

NucSys Newsletter

Issue No. 6. – The End of the Beginning

November 2008

A number of significant events have occurred over the last several months in the evolution of NucSys. The clearest example of this is the submission of **NucSys II** application to the European Commission. The very high standard of this proposal reflects our progress as a collective and our individual experiences of the last few years. Certainly we have developed a much more practical understanding of what makes the ideal balance of training and research components. An equal balance of wet and dry lab support has been allocated to more rigidly defined research questions. These developments also reflect a significant input from the ESRs. Of course there are no certainties in funding (NucSys I had to be in the top 5% to be funded). If not funded in this round it is reasonable to anticipate the proposal becomes stronger for subsequent applications.

Other significant, but less obvious steps, in our development have been the spin-off of parallel applications and collaborative papers from the NucSys network. NucSys interacts with an ever-increasing range of local, national and international projects and networks. By no means an exhaustive list includes ongoing interactions with networks such as NuGo, the establishment of a formal strategic relationship between University of Luxembourg (Carsten Carlberg) and the Institute for Systems Biology in Seattle, USA. Similarly, other trans-Atlantic

applications are underway to create, for example, a MSc training program between partners within NucSys and colleagues in the USA. In this was the legacy of NucSys appears firmly established and woven into the academic fabric of all partners.

Of course the other way in which this is the end of the beginning is that this newsletter is the last to include updates from Tatjana, Sebastiano and Claudia, as current students. At the time of writing they are planning the next moves, including finishing the experiments for their thesis (TD has already submitted), completing papers and looking for jobs. Tatjana will join the lab of Ernest Fraenkel Department of Biological Engineering, MIT, Cambridge, MA and work on the combination of gene/protein expression and ChIP-Seq data in health and disease combined with systems biology modeling. Sebastiano too is planning to look for post-doctoral positions in the US, whereas Claudia is planning to look for posts in industry. We obviously wish them good luck!

In other ways the field of systems biology in human health and disease is perhaps also at the end of the beginning. I spent the last few days at the MD Anderson Cancer Center in Houston, Texas, attending the **61st Annual Symposium on Cancer Research Systems Biology of Cancer**.

Many of the key researchers in the US presented and I was left with the

impression that at its best the fusion of disciplines really can be used as a piercing beam of light to illuminate cancer in a manner that is totally revealing and unprecedented. At its worse, unfortunately, it is little more than re-packaging of traditional reductionism centred around candidate and intuition-driven biology. Indeed I was surprised by the extent to which some (very senior) investigators were merely re-naming very standard cancer research; I won't name and shame!

The best of the best was perhaps still focussed around model organism studies and work on *C. Elegans* development by **A. J. Marian Walhout** (University of Massachusetts Medical School) presented some very interesting examples of network motif identification in development. In particular, she dissected network topology and identified the interaction between miRNA and transcription factors to generate negative feedback loops; motifs that other workers have found previously to be under-represented.

Similarly **Jeff Hasty** (University of California, San Diego) presented a very elegant series of studies attempting, successfully, to build oscillating transcriptional modules based around negative and positive feedback and using two colour gene reporter systems.

Using mammalian systems various workers outlined the challenges in terms of data collection and modelling; notably **Pedro Mendes** (Manchester University/Virginia Bioinformatics Institute) and **Bernard Palsson** (UCSD) both spoke with particular clarity. These talks are no doubt important but have the tendency to present the "30000 ft" view that can be stimulating but ultimately unsatisfying.

Others presented more specific findings modelling key cellular events. For example, **Michael Yaffe** (MIT Department of Biology) examining DNA damage response and **Peter Sorger** (Harvard

Medical School) examining cytokine signalling both presented the key challenges and successfully illustrated how the developed models generated novel predictions and insight that could be exploited therapeutically.

