JÄSENKIRJE 4/2011
ABSTRAKTILEHTI

SUOMEN REUMATOLOGINEN YHDISTYS
REUMATOLOGISK FÖRENING I FINLAND - THE FINNISH SOCIETY FOR RHEUMATOLOGY

MUUTTUVATKO YHTEYSTIETOSI?
ILMOITATHAN MUUTOKSISTA!

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Vain sähköpostitse kirjeensä haluavat, ilmoittathan osoitteenne (myös muutokset) Pialle tai Maijulle: maiju.kivisto@helsinki.fi Kiitos!

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KOKOUS- ja KOULUTUSTAPAHTUMIA 2012-13

26.-27.1.12	**SRY vuosikokous, Turku**
1.3.2012	**Advances in Rheumatology, Helsinki**
26.-27.4.2012	**Nivelten uä-tutkimus / jatkokurssi, Helsinki Meilahden Kolmiosairaala**
10.-11.5.12	**SRY kevätkokous, Lahti/Vierumäki, yhteiskokous reumaortopedien kanssa**
6.-9.6.12	**EULAR Berliini, Saksa**
5.-8.9.12	**SCAND Kööpenhamina, Tanska**
9.-13.11.12	**ACR Washington, USA**
24.- 25.1.13	**SRY vuosikokous, Kuopio**

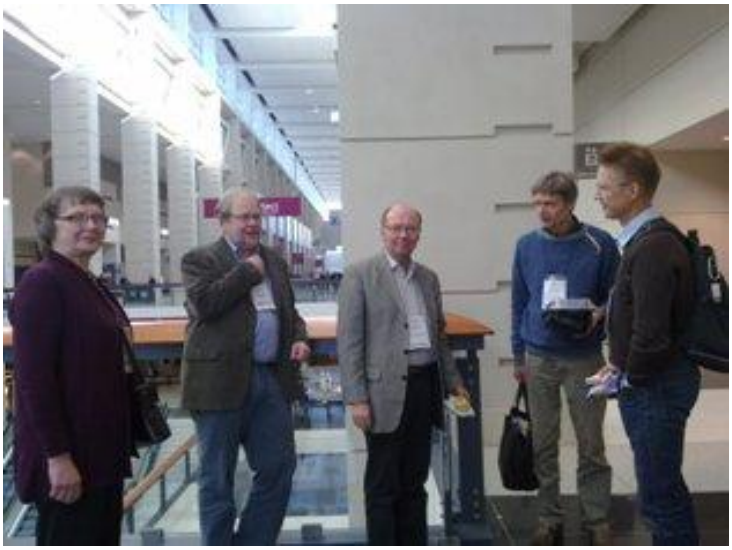
Puheenjohtajalta:

Kävimme Chicagossa päivittämässä tietojamme kertauskurssilla mm. SLE:n keskushermostomanifestaatioista, suurten suonten vaskuliiteista, perifeerisistä neuropatioista, reumatautien silmäilmentymistä, kroonisesta kivusta, entesopatioista ja immuunipuolustuksesta. Varsinaisessa kokouksessa oli tarjolla runsaasti tietoa immuunijärjestelmän eri osien toimintamekanismeista ja merkityksestä. Viime vuosien havainnot ovat nostaneet luontaisen immuniteetin tutkimuksen edistymisen kiinnostavaksi seurattavaksi.

Kokouksessa oli esillä uusia kuvantamistapoja. Nivelten ultraäänitutkimukset ovat tulossa myös yhdysvaltaisten reumatologien praktiikkaan. On myös kannettu runsaasti huolta uusien lääkehoitojen pitkäaikaisesta turvallisuudesta, mutta biologisten lääkkeiden käytön yhteydessä ei ole näyttöä kiinteiden kasvainten lisääntymisestä sisäelimissä. Ihosyöpien osalta seuranta jatkuu.

Kokouksessa esitettiin myös mahdollisuuksia lopettaa hyvin mennyt lääkitys mielestäni aika vaatimattomin tuloksin. Esityksissä kävi myös ilmi, että potilaan BMI vaikuttaa TNFα-vasta-aineita saavien potilaiden hoitovasteeseen. Tulehdusreaktion immunologiaa käsiteltiin eri näkökulmista. Uudet lääkkeet, pienet molekyylit JAK- ja SYK-kinaasien estäjät, olivat toistuvasti esillä. Pisimmällä olevia valmisteita on testattu jo faasi III kokeissa. Niillä saadut hoitovasteet vastaavat biologisilla lääkkeillä saatuja vasteita. Turvallisuustietoja seurataan kiinnostuneina, koska näiden entsyymien kautta signaalin välitystä tapahtuu muissakin kudoksissa kuin immunologisiin reaktioihin osallistuvissa soluissa.

Kihdin lisääntyminen ja hoito tuottaa ongelmia kaikkialla, missä väestö pulskistuu ja vanhenee. Uusia hoitokeinoja haetaan. Liikunnan ja ruokavalio-ohjauksen merkitystä nivelrikon hoidossa oli ansiokkaasti tutkittu ja todettu molempien olevan tärkeitä tuloksiin pyrittäessä, mutta ruokavalio-ohjauksen olevan merkittävämpi painon pudotuksen kannalta.



Huomattava osa reumatologijoukostamme on lähivuosina siirtymässä senioriteettiin. Eläköitymisjuhlat ovat työn ja työntekijän juhlia. Monesti niissä tulee esille se valtava työn määrä, jonka muutamat kollegat ovat työvuosinaan tehneet. Monet reumatologeistamme ovat perustaneet keskussairaaloihimme reumatologiset yksiköt ja hoitaneet niitä 20 - 30 vuoden ajan, suuren osan ajasta yksin. Onneksi jotkut nuoremmat kollegat ovat kuitenkin innostuneet alasta ja kouluttautuneet seuraajiksi. Heitä ei kuitenkaan ole riittävästi. Toivottavasta onnistunut rekry-kampanjamme tuottaa konkreettista tulosta! Työ tekijäänsä kiittää vanhan sananparren mukaan ja sen aistii työtä tehnytkin. Potilailta saatu arvostus tulee esiin monissa hoitokontakteissa. Kollegojen arvostus osaltaan on myös kiitos, jota niukasti sanallisesti arjessa toisillemme jakelemme. Onneksi edes juhlatilanteissa sekin tulee sanotuksi!

