and also pain symptoms with the barostat procedure. Ex-vivo stress challenge of mucosal samples will be tested in Ussing Chambers where stressors can be added ex-vivo and thereafter we can measure short circuit current as an indicator of ion transport over an epithelium.

The aim of this project is to systematically describe the pathophysiological link between the environment in the colon lumen (mainly contingent by bacteria), immune response and activation of the ENS in patients with microscopic colitis and post-infectious IBS.

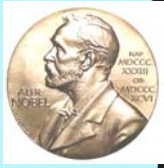
POSTER 12

Occurrence of ENaC subunits in airway epithelial cell lines and nasal epithelia

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The epithelial sodium channel (ENaC) gene encodes sodium channels that mediate Na^+ transport in epithelia and are essential for sodium and water homeostasis. The channel is expressed in a variety of epithelial-lined organs and has a recognized functional importance in the kidney, colon, sweat duct, and lung. An imbalance in the epithelial transport of Na^+ in the airways leads to disturbances in airway surface liquid volume (ASL). ASL depletion and airway flooding have serious consequences. To assess the occurrence, and to analyse the mRNA levels of α -, β -, and γ -ENaC subunits in cystic fibrosis (CF) and non-CF airway epithelial cells, we carried out a relative quantitative analysis of these subunits by a real time-polymerase chain reaction (RT-PCR) assay specific for each subunit, using two human respiratory epithelial-cell lines, and nasal epithelial cells (biopsy) obtained by bursh. We found about the same expression levels of α -subunits, an increase in the mRNA levels of β -subunit and a decrease in the mRNA levels of γ -subunit in CF cells when compared with normal cells. The expression level of ENaC subunits found in nasal biopsies were $\alpha > \beta > \gamma$. Whether these differences in mRNA levels result in differences in protein levels remains to be investigated. Our finding of an increased in the mRNA level of the β -subunit in CF-cells is of interest in view of an animal model for CF disease based on overexpression of the β -ENaC subunit in transgenic mice.



Menu Nobel Days Dinner

- ◆ Rostbiff på ruccola toppad med jungfruolivolja, balsamico samt hyvlad parmesan.
- ◆ Sallad på små saftiga tomater, cocktailmozzarella, borretanalök och riven basilika samt oregano.
- ◆ Frittata med zucchini, paprika och parmesanost.
- ◆ Pestomarinerade gröna musslor toppad med citronolivolja.
- ◆ Grillad/stekt kycklingklubba
- ◆ Italienska charkuterier som salami Milano och prosciutto.
- ◆ Mustig jordärtskocksoppa kryddad med fänkål och apelsin.
- ◆ Italienskt bondbröd med tapenade.
- ◆ Italienskt rödvin (Paxa Lazio Rosso) alternativt alkoholfritt alternativ