Marc Vidal (Dana Faber Cancer Inst) summarised the development in this discipline as the transition from learning to fly, to learning to fly, robustly. He, and other speakers, re-iterated the point that it is necessary for all stakeholders to work together. Biologists, modellers, bioinformaticians, computer scientists etc. all have a responsibility to be aware of the needs of each other. More specifically he likened the field to the position of the genomic era in the early 1990s, and predicted (boldly?) that unprecedented strides will be made within the next 10 years. This theme was echoed by **John N. Weinstein** (MD Anderson Cancer Ctr), who made the point that the number of publications in SB is not growing exponentially, as might be imagined. In part future growth requires the widespread application of certain enabling technologies – not least of which is bioinformatics.

Thus it seems that many of the key resources, techniques and approaches are in place for the rapid future progress in systems biology in human health.

Finally apologies for late release of this newsletter – remember to always back-up your work!

MJC Nov 2008

Network news.

Bold = PI

Bold = ESR

Team 1, Prof. Carlberg, University of Kuopio, Finland.



ESR1: Tatjana Degenhardt, (4/06 to 3/09)

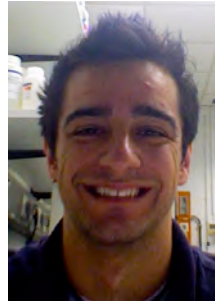
Publications

Mager U, **Degenhardt T**, Pulkkinen L, Kolehmainen M, Tolppanen AM, Lindström J, Eriksson JG, **Carlberg C**, Tuomilehto J, Uusitupa M; Finnish Diabetes Prevention Study Group. Variations in the ghrelin receptor gene associate with obesity and glucose metabolism in individuals with impaired glucose tolerance *PLoS ONE*. 2008 Aug 13;3(8):e2941



ESR2: Aleksandra Tomaszewska (12/06 to 11/09)

Team 2, Drs Campbell & Bunce, University of Birmingham, UK



ESR3: Sebastiano Battaglia, (3/06 to 2/09)

Publications

Abedin SA, Thorne JL, **Battaglia S**, Maguire, O, Hornung, L, Doherty AP, Mills IG, **Campbell MJ** (2008). Elevated NCOR1 disrupts a network of dietary-sensing nuclear receptors in bladder cancer cells (*Carcinogenesis* – In press)

Attended meetings

International Conference of System Biology, Goteborg (Sweden), 22-28 Aug 2008; poster: NCoR Activity in the Prostate System

The first two days were dedicated to tutorials, mostly based on math applied to biology. The one that interested me the most was "System Biology Workbench", this is the software that I normally try to play with and the tutorial showed how to model using commands line...pretty difficult!

Several talks were focused on integration of high throughput data; Frank Holstege, from Utrecht (NL), generated microarray data from targeted mutations in components of the signaling and transcription machinery in the yeast *S. cerevisiae* in order to uncover new regulatory mechanisms, with focus on the Mediator complex.

Some talks and loads of posters were indeed explaining models of cell cycle in yeast, breaking down kinases functions and their regulations; other main topic were also NFkB and MAP kinases activity,

transcriptional regulation, miRNA function and drug discovery.

At the end of the conference I attended a workshop on "Inferring Network for Disease" where the main topic was the integration of experimental and clinical data in order to describe mathematically most common diseases and cancers (colon, lung and prostate).



ESR4: Pedro Velica, (9/06 to 8/09)

Attended meetings

European Muscle Conference, Oxford (Sep 13-16)

My abstract was selected for a talk on the "Muscle Development and Redevelopment" session and was awarded with the young investigator prize. The abstracts will be published in the Journal of Muscle Research and Cell Motility. Also, for winning the award I was invited to write a short report for this same journal.