Reumatologisen yhdistyksen historiikkia pitäisi jälleen päivittää. Toivoisin, että eri puolilla maatamme työskennelleet kollegat kirjoittaisivat oman alueensa reumatautien hoidon kehityksestä ajalta, jonka muistavat tai johon löytyy paikkakunnalta kirjallista materiaalia. Niistä saisimme kootuksi historiikkia, kun vajaan viiden vuoden kuluttua tulee kuluneeksi 70 vuotta yhdistyksemme perustamisesta. Edellisten juhlien aikana Lordi voitti euroviisut. Tulevasta emme tiedä, mutta ehkäpä jotain jännittävää tapahtuu reumatologian kentällä.

Tulevaan vuosikokoukseen valmistaudumme odottavin mielin. Esille tulee mielenkiintoisia raportteja. Kliinisen työn kuorma vähentää jäsenistön mahdollisuuksia käyttää aikaansa tutkimustyöhön. Oman työn tuloksia kannattaa kuitenkin jakaa myös muille. Huomioikaa muutokset vuosikokouksen aikataulussa. ALOITAMME PERINTEISESTÄ OHJELMARUNGOSTA POIKETEN VUODEN REUMALUENNOLLA. Muistakaa ilmoittautuminen tulevaan kokoukseemme! Sihteerimme kaipaa myös sähköpostiosoitteiden päivitystä. Kirjeessämme on bittiavaruudesta pelastettua kuvitusta syyskokouksestamme. Talouden epävarmuudesta huolimatta kevätkaudelle on luvassa sekä tutkimus- että koulutusapurahoja!

Hyvän tulevan vuoden toivotuksin
Oili K-S

SRY:n vuosikokous Turussa 26-27.1.12.

KOKOUSINFO JA ILMOITTAUTUMINEN

Suomen Reumatologisen Yhdistyksen vuosikokous järjestetään 25-27.1.2012 Turussa. Kokouspaikkana Radisson Blu Marina Palace (Linnankatu 32), jossa myös illallinen, majoitukset ja satelliittisymposiumit Pfizer 25.1, Lilly 26.1, ja MSD 27.1.
Ilmoittautumiset 9.1 mennessä SRY:n tapahtumakalenterin kautta tai internetosoitteeseen www.josmir.fi/ilmoittautuminen. Ilmoittautumislomakkeen voi myös lähettää osoitteeseen Johanna Reinikainen / Josmir Oy, Imppalanmäki 1, 04200 Kerava.
Majoitukset Radisson Blu hotellissa:
Majoitusvaraukset Josmir Oy:n kautta ilmoittautumisen yhteydessä. Huonehinnat: 1hh/97€/vrk ja 2hh/117€/vrk. Kukin vastaa majoituskuluista itse.
(Huom! Pfizer kustantaa satelliittisymposiumiinsa osallistuvien majoituksen 25-26.1. väliseltä yöltä Radisson Blu Marina Palace hotellissa)
Osallistumismaksut: Ei osallistumismaksua. Kokous on tarkoitettu Suomen Reumatologisen yhdistyksen jäsenille ja reumatologiaan perehtyville ja erikoistuville lääkäreille.
Lisätietoja SRY:n syyskokouksesta antaa SRY:n puheenjohtaja Oili Kaipiainen-Seppänen, oili.kaipiainen-seppanen@kuh.fi tai puh. +35844 717 2555.
Järjestelyihin ja näyttelyyn liittyvissä kysymyksissä ota yhteyttä Josmir Oy / Johanna Reinikainen, johanna.reinikainen(a)josmir.fi tai puh. +35840 768 4537.

ILMOITTAUTUMINEN (pakollinen kenttä*)
Sukunimi*: _____
Etunimi*: _____
Kotiosoite: _____
Puhelin: _____
Sähköposti*: _____
Toimipaikka*: _____
Osallistun torstaina 26.1.2012
- lounaalle _____
- SRY:n syyskokouksen 1. kokouspäivään _____
- SRY illalliselle klo 19.00 _____

Osallistun perjantaina 27.1.2012
- SRY syyskokouksen 2. kokouspäivään _____
- Lounaalle (huom! Niille, jotka eivät osallistu MSD:n lounassymposiumiin) ___

Erikoisruokavalio (ei/kyllä, mitä)? _____
Haluan osallistumistodistuksen _____
Olen SRY:n jäsen _____
Muuta: _____

SRY:n vuosikokous Turussa 26. - 27.1.2012

(Satelliittisymposiumit vuosikokouksen yhteydessä: Terveystalous moduuli III, Pfizer, ke 25.1.12 klo 17-20.00)

OHJELMA TORSTAINA 26.1.2012

klo 9-11.00	Satelliittisymposium - Osteoporoosi – GIOP, Lilly
11.00 – 12.00	LOUNAS
12.00 – 12.05	Vuosiokouksen avaus, dos Oili Kaipiainen-Seppänen

12.05 – 12.35 VUODEN REUMALUENTO

Minisymposium – Osteoporoosi

	pj prof. Timo Möttönen
12.35 – 13.10	Osteoporoosi lääkkeiden vaikutus luun aineenvaihduntaan, LT Riku Kiviranta, Turun yliopisto
13.10 – 13.45	GIOP. prof. Timo Möttönen, TYKS
13.45 – 14.20	Murtumien esto osteoporoosihoidolla: onnistuuko myös käytännössä? prof. Hannu Aro, TYKS
14.20 – 14.55	D-vitamiini ja kalsium, LT Marja Lehtonen-Veromaa, Lääkärikeskus Pulssi
14.55 – 15.30	KAHVI JA NÄYTTELYYN TUTUSTUMINEN
ABSTRAKTEJA I	pj dos Dan Nordström
15.30 – 16.00	Abstrakteja (kesto 10 min sisältäen keskustelun, 3 kpl)
16.00 – 16.10	SRRF:n apurahan 2011 jakaminen, pj. Oili K-S
16.10 – 16.20	Tauko
16.20 – 17.20	Yhdistyksen vuosikokous
19.00 –	ILLALLINEN