The European Muscle Congress took place in Keble College, Oxford. The sessions covered muscle physiology, disease, development, new therapies as well as muscle proteomics and genomics. Some works were particularly interesting, such as the combination of electric stimulation and muscle precursors to obtain better tissue engineering. Also, a therapy aiming muscle dystrophy consisting of injecting splicing-promoting oligonucleotides showed promising results by rescuing the re-expression of the dystrophin protein. The informal scientific exchange was very good as the meals and coffee breaks took place in the very pleasing halls and quads of the college. It

was good for me to learn about what is going on in muscle research

Team 3, Prof. Van Leeuwen, Erasmus University Medical Centre, Rotterdam The Netherlands



ESR5: Claudia Bruedigam (3/06 to 2/09)

Publications

Bruedigam C, Koedam M, Chiba H, Eijken M, **van Leeuwen JP**. Evidence for multiple peroxisome proliferator-activated receptor gamma transcripts in bone: fine-tuning by hormonal regulation and mRNA stability. *FEBS Lett.* 2008 May 14;582(11):1618-24. Epub 2008 Apr 22.

Attended meetings

35th Symposium on Calcified Tissues, Barcelona, 2008 (poster)

The 35th European Symposium on Calcified Tissues took place in Barcelona from 24 - 28 May this year. I attended this meeting in order to share my recent data concerning the role of peroxisome proliferator-activated receptors in bone biology, and to receive new insights into the current research directions and novel approaches in the bone field. The meeting addressed both biological and clinical questions, therefore was stimulating "from bench-to bedside" discussions. It offered a variety of symposia with highly qualified invited speakers, workshops and poster sessions. From a cell-biological point of view, the presentations about crosstalk between the osteoblast and osteoclast, and as well a new player, the T cell which has been shown to mediate effects of estrogen and PTH in bone, were very interesting. My further interest was taken by the developments in the genetic field.

Large effort has been put into the fine-mapping of quantitative trait loci in mice. By using a stock of genetically heterogeneous mice, genome-wide high resolution mapping of multiple phenotypes including several human disease models was successful with an average of 2.8 megabases. The second interesting development in the genetic field is the application of genome wide association analysis in order to find novel targets for bone-related disorders in an unbiased way. Most aging- and bone-related disorders, such as osteoporosis or atherosclerosis, are multi-factorial diseases, which means that many factors share the control over the phenotypical outcome. By collecting and merging large population data from several European cohorts, the relatively small effects of such factors will hopefully become visible due to increases in statistical significances.

ESR 6: Viola Woeckel (1/07 – 12/09)



Attended meetings

Wetenschapsdagen 2008 in Antwerp

The biggest learning moment was for sure the creating and presenting a poster.

ECTS in Barcelona

In this European meeting a lot of clinicians and scientists working in the bone field came together. It was my first international meeting. I learned that you really have to have good preparations and should attend meetings and workshops with the professors otherwise you hardly get a chance to talk to them. Additionally it was hardly impossible to find people in the mass.

Osteoimmunology in Rhodos

This international meeting on osteoimmunology brought together the top people from Japan and USA. Because it was a relatively small meeting it was easy to get in touch with them and the other participants. Although knowing the fact that Japanese have very often problems with the English language, it was still frustrating in getting (or better not getting) information from younger Japanese scientists. Networking was one of the most important actions taking place there. Although the background was also bone, there was no overlap with the ECTS. This underlines the wide variety of the field.

Courses Attended

Apr-Jul 08 Scientific English Writing

Learning tips and tricks with the English language and having a lot of discussions and feedback over your own work.

Sep 08 ECTS PhD training course (presentation)

This meeting felt like a Bone-NucSys. More than 50 PhD students from Europe and the field of bone attended this course. Europeans main professors of bone biology organised and attended the course. Beside basics on all possible fields of bone, new theories were discussed. High quality of networking.

Sep 08 Neuro-Endocrinology-Immunology (presentation)

Learning about the interactions of the neuro-endocrine and immunosystem with way more interactions than I thought.

Team 4, Profs Goldfarb & Gibson and Dr. Plant, University of Surrey, UK



ESR7: Ellen Wiedemann, (10/06 to 9/09)

Team 5, Prof. Westerhoff and Drs.