OHJELMA PERJANTAINA 27.1.2012

ABSTRAKTEJA II	pj LT Timo Yli-Kerttula
8.30 – 10.00	Abstrakteja (kesto 10 min sisältäen keskustelun, 9 kpl)
10.00 – 10.30	KAHVI JA NÄYTTELYYN TUTUSTUMINEN
ABSTRAKTEJA III	pj LT Heidi Mäkinen
10.30 – 11.20	Abstrakteja (kesto 10 min sisältäen keskustelun 8 pl)
11.20-11.50	Tutkimus- ja väitöskirja-apuraharaportteja
AJANKOHTAISTA	*pj dos Oili Kaipiainen-Seppänen*
11.50 – 12.20	Ajankohtaisia teemoja
12.20 -	Uuden hallituksen kokous
12.30 -14.00	Satelliitti- MSD – Spondylartriitit

1. CORRELATION OF [^{18}F]FDG PET ASSESSMENTS WITH DISEASE ACTIVITY AND MARKERS OF INFLAMMATION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS FOLLOWING INITIATION OF TRIPLE COMBINATION ORAL ANTIRHEUMATIC THERAPY

Roivainen A[1], Hautaniemi S[1], Möttönen T[2], Nuutila P[1,2], Oikonen V[1], Parkkola R[3], Pricop L[4], Ress R[4], Seneca N[5], Seppänen M[1], Yli-Kerttula T[2]. [1]Turku PET Centre, [2]Department of Internal Medicine, [3]Department of Radiology, Turku University Hospital, Turku, Finland, [4]Hoffmann-La Roche Inc, Nutley, NJ, USA, [5]Hoffmann-La Roche Ltd., Basel, Switzerland.

2. THE EFFECT OF BIOLOGIC DRUGS ON JOINT REPLACEMENT SURGERY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A REGISTRY STUDY

Kalle Aaltonen[1], Liisa Virkki[1], Esa Jämsen[2,3], Tuulikki Sokka-Isler[4], Yrjö T. Konttinen[1,2], Peltomaa Ritva[5], Tuompo Riitta[5], Yli-Kerttula Timo[6], Lähteenmäki Jukka[7], Kortelainen Saara[8], Ahokas-Tuohinto Pirkko[9], Marja Blom[1], Dan C.E. Nordström[5]. [1]University of Helsinki; [2]Coxa, Hospital for Joint replacement, Tampere; [3]Tampere University Hospital; [4]Central Finland Central Hospital; [5]Helsinki University Central Hospital; [6]Rauma Regional Hospital; [7]North Karelia Central Hospital; [8]Turku University Hospital; [9]Raahe Hospital

Objectives: The aim was to evaluate the effect of biologic drugs on the need for joint replacement surgery during follow-up or the survival of implanted endoprostheses during or prior to follow-up in patients with rheumatoid arthritis (RA).
Patients and methods: The study population comprised two cohorts of patients (Registry of biologic drugs in Finland (ROB-FIN) and the Central Finland RA database from years 1999-2010. Records of joint replacements performed 1980-2010 were acquired from the Finnish Arthroplasty Registry. Patient characteristics were equalized using propensity score matching. The rates of primary and revision operations were compared between the biologic drugs and disease modifying anti-rheumatic drug (DMARD) users. The lifetimes of the prosthetic joints were compared using Kaplan-Meier survival analyses.
Results: Of the 2102 biologics and 2710 (DMARD) users identified from the registries, 1587 remained in both groups after the matching procedure with median follow-up times of 3.05 and 8 years, respectively. Primary operations per 100 patient years during follow-up were more prevalent in the biologics group compared to control group (3.89 vs. 2.63, p=0.038), but the rates of revision operations were lower (0.65 vs. 0.85, p=0.007). According to survival analyses biologics users are more likely to undergo primary joint replacement surgery during follow-up. Survival of the installed endoprostheses during or prior to follow-up was not significantly improved.
Conclusion: The use of biologic drugs failed to reduce the need for joint replacement surgery in patients with a similar (matched) on-medication disease activity. Despite the lower rate of revisions among biologic users, the durability of endoprostheses was not statistically significantly different from that among DMARD users.

3. ASSOCIATION OF ADIPOKINES ADIPSIN, RESISTIN AND LEPTIN WITH INTERLEUKIN 6 AND METALLOPROTEINASES 1 AND 3 IN SYNOVIAL FLUID FROM OSTEOARTHRITIS PATIENTS

A Koskinen[1], K Vuolteenaho[1], R Nieminen[1], T Moilanen[2] and E Moilanen[1]
[1]The Immunopharmacology Research Group, University of Tampere School of Medicine and Tampere University Hospital, Tampere, Finland, [2]Coxa Hospital for Joint Replacement, Tampere, Finland

Objectives: Recent studies suggest that adipocytokines are involved in the pathogenesis of arthritis. The aim of the present study was to investigate the connection of synovial fluid leptin, and two less studied adipokines, adipsin and resistin, to the proinflammatory cytokine IL-6 and matrix metalloproteinase (MMP) levels in OA patients.

Methods: Synovial fluid samples and clinical information were collected from 91 patients (age 70.2 (9.6) years, BMI 30.8 (5.8) kg/m^2; mean (sd); females 66%) with osteoarthritis undergoing total knee replacement surgery. Levels of adipokines adipsin, resistin, and leptin, and IL-6, MMP-1 and MMP-3 were determined in the synovial fluid samples by immunoassays.

Results: Resistin and leptin showed positive correlations with synovial fluid levels of IL-6, MMP-1 and MMP-3. Interestingly, adipsin correlated negatively with IL-6 and MMP-1. When the patients were divided into two groups by BMI (BMI>30 = obese, n=46; BMI<30 = non-obese, n=45), the negative correlations of adipsin with MMP-1 and MMP-3 became more evident in the non-obese group whereas no correlations were found in the obese group. Positive correlations of leptin with MMP-1 and MMP-3 were more evident in the obese group than in the whole group, and no correlations were found in the non-obese group. Synovial fluid leptin levels were higher in the obese group compared to non-obese group. Levels of other adipokines studied did not differ in the two BMI groups.

Conclusions: Adipokines resistin and leptin were found to correlate positively and adipsin negatively with the proinfammatory mediator IL-6 and MMP enzymes in synovial fluid from OA patients. Negative correlations of adipsin with MMPs were more evident in non-obese patients whereas leptin correlated with MMPs in obese, but not in non-obese subjects. The results suggest that leptin might act as a proinflammatory factor especially in obese patients, whereas adipsin might have protective role in non-obese patients.

4. HIGH SYNOVIAL FLUID IL-6 LEVELS ARE ASSOCIATED WITH INCREASED MMP LEVELS AND WITH THE MOST SEVERE RADIOGRAPHIC CHANGES IN OSTEOARTHRITIS PATIENTS

K. Vuolteenaho[1], A. Koskinen[1], T. Moilanen[1,2] and E. Moilanen[1]. [1]The Immunopharmacology Research Group, University of Tampere School of Medicine and Tampere University Hospital, Tampere, Finland, [2]Coxa Hospital for Joint Replacement, Tampere, Finland.

Objectives: IL-6 is a proinflammatory cytokine contributing to the pathogenesis of rheumatoid arthritis. The purpose of the present study was to investigate if IL-6 is also a significant cytokine in osteoarthritis, by assessing the association of synovial fluid IL-6 with cartilage destructing MMPs, and further, with the radiographic severity of OA.
Methods: Plasma and synovial fluid samples were obtained from 100 OA patients (62 females, BMI 30.8±0.6kg/m2, age 70.0±1.0 years; mean±SEM) undergoing total knee replacement surgery. Concentrations of MMPs and IL-6 were measured by immunoassays. Preoperative radiographs from a subgroup of 31 patients were evaluated according to the Ahlbäck classification.
Results: Synovial fluid levels of IL-6 (228.6 ± 32.2 pg/ml) were considerably higher compared to plasma levels (3.7 ± 0.3 pg/ml) and there was no correlation between these two, suggesting that IL-6 is produced locally within the joint. Synovial fluid IL-6 correlated with MMP-1 (Spearman´s
r = 0.446, p < 0.001, 18.9 ± 2.0 ng/ml) and MMP-3 (Spearman´s r = 0.486, p<0.001, 986.6 ± 103.9 ng/ml). Further, synovial fluid IL-6 levels were twice as high in patients with radiologically most advanced OA (Ahlbäck grades 4-5, 231.0 ± 55.0 pg/ml, n=8) than in patients with less severe disease (grades 1-3, 110.0 ± 24.6 pg/ml, n=23; p < 0.03).
Conclusions: According to our results, IL-6 produced within the osteoarthritic knee joints, is associated with increased levels of cartilage destructing MMPs and radiographic severity of OA, implicating a remarkable role for IL-6 in the pathogenesis of OA.

5. MAP KINASE PHOSPHATASE-1 INCREASES THE EXPRESSION OF INTERLEUKIN-12 THROUGH INTERFERON REGULATORY FACTOR 1 IN ACTIVATED MACROPHAGES

Riku Korhonen, Noora Huotari, Tuija Hömmö, Tiina Leppänen and Eeva Moilanen. The Immunopharmacology Research Group, University of Tampere School of Medicine, Tampere, Finland and Tampere University Hospital, Tampere, Finland.

Mitogen-activated protein kinase phosphatase-1 (MKP-1) is a nuclear serine/threonine phosphatase that inhibits p38 mitogen-activated protein kinase (MAPK) signaling and inflammatory gene expression. MKP-1 deficient mice also display excessive inflammatory response and increased mortality during endotoxemia. Surprisingly, the present study shows that MKP-1 augments interleukin (IL)-12 expression in macrophages suggesting a stimulatory effect on Th1 type immune response. In the present study, LPS-induced expression of IL-12p40 was lower in primary mouse

peritoneal macrophages and bone marrow-derived macrophages from MKP-1 deficient mice than in cells from wild-type mice, whereas TNF expression was enhanced as expected. Correspondingly, p38 MAPK inhibitors BIRB 796 and SB202190 enhanced LPS-induced IL-12p40 production. Silencing of a transcription factor interferon-regulatory factor 1 (IRF1) by siRNA resulted in the inhibition of IL-12p40 expression in J774 mouse macrophages, which shows that IRF1 regulates IL-12p40 expression. p38 MAPK inhibitor BIRB 796 enhanced LPS-induced expression of IRF1 in J774 mouse macrophages and primary mouse peritoneal macrophages from wild-type mice, and IRF1 expression was reduced in primary mouse peritoneal macrophages from MKP-1 deficient mice. In conclusions, we suggest that MKP-1 increases and p38 MAPK decreases the expression of IL-12 by enhancing the expression of IRF1. MKP-1, through regulation of IRF1 and IL-12, may be an important factor in the induction of Th1 type of immune response and anti-microbial defense.