Bruggeman & Bakker, Vrije Universiteit Amsterdam, The Netherlands



ESR8: Katja Rybakova, (9/06 to 8/09)



ESR9: Alexey Kolodkin. (9/06 to 8/09).

Attended meetings

April 2008 ESF conference in St Feliude Guixols, Spain, poster presentation:

Glucocorticoid receptor signalling in detailed and simplified models- searching for design principles. A.N. Kolodkin, F.J. Bruggeman, M.J. Moné, E.N. Rybakova, B.M. Bakker, H.V. Westerhoff

July 2008 Marie Curie and ESOF conference in Barcelona, Spain

poster presentation: The emergence of nuclear receptor signalling from molecular interactions: Understanding emerges from the Marie Curie research training network

NucSys. A.N. Kolodkin, H.V. Westerhoff, F.J. Bruggeman, M.J. Moné, E.N. Rybakova, B.M. Bakker, J.P.T.M. van Leeuwen and C. Carlberg

August 2008 ISGSB in Helsingore, Denmark poster presentation: NR signaling and nucleo-cytoplasmic transport:

Towards understanding of design principles. A.N. Kolodkin, F.J. Bruggeman, M.J. Moné, H.V. Westerhoff

August 2008 ICSB in Guteburg, Sweden poster presentation: NR signaling and nucleo-cytoplasmic transport:

Towards understanding of design principles. A.N. Kolodkin, F.J. Bruggeman, M.J. Moné, H.V. Westerhoff

September 2008 BioSim meeting in Budapest, Hungary oral presentation:

Design principles of steroid hormone receptor signalling. A.N. Kolodkin, F.J. Bruggeman, M.J. Moné, H.V. Westerhoff

Team 6, Dr. Kersten and Prof. Müller, Wageningen University, The Netherlands.



ESR 10: Anastasia Georgiadi. (08/06 to 07/09)

Attended meetings

7th Dutch Endo-Neuro-Psycho Meeting (June 2008):

An annual meeting, which aims to update and stimulate endocrine and brain science in the Netherlands. My talk was under the session of Nuclear receptors and Metabolism, with the title "**Role of PPARs in fatty acid dependent gene regulation in the mouse heart: a transcriptomics approach.**"

Obesity meeting (June 2008):

One day meeting covering new insights on the causes and pathogenesis of obesity, as well as prevention policies at the level of the population.

49th International Conference on the Bioscience of Lipids (August 2008):

A meeting covering all different aspects of lipid metabolism from their packaging and transport through the cell membrane into the cytoplasm till their role in the development of metabolic syndrome. My talk was under the session of Fatty acids, Lipids and Metabolic Syndrome, with the title: **“Feedback regulation of cardiac fatty acid uptake is mediated by Angptl4.”**

Team 7, Dr. Hakkola and Prof. Pelkonen, University of Oulu, Finland



ESR 11: Marcin Buler (1/07 to 12/09)

Conferences:
Scandinavian Physiological Society
Annual Meeting 2008, Oulu,
Finland, August 15-17, 2008

Courses:
Mouse Embryonic Stem Cell Culture
Training Course, Max-Planck
Institute for Molecular Genetics, Berlin,
June 23 – 28, 2008,
Bioinformatics, University of Oulu, Oulu,
March 13-27, 2008
Molecular Medicine - Nutrigenomics ,
University of Kuopio January 1.-15.2.2008

System Biology, University of Oulu,
February, 2008

*Team 8, Dr. Verstuyf, Prof. Bouillon,
Katholieke Universiteit Leuven, Belgium*



ESR 12: Carsten Kriebitzsch (09/06 to
08/09)

ASBMR meeting Montreal (no
contribution) 11-16 September

The annual meeting of the American Society of Bone and Mineral Research took place in Montreal. Several poster sessions and oral presentations offered the opportunity to get more insights about new findings and latest results in bone biology. Interesting talks in the Symposia about “Vitamin D – clinical and scientific advances” or “Novel treatments of bone disease” offered further information about these topics. During the meeting the effects of Vitamin D in the treatment of Osteoporosis and cancer were discussed. Furthermore, it was interesting to learn more about the crucial role of canonical Wnt signalling pathway in bone biology, a topic that is currently extensively investigated and discussed in many posters and talks. Moreover, the meeting offered the opportunity for discussion and exchange of ideas with other young scientists. Interesting for me as an ESR from NucSys nuclear receptor biology was addressed in the “Vitamin D workshop working group”.