6. STAT3 PHOSPHORYLATION OF CIRCULATING LEUKOCYTES CORRELATES WITH DISEASE ACTIVITY IN EARLY UNTREATED RHEUMATOID ARTHRITIS

K Kuuliala[1], A Kuuliala[1], S Aittomäki[1], S Oksanen[1], S Siitonen[2], H Kautiainen[3], M Leirisalo-Repo[4] and H Repo[1. 1]Haartman Institute, University of Helsinki, Helsinki, [2]Laboratory Services (HUSLAB), Helsinki University Central Hospital, Helsinki, [3]Central Finland Central Hospital, Jyväskylä, and [4]Department of Medicine, Division of Rheumatology, Helsinki University Central Hospital, Helsinki

Objectives: To evaluate STAT3 activation in peripheral blood leukocytes in early untreated RA in relation to disease activity.
Methods: Blood samples were obtained from 39 patients with early untreated RA. Median age of patients was 51 years (IQR 33-63), median duration of symptoms 8 months (IQR 4-21), 77% were women, and 82% anti-CCP positive. Disease activity was evaluated by the DAS28 score (available for 36 patients). Phosphorylated STAT3 (pY705) levels in leukocyte subsets (CD14+, CD3+CD4+, CD3+CD8+, CD19+) were determined by flow cytometry. The proportion of pSTAT3 positive cells was determined using an electronic gate set to include <5% of positively fluorescing cells from a healthy control subject. Correlation coefficients were calculated by Spearman method.
Results: The proportion of pSTAT3 positive CD4+ cells was increased compared to controls in 22/37 patients (57%), CD8+ in 16/37 (43%), CD19+ in 11/37 (30%), and CD14+ in 22/39 (56%). DAS28 correlated with the proportion of pSTAT3+ CD4+ cells [r=0.43 (95% CI: 0.14 to 0.67), p=0.010].
Conclusions: STAT3 is constitutively activated in circulating leukocytes in early RA. The proportion of pSTAT3+ CD4+ cells correlates with disease activity evaluated by DAS28. Our results emphasize the heterogeneous involvement of immune inflammatory cells and may provide a novel strategy for personalized medicine in the treatment of early RA.

7. ALTERED HUR EXPRESSION IN HLA-B27 -EXPRESSING U937 MONOCYTIC CELLS

Anna S. Sahlberg [1, 2], Marja Ruuska [1, 2], Kaisa Granfors [1], Markus A. Penttinen[2]
[1]National Institute for Healthand Welfare, Turku, Finland, [2]Department of Medical Microbiology, University of Turku, Turku, Finland.

Development of reactive arthritis (ReA) is strongly associated with tissue antigen HLA-B27. Here we aimed to investigate the role of HLA-B27 in regulation of RBP human antigen R (HuR) expression in *Salmonella*-infected or *Salmonella* LPS-stimulated human U937 monocytic cells, since HuR is a critical regulator of the post-transcriptional fate of certain transcripted genes like TNFα. Activated p38 may induce the cytoplasmic accumulation of HuR. In cytoplasm, HuR can be cleaved to two cleavage products (CPs), HuR-CP1 (24 kDa) and HuR-CP2 (8 kDa), that have been linked to promotion of apoptosis. The cleavage of HuR is shown to be protein kinase RNA (PKR)-dependent. Intriguingly, we have previously observed altered p38 kinase- and PKR-related signalling in HLA-B27-expressing monocytic cells suggesting that HuR regulation might be altered in these cells. Our studies show that in cells expressing misfolded B27 (B27g and H9F), HuR (36kDa) expression is increased but generation of CPs is decreased when compared to cells expressing rapidly folding B27 molecule (E45M) or control (Mock) cells. Also, HuR expression

and generation of CPs show reduced PKR- or p38- dependency in HLA-B27-transfected cells compared to control cells. Our results show that the expression of HLA-B27 disturbs the HuR-mediated signalling pathway. Moreover, altered signalling is related to misfolding-linked Glu45 in the B pocket of the HLA-B27 heavy chain. Taken together, HLA-B27 HCs modulates the intracellular environment of monocyte/macrophages and the mechanisms that are important in controlling interaction between ReA-triggering bacteria and host cell. This phenomenon is at least partly dependent on the misfolding feature of the B27 molecule. These observations offer a novel mechanism by which HLA-B27 may modulate inflammatory response induced by ReA-triggering bacteria.

8. ALTERED PHOSPHORYLATION OF STAT1 IN HLA-B27 EXPRESSING U937 HUMAN MONOCYTIC CELLS IS DEPENDENT ON PKR ACTIVITY.

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The development and severity of reactive arthritis (ReA) and the susceptibility to other spondyloarthropathies are strongly associated with the tissue antigen HLA-B27. Several findings suggest that tendency of HLA-B27 heavy chains (HCs) to misfold during assembly may play an important role in disease pathogenesis. We have previously reported that some signaling pathways might be disturbed in cells expressing misfolding HLA-B27 molecules. For example the expression and activation and double-stranded RNA activated kinase (PKR) is altered in B27-expressing cells. PKR is known to associate with an important regulator of inflammatory responses, signal transducer and activator of transcription 1 (STAT1), which is a major mediator of interferon (IFN) signaling. We have earlier detected that in HLA-B27 expressing cells the phosphorylation of STAT1 tyrosine 701 residue is enhanced, even prior any stimulation. Moreover this phosphorylation is dependent on PKR activity. The aim of this study was to determine whether HLA-B27 modulates the phosphorylation of serine 727, which is another important phosphorylation site of STAT1. Intracellular localization of STAT1 in Salmonella-infected human monocytic cells was also studied. In addition, we studied the role of signaling molecule PKR in these modulatory effects.
We observed that phosphorylation of STAT1 serine 727 is prolonged in cells expressing misfolding forms of HLA-B27 after *S enteritidis* infection, whereas in Mock and in cells expressing mutated, correctly folding HLA-B27 the phosphorylation of serine 727 is transient. Studies using a specific inhibitor of PKR revealed that in cells expressing misfolding forms of HLA-B27 molecule phosphorylation of STAT1 serine 727 is only partially dependent on PKR activity at the early time points of infection but the dependency increases in time. In addition, more STAT1 is localized in nucleus in HLA-B27 expressing cells, even before external trigger, when compared to Mock cells. Our results show that phosphorylation of STAT1 serine 727 residue is prolonged in HLA-B27 expressing monocyte-macrophage cell lines cells after bacterial infection. This is of interest since phosphorylation of serine 727 on STAT1 is suggested to contribute to macrophage activation and promote inflammatory responses. Therefore, our results offer a mechanism how expression of HLA-B27 molecule can impact the course of Salmonella infection and ReA.

9. EARLY RHEUMATOID ARTHRITIS IN JYVÄSKYLÄ 2008-11; DESCRIPTION OF PATIENTS SEEN IN NORMAL CLINICAL CARE

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Objective: Remission is the target of treatment of early rheumatoid arthritis (ERA)- patients nowadays, and it should be achieved as quickly as possible to avoid permanent disability and damage. There is a great amount of knowledge from many ERA RCT:s in order to make treatment recommendations, however, the data from observational studies considering usual rheumatologic care of ERA is somewhat scarce. We analyzed data of Finnish ERA-patients treated in Jyväskylä Central Hospital rheumatology clinic between 2008 and 2011.

Methods: All patients with adult-onset (16 years or more) new RA diagnosis were monitored as part of normal clinical care with GoTreatIT –computer software (published earlier) in Jyväskylä Central Hospital outpatient clinic. Patients are treated and followed according to structured multiprofessional routine clinical practice where every ERA-patient from the region (ca 280 000 inhabitants) is treated and followed at 3, 6, 12 and 24 months after RA-diagnosis is made using ”treat-to-target” and ”tight control”- principles. Data are recorded by the treating rheumatologist as part of normal clinical visit and used for clinical decision making.

Results: Data were available from 410 ERA-patients (68%F, 70% RF/CCPab+). Median (IQR) duration of symptoms was 6(3,11) mo. Data were available from 235, 243, 199, 256 and 178 patients at 0, 3, 6, 12 and 24 mo respectively. Data of disease activity and used medication are presented in TABLE. DAS28-remission was achieved by 55.7%, 51.6%, 62.7%, and 62.9% of patients at 3, 6, 12 and 24 mo, respectively. At the baseline 21% of patients had erosions.

Conclusions: Remission is a realistic goal of treatment in real-life rheumatologic settings and it is achievable with non-biologic treatment for the majority of ERA-patients during the first 2 years after diagnosis.

TABLE. Values of clinical status measures as median (IQR) and medications.

	0 months	3 months	6 months	12 months	24 months
DAS28	4.2(3.1,5.0)	2.4(1.5,3.1)	2.4(1.7,3.3)	2.2(1.4,3.0)	2.1(1.4,2.9)
PtGl(0-100)	38(18,55)	24(6,46)	24(9,47)	22(6,48)	22(6,40)
InvGl(0-100)	30(20,50)	5(0,20)	9.5(0,20)	6(0,15)	5(0,15)
SJC28	3(1,7)	0(0,1)	0(0,1)	0(0,1)	0(0,1)
TJC28	3(1,7)	0(0,2)	1(0,2)	0(0,2)	0(0,1)
CRP	6(2,17)	2(1,5)	2(1,5)	2(1,4)	2(1,5)
ESR	18(8,32)	8(5,16)	8(5,16.5)	7(5,14)	7(5,13.5)
HAQ (0-3)	0.9(0.5,1.4)	0.4(0,0.9)	0.5(0.1,1.0)	0.4(0,0.9)	0.4(0,0.9)
Medications					
FIN-RACo-combination	15.7%	18.5%	20.1%	18.8%	13.5%
Other MTX-combo	31.1%	35%	31.7%	32.8%	34.8%
MTX	37%	31.7%	29.1%	27.3%	29.2%
Other mono	10.2%	7.0%	10.1%	7.8%	12.4%
Other combo	0.9%	2.5%	5.0%	7.8%	6.2%
No DMARDS	5.1%	5.3%	4.0%	5.5%	3.9%
Prednisolone	76.6%	76.1%	75.9%	67.2%	50.0%
Biologics	0	0.4%(n=1)	1.5%(n=3)	3.1%(n=8)	6.2%(n=11)

10. SIMILAR CLINICAL OUTCOMES IN RHEUMATOID ARTHRITIS WITH MORE VS. LESS EXPENSIVE TREATMENT STRATEGIES

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11. MONITORING OF TNF-ALPHA BLOCKERS INFLIXIMAB AND ADALIMUMAB BY MEASURING TROUGH LEVEL CONCENTRATIONS AND ANTI-DRUG ANTIBODIES

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Use of TNF-alpha blockers for patients with rheumatoid arthritis and chronic bowel disease is continuously increasing. These biologicals are costly and therefore optimization of the drug dosage is especially desirable. In addition, elimination of these macromolecular drugs can be substantially accelerated by antibodies against them - if antibodies are detected the drug is normally not clinically useful. Choice of the dose or discontinuation of the therapy may be based on clinical efficacy but challenges are reliability of efficacy assessment or slowness in clinical response. Our objective was to evaluate spectrum of infliximab or adalimumab trough levels and antibody levels from 200 serum samples with a clinical request of at least one of the analyses.

From the 139 requested infliximab measurements the level was within the usual target range (2-10 µg/ml) in 43%, lower in 36%, and higher in 21% of the patients. Anti-infliximab antibody testing was performed for a total of 45 patients and antibodies were detected in 24% of them. The level of antibodies varied a lot but all samples positive with anti-infliximab antibodies had infliximab concentration below 0.06 µg/ml. Therefore it seems that measument of infliximab (and probably adalimumab) trough level is the best first-line analysis for clinical use in optimization of drug dosing. In our material increase of the dose would have been indicated in 36% and decrease in 24% of the patients. In the case of low drug concentration the anti-infliximab antibody measurement can be used in helping decision on discontinuation of the paricular biological drug for that patient. If antibodies are detected an alternative anti-TNF biological can be used since cross-reaction of the antibodies is unlikely to occur.

In conclusion, we state that monitoring of anti-TNF drug trough level can be used to guide dose of these costly biological drugs. For the patients with low drug level it is justified also to examine possible antibodies against the used anti-TNF agent. In future we aim to evaluate clinical effectiveness of trough level and antibody testing.