Vitamin D Analogs in Cancer Prevention
and Therapy” in Krefeld 17-18 May (talk)

In May I attended the Symposium “Vitamin
D Analogs in Cancer Prevention and
Therapy” In Krefeld. I had the opportunity

to present my data concerning Cystathionine beta synthase (CBS) in the talk "Gene expression profiling in 1,25-dihydroxyvitamin D3-treated MC3T3-E1 mouse osteoblasts". In the meeting the use of Vitamin D in cancer therapy was discussed but also its limitations like calcemic side effects. Due to these limitations the necessity to develop analogs which show a nice dissociation between beneficial antiproliferative effects and negative calcemic side effects was expressed. Furthermore, the connection between sunlight exposure/vitamin D status and cancer risk was addressed. The need of a sufficient Vitamin D status was depicted leading to an interesting discussion about the required daily amount of Vitamin D. Remarkably, almost every high level researcher in the field present in Krefeld suggested a different dose starting from 400 IU up to 4000 IU or even more.

Marie Curie Workshop (poster) + ESOF2008 in Barcelona 17-22 Jul

The Marie Curie Workshop in Barcelona was a nice opportunity to meet other Marie Curie fellows. Different topics were addressed during the meeting like funding possibilities by the EU, how to write a grant or different job possibilities for young researchers. During these different talks all fellows had the opportunity to present their work in poster sessions.

After the meeting the European Science Open Forum 2008 (ESOF2008) started. I liked the meeting because it offered insights into different fields of research and it was possible to talk with other fellows about their projects. Universities and research institutes presented their work and showed the various possibilities young Post Docs may have in the institutes. The highlight of ESOF2008 was for me the session with the Nobel prize laureates (Richard J Roberts and Aaron Ciechanover) which gave a overview about their scientific life. The best for me was that they depicted that you do not

need a Nature paper to obtain the Nobel prize.

Courses attended

Mouse Embryonic Stem cell Culture training course

Team 9, Drs. Mazzatti & Mayes, Unilever R&D, United Kingdom



ESR13: Oita Radu Cristian, (1/07 to 12/09)

Publications

Mazzatti DJ, Smith MA, **Oita RC**, Lim FL, White AJ, Reid MB. Muscle unloading-induced metabolic remodeling is associated with acute alterations in PPARdelta and UCP-3 expression. *Physiol Genomics*. 2008 Jul 15;34(2):149-61.

Team 10, Prof. Muñoz and Dr. González-Sancho, Instituto de Investigaciones Biomédicas, Spain



ESR 14: Fabio Pires, (10/06 to 09/09)

Publications

Pendás-Franco N, Aguilera O, **Pereira F**, González-Sancho J, **Muñoz A**. Vitamin D and Wnt/b-catenin pathway in colon cancer: role and regulation of DICKKOPF Genes". *Anticancer Research* 2008 (in press).

Attended meetings

Pereira F, Larriba MJ, Herrera M, Muñoz-Alonso MJ, Bonilla F, **Muñoz A** Effect of 1,25-dihydroxyvitamin D3 on dna damage and survival of platinum-treated human cancer cells". 8th International Conference of Anticancer Research. Kos, Greece, 2008. Published in Anticancer Research 28: 3442, 2008.

The Anticancer Research Conference held in Kos was a big meeting dedicated to preventive medicine. I found particularly interesting the symposium on epidemiology of Vitamin D. Some works from Norway, published this year in PNAS, showed that the people of Tibete, where the UV exposure is high, are vitamin D deficient, while apparently in Norway, this deficiency was absent, maybe due to Norwegian food habits (rich in fish and some dishes prepared with cod liver oil). Moreover, there were nice talks on prostate stem cells and circulating tumor cells.

Course attended

In Vivo Imaging - from Molecule to Organism. Erasmus MC, Rotterdam, Netherlands.

Team 11, Dr. Heinrich Schrewe, Max-Planck Institute for Molecular Genetics, Germany.



ESR 15: Pedro Rocha, (01/07 to 12/09)

Benzon Symposium No 55 Transcription Chromatin and Disease.

18/08 21/08 August Copenhagen.

The aiming of this meeting was discussion of the latest topics involving eukaryotic transcription and how epigenetic mechanisms can provide for extra levels of regulation. Several talks showed also how it is possible to translate into medical applications what is discovered in the basic science lab. The meeting had a good mixture of names established in the scientific community like Nobel Prize laureate Roger Kornberg, Robert Roeder, Thomas Jenuwein, Tony Kouzarides, etc; and some exciting short-talks by new established labs. From the talks that impressed me the most I would like to highlight the one given by Robert Tjian where he described a switch of the core promoter recognition complex that occurs during skeletal muscle differentiation. He showed that during differentiation of myoblasts, MyoD stops targeting myogenin using TFIID as a recognition element and uses an alternative transcription factor called Taf3. Inherent to this switch in the core transcription machinery he described that subunits of the Mediator (which are thought to be ubiquitously expressed) are no longer found in fully differentiated myotubes. Without showing any data he implied also that muscle cells might not be the only ones where this happens and for instance

in liver hepatocytes the same might be happening. But I guess that is a story for another Cell paper.

Team 12, Dr. Kay Colston, St. George's Hospital Medical School, UK



ESR 16: Carole Brosseau – France (11/06 to 10/09)

Team 13, Prof. Cross and Drs Kallay & Thalhammer, Medical University of Vienna, Austria



ESR 17: Thomas Nittke, (09/06 to 08/09)

Team 14, Dr. Luciano Adorini, BioXell S.p.A., Italy



ESR 18: Gilles Laverny, (10/06 to 09/09)