12. FIVE CASES OF INTERSTITIAL LUNG DISEASE AFTER COMBINING LEFLUNOMIDE TO METHOTREXATE THERAPY

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Background. Interstitial lung disease (ILD) is a rare complication of methotrexate (MTX) treatment. It is suggested that another anti-rheumatic drug leflunomide (LEF) may also have toxic lung effects in Asian populations. However, in Caucasian populations LEF is considered lung safe. We observed five cases of ILD after LEF was combined to MTX treatment in Finnish patients.

Methods. Review of clinical characteristics, laboratory parameters, radiological and lung examinations, treatment and clinical course of five cases observed between 2005 and 2010.

Results: Of the five patients (two men) four had rheumatoid arthritis and one ankylosing spondylitis with hip synovitis. Patients were 49-74 years old and they had no previous lung diseases. Four were non-smokers and one ex-smoker. Four patients had used MTX 16.9-142.3 months without LEF. However, they developed ILD 3.3-5.3 months after LEF was combined to MTX. One patient had used MTX 31.7 months without LEF and 16.9 months combined to LEF. LEF was temporarily stopped and when re-started she developed ILD in 4.6 months. At the time of ILD all patients used LEF 20 mg daily and MTX 20-25 mg weekly (four intra-muscularly). All patients had new parenchymal infiltrates in chest x-ray and broncho-alveolar lavage was performed in four patients without evidence of infection. MTX and LEF were permanently stopped from all patients, high dose corticosteroids were given for four and cholestyramine for two. Three patients needed non-invasive ventilation and one also invasive ventilation. Full recovery was observed in three patients. Two patients were significantly disabled, one died a year later on heart failure and the other one is considered for lung transplantation.

Conclusion. Combining LEF to MTX treatment may have serious toxic lung effects and this issue should be examined in larger populations.

13. JOINT SYMPTOMS AFTER A LARGE WATERBORNE GASTROENTERITIS OUTBREAK – A CONTROLLED, POPULATION-BASED QUESTIONNARE STUDY

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14. CNS VASCULITIS – DIAGNOSIS, TREATMENT AND PROGNOSIS BASED ON PATIENT RECORDS COVERING A 10 YEAR PERIOD

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Objectives: To identify patients suffering from CNS vasculits (primary vasculitis or secondary) using patient records accumulated at Helsinki University Central Hospital (HUCH) over 10 years. Special focus was put on specific diagnosis, therapy and prognosis of disease.

Methods: Patients were identified using specific electronic patient records (Miranda/Cressida) including individualized ICD10 diagnosis documentation of patients being treated for CNS vasculits at HUCH. When needed for clarification and in patients being entered before 2004, manual paper records were consulted**.**

Results: 57 patients were identified and carefully documented**.** Specific diagnoses resulting in CNS vasculitis included: 23 patients with primary angitis of CNS (PACNS or no indication of systemic vasculitis); 8 patiens with SLE; 5 patients with antiphospholipid syndrome (aPL syndrome); 5 with systemic vasculitis; 2 with reversible cerebral vasoconstrictive syndrome (RCVS); 1 Wegener´s granulomatosis; 1 drug abuse and, 12 with not specified CNS vasculitides**.** The diagnosis was based on radiographic [(dator tomography (DT), magnetic resonsnce imiging (MRI), magnetic resonance angiography (MRA) and angiography)] and clinical grounds; no patient had been diagnosed using brain biopsy. Mean age of patients were 44 yrs (range 17-66; woman/man ratio: 3.1:1). 33/27/10/37% had reported classic risk factors including high lipids, high blood pressure, DM, and were smokers, respectively.

Main neurologic symtoms included hemiparesis; headache; speach imparement; vertigo; and sight impairment in 44/35/35/12 and 7% of patients, respectively. Treatments consisted of glucocorticoids; immunosupressants; cytostatic therapy (cyclophosphamide), immune globulins and biologics in; 74/43/14/7 and 1 %, respectively. 20% of patients used also antivasospastic antihypertensive medication.

48/57 patients were included in the working force prior to diagnosis and at last visit 30/54 had returned back to work, 21 were pensioned; 1 was on sick leave and 3 had died during follow-up.
Conclusions: CNS vasculitis is an uncommon and poorly understood condition. Diagnosis is made according to proposed criteria, and treatment is based on clinical ground as no randomized studies exist. When diagnosis of sytemic vasculitis or secondary diagnosis is made, treatment is based on the proposed guidelines used in these conditions. Prognosis is perhaps better than expected as 30/54 had returned to work at last medical visit.

15. PATIENTS WITH GOUT IN KUOPIO UNIVERSITY HOSPITAL.

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Objective. To assess the clinical picture, therapy and co-morbidities of the patients with gout in Kuopio University Hospital.
Methods. Data from the files of the patients with gout, ICD-10 codes M10.0-10.9, visiting the emergency unit, department of medicine or rheumatological outpatient department between 1 January 2007 and 31 December 2007 were evaluated.
Results. Of 66 patients, 48 (73 %) were male and 18 female. The mean age at evaluation was 67 ± 14.5 years, 65.2 ± 12.8 years in males and 72.2 ± 17.7 years in females, p = 0.082, range 23-101. Fourteen patients were electively sent for consultation, 44 patients were referred from the emergency unit, 8 patients from the other wards of the hospital and 5 cases as emergency cause during their stay in the hospital for other reasons. Fourteen (21 %) patients had podagra, 22 (33 %) other joint involvements and 29 (44 %) had a polyarticular disease.
Crystals were studies in 20 cases and 70 % showed sodium urate crystals. New gout diagnosis was established in 21 cases. Serum urate was measured in 59/66 cases and the result was > 450 mmol/L in 74 %.
The mean BMI was 31 ± 5 kg/m^2, among men 32 ± 5 kg/m^2, range 23 - 47, and among women 29 ± 4 kg/m^2, range 22 - 36.
Thirty-nine (59 %) patients, 15 (83 %) women and 24 (50 %) men were on diuretics. They were older than the non-users, the mean age at evaluation was 75 ±10 years and 55±11 years, respectively, p<0.001. Their serum creatinine values were 149 ± 86 umol/L, whereas in non-diuretic users the values were lower 78 ± 20 umol/L, p < 0.001. With MDRD formula creatinine clearance among diuretic users was 46 ± 22 ml/min/1.73 m^2 and among non-users 93 ± 23 ml/min/1.73 m^2, p < 0.001. Only 5 (8 %) patients had no hypertension, diabetes, hyperlipidaemia, cardiovascular diseases or renal failure. Nine (14 %) patients had all of them.
Diet therapy was mentioned in 89 % of the files. NSAIDs were described in 85 % of the cases. Corticosteroid injection was given in 22 (33 %) cases. Peroral corticosteroid was established in 29 % of the cases.
Conclusion. Polyarticular gout is common in patients seen either as emergency cases or in hospital wards. Co-morbidities are regularly associated with gout.

16. PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN KUOPIO UNIVERSITY HOSPITAL.

Lotta Sydänmaa and Oili Kaipiainen-Seppänen. Department of Medicine, Kuopio University Hospital.

Objective. To assess the clinical picture, therapy and co-morbidities of the patients with systemic lupus erythematosus (SLE) at the rheumatological outpatient clinic of Kuopio University Hospital.
Methods. Data from the files of the patients with SLE, ICD-10 codes M32.0-32.9, visiting the rheumatological outpatient clinic between 1 September 2007 and 31 August 2008 with were evaluated.
Results. Of 48 patients, 43 (90 %) were female. The mean age at disease onset was 37.3±19.2 years, in female 35.6±19.4 and in male 51.3±10.7 years, p=0.083. Forty (83 %) patients fulfilled

4/11 criteria, mean 5.7±1.5 criteria, range 4–10. The most common positive classification criterion was antinuclear antibodies, 93 %. Arthritis/arthralgia occurred in 85 %, immunological abnormalities in 63 %, discoid skin changes in 63 % and butterfly skin dash in 58 % of the patients. Patients with butterfly skin dash had also discoid changes, p=0.039. Patients with juvenile SLE had most frequently nephritis, p =0.002. At some time period 96 % of the patients were on corticosteroids. Other commonly used drugs were antimalarials, 92 %, azathioprine, 79 %, and methotrexate, 46 %. Eleven (23 %) patients had hypertension. During the last 5 years lipid profile was studied in 63 % and bone density was measured in 77 % of the patients. In bone density measurement 59 % had abnormal findings: osteopenia in 43 % and osteoporosis in 16 % of the cases. Among 24 patients, who were in fertile age during the disease, 29 % of pregnancies were aborted.
Conclusion. The criteria of SLE were fulfilled as described in the literature. In addition to the therapy of the disease itself prevention of side-effects and co-morbidities should be taken into account.

17. PATIENTS WITH SYSTEMIC SCLEROSIS IN KUOPIO UNIVERSITY HOSPITAL.

Anna Juuti and Oili Kaipiainen-Seppänen. Department of Medicine, Kuopio University Hospital.

Objective. To assess the clinical picture, therapy and co-morbidities of the patients with systemic sclerosis (SSc) at the rheumatological outpatient clinic of Kuopio University Hospital.
Methods. Data from the files of the patients with SSc, ICD-10 codes M34.0-34.9, visiting the rheumatological outpatient clinic between 1 September 2007 and 31 August 2008 with were evaluated.
Results. Of 64 patients, 58 (91 %) were female and 6 (9 %) male. The mean age at diagnosis was 50.5±11.4 years in female and 56.2±11.7 years in male, p=0.298. The duration of the disease was 5.7±4.3 years in female and 2.3±3.8 years in male, p=0.077. Raynaud's phenomenon occurred in 49/58 (85 %) among females and in 4/6 (67 %) among males. Reflux occurred in 53 % and synovitis in 39 % of the cases. Digital ulcers had occurred in 20 % of the cases, one patient had had amputation and one suffered from pulmonary hypertension. As clinical finding abnormal changes in nail walls were recorded in 72 % of the female and 50 % of the male patients and in capillaroscopy, performed for all patients, findings reflecting to systemic sclerosis in 86 % of the patients. Of 64 patients, 20 % had abnormal findings in chest x-ray and 19 % in lung function tests. Positive antinuclear antibodies were recorded in 42 % and anticentromere antibodies in 52 % and anti-Scl70 antibodies in 6 % of the patients. Other autoimmune co-morbid conditions were described in 33% of the cases. At some period of the disease course 80 % of the patients were on corticosteroids, 75 % on hydroxychloroquine, 69 % on azathioprine, 48 % on cyclosporine, 31 % on methotrexate and 17 % on cyclophosphamide. Of females 41 % and of males 33 % had hypertension. Twenty-six per cent of the females and 67 % of the males had hypercholesterolemia. Osteoporosis occurred in 10 and osteopenia also in 10 patients.
Conclusions. The clinical picture was similar to that described in the literature except that serious internal organ involvement was infrequent and arthritis was common in this series. Therapy of the disease was tailored according to the disease manifestations and therefore use of corticosteroids and immunosuppressive drugs were common. Corticosteroids were used for most patients with modest dosage because of arthritis, vasculitis or oedematous skin changes. Prevention of side-effects of the therapy and co-morbidities should also be taken into account.

Toimituksesta

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Toimituksen väki toivottaa kaikille yhdistyksen jäsenille hyvää uutta vuotta 2012 ja jaksamista tärkeässä työssään! Toisilla tosin on eläkepäivät jo ansaitusti menossa; vireyttä heille!
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Tiedoksi vielä uusille jäsenille ja muistutukseksi vanhoille: yhdistyksen sivut: www.reumatologinenyhdistys.com pitävät sisällään kaikenlaista tarpeellista, joten poiketkaa siellä kun kiireiltänne ehditte!
ensi vuoteen…., Maiju K

Tervetuloa uudet jäsenet!

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ROB-FIN rekisteri paikalla myös Turussa.
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