Attended meetings

International immunology meeting, Paris, France

Group Publications 1/5/08 to 7/11/08

Bold = PI

Bold = ESR

1. Mager U, **Degenhardt T**, Pulkkinen L, Kolehmainen M, Tolppanen, Lindström J, Eriksson JG, **Carlberg C**, Tuomilehto J, Uusitupa M. Variations in the *ghrelin receptor* gene associate with obesity and glucose metabolism in individuals with impaired glucose tolerance. (2008) *PLoS ONE* **3**, e2941
2. Martens K, van Themaat E, van Batenburg MF, Heinänen M, Huyghe, S, van Hummelen P, **Carlberg C**, van Veldhoven PP, van Kampen A, Baes M. Coordinate induction of PPARα and SREBP2 in multifunctional protein 2 deficient mice. (2008) *Biochim Biophys Acta* in press
3. Thorne J, **Campbell MJ**, Turner BM. Transcription factors, chromatin and cancer. *Intl J Biochem Cell Biol* 2008 In press
4. Abedin SA, Thorne JL, **Battaglia S**, Maguire, O, Hornung, L, Doherty AP, Mills IG, **Campbell MJ** (2008). Elevated NCOR1 disrupts a network of dietary-sensing nuclear receptors in bladder cancer cells. *Carcinogenesis In Press*
5. Hayden RE, Pratt G, Davies NJ, Khanim FL, Birtwistle J, Delgado J, Pearce C, Sant T, Drayson MT, **Bunce CM**. Treatment of primary CLL cells with bezafibrate and medroxyprogesterone acetate induces apoptosis and represses the pro-proliferative signal of CD40-ligand, in part through increased 15dDelta(12,14,)PGJ(2). *Leukemia*. 2008 Oct 16. [Epub ahead of print]
6. Akagi T, Luong QT, Gui D, Said J, Selektar J, Yung A, **Bunce CM**, Braunstein GD, Koeffler HP. Induction of sodium iodide symporter gene and molecular characterisation of HNF3 beta/FoxA2, TTF-1 and C/EBP beta in thyroid carcinoma cells. *Br J Cancer*. 2008 Sep 2;99(5):781-8.
7. Nijenhuis T, van der Eerden BC, Hoenderop JG, Weinans H, **van Leeuwen JP**, Bindels RJ. The Bone Resorption Inhibitor Alendronate Normalizes the Reduced Bone Thickness of TRPV5(-/-) Mice. *J Bone Miner Res*. 20mo08 Jul 2. [Epub ahead of print]
8. Williams AJ, Robson H, Kester MH, **van Leeuwen JP**, Shalet SM, Visser TJ, Williams GR. Iodothyronine deiodinase enzyme activities in bone. *Bone*. 2008 Jul;43(1):126-34. Epub 2008 Apr 4.
9. **Bruedigam C**, Koedam M, Chiba H, Eijken M, **van Leeuwen JP**. Evidence for multiple peroxisome proliferator-activated receptor gamma transcripts in bone: fine-tuning by hormonal regulation and mRNA stability. *FEBS Lett* 2008 May 14;582(11):1618-24. Epub 2008 Apr 22.
10. van der Kolk JH, **van Leeuwen JP**, van den Belt AJ, van Schaik RH, Schaftenaar W. Subclinical hypocalcaemia in captive Asian elephants (*Elephas maximus*). *Vet Rec* 2008 Apr 12;162(15):475-9.
11. **Plant N** Can systems toxicology identify common biomarkers of non-genotoxic carcinogenesis? *Toxicology* (2008) in press.
12. Hornberg JJ, **Bruggeman FJ**, **Bakker BM**, **Westerhoff HV**, Metabolic control analysis to identify optimal drug targets IN: *Progress in drug research*, eds H.I. Boshoff and C.E. Barry III, Birkhäuser Verlag Basel Switzerland Vol 64 pp 172-189.
13. Lemke U, Krones-Herzig A, Diaz MB, Narvekar P, Ziegler A, Vegiopoulos A, Cato AC, Bohl S, Klingmüller U, Sreaton RA, Müller-Decker K, **Kersten S**, Herzig S. The glucocorticoid receptor controls hepatic dyslipidemia through Hes1. *Cell Metab* 2008 Sep;8(3):212-23.
14. Stienstra R, Duval C, Keshtkar S, van der Laak J, **Kersten S**, **Müller M**. Peroxisome proliferator-activated receptor

- gamma activation promotes infiltration of alternatively activated macrophages into adipose tissue. *J Biol Chem* 2008 Aug 15;283(33):22620-7. Epub 2008 Jun 9.
15. Joosten MM, Beulens JW, **Kersten S**, Hendriks HF. Moderate alcohol consumption increases insulin sensitivity and ADIPOQ expression in postmenopausal women: a randomised, crossover trial. *Diabetologia*. 2008 Aug;51(8):1375-81. Epub 2008 May 27.
16. Arpiainen S, Järvenpää SM, Manninen A, Viitala P, Lang MA, **Pelkonen O**, **Hakkola J** Coactivator PGC-1 α regulates the fasting inducible xenobiotic-metabolizing enzyme CYP2A5 in mouse primary hepatocytes. *Toxicol. Appl Pharmacol* (2008), 232, 135-141.
17. **Pelkonen O**, Turpeinen M, **Hakkola J**, Honkakoski P, Hukkanen J, Raunio H Inhibition and induction of cytochrome P450 enzymes current status. *Arch. Toxicol.* (2008), in press.
18. **Bouillon R**, Carmeliet G, Verlinden L, van Etten E, **Verstuyf A**, Luderer HF, Lieben L, Mathieu C, Demay M. Vitamin D and Human Health: Lessons from Vitamin D Receptor Null Mice. *Endocr Rev* 2008 Oct 29(6):726-776.
19. Eelen G, Vanden Bempt I, Verlinden L, Drijkoningen M, Smeets A, Neven P, Christiaens MR, Marchal K, **Bouillon R**, **Verstuyf A**. Expression of the BRCA1-interacting protein Brip1/BACH1/FANCJ is driven by E2F and correlates with human breast cancer malignancy. *Oncogene*. 2008 Jul 10;27(30):4233-4241.
20. Masuyama R, Vriens J, Voets T, Karashima Y, Owsianik G, Vennekens R, Lieben L, Torrekens S, Moermans K, Vanden Bosch A, **Bouillon R**, Nilius B, Carmeliet G. TRPV4-mediated calcium influx regulates terminal differentiation of osteoclasts. *Cell Metab* 2008 Sep;8(3):257-265.
21. **Bouillon R**. How effective is nutritional supplementation for the prevention of stress fractures in female military recruits? *Nat Clin Pract Endocrinol Metab*. 2008 Sep;4(9):486-487.
22. **Bouillon R**, Bischoff-Ferrari H, Willett W. Vitamin D and health: perspectives from mice and man. *J Bone Miner Res*. 2008 Jul;23(7):974-979.
23. Roux C, Bischoff-Ferrari HA, Papapoulos SE, de Papp AE, West JA, **Bouillon R**. New insights into the role of vitamin D and calcium in osteoporosis management: an expert roundtable discussion. *Curr Med Res Opin* 2008 May;24(5):1363-1370.
24. Benn BS, Ajibade D, Porta A, Dhawan P, Hediger M, Peng JB, Jiang Y, Oh GT, Jeung EB, Lieben L, **Bouillon R**, Carmeliet G, Christakos S. Active intestinal calcium transport in the absence of transient receptor potential vanilloid type 6 and calbindin-D9k. *Endocrinology* 2008 Jun;149(6):3196-3205.
25. Eelen G, Valle N, Sato Y, Rochel N, Verlinden L, De Clercq P, Moras D, **Roger Bouillon R**, **Muñoz**, **Verstuyf A**. Superagonistic fluorinated vitamin D3 analogs stabilize helix 12 of the vitamin D receptor. *Chem & Biol*, **15**, 1029-1034 (2008).
26. Wilson S, **Mazzatti DJ**. Current status and future prospects in the search for protein biomarkers of immunosenescence. *Expert Rev Proteomics* 2008 Aug;5(4):561-9.
27. **Mazzatti DJ**, Smith MA, **Oita RC**, Lim FL, White AJ, Reid MB. Muscle unloading-induced metabolic remodeling is associated with acute alterations in PPARdelta and UCP-3 expression. *Physiol Genomics* 2008 Jul 15;34(2):149-61.
28. Larbi A, Franceschi C, **Mazzatti D**, Solana R, Wikby A, Pawelec G. Aging of the immune system as a prognostic factor for human longevity. *Physiology* (Bethesda). 2008 Apr;23:64-74.

29. **Mazzatti DJ**, Malavolta M, White AJ, Costarelli L, Giacconi R, Muti E, Cipriano C, Powell JR, Mocchegiani E. Effects of interleukin-6 -174C/G and metallothionein 1A +647A/C single-nucleotide polymorphisms on zinc-regulated gene expression in ageing. *Exp Gerontol* 2008 May;43(5):423-32.
30. **Mazzatti DJ**, Mocchegiani E, Powell JR. Age-specific modulation of genes involved in lipid and cholesterol homeostasis by dietary zinc. *Rejuvenation Res.* 2008 Apr;11(2):281-5.
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