

NucSys Newsletter,
Issue No. 4. – Bumps on the road
October 2007

All PhD periods have their highs and lows. Probably the highs teach us to enjoy the thrill of discovery and lows teach us to be resilient.

From my first hand experience and subsequently watching my own students I know each phase is important. In my own case I learnt at an early stage the value of labeling all tubes clearly and permanently!

It's important to feel the bumps on the road; to get unanticipated results, or no results, to set the experiment up incorrectly, to throw away the wrong tube, to run out of reagents and to contaminate cells. These experiences probably teach us more about ourselves as researchers and experimentalists compared to when the experiment works first time, and the results are just what the PI has been waiting for.

Of course mistakes are only one serendipitous step away from discovery.

The anecdotes below celebrate these provocative research moments, also known as the bumps on the road, of our ESRs.

Pedro Velica. After spending several weeks cloning Akr1c18 cDNA in an expression vector, transforming bacteria with it, growing them and spending

almost a whole day purifying the his-tagged recombinant protein... nothing came out. After checking the sequence of the vector to confirm the cloning I have now picked a few clones and grew them at different temperatures and will do small preps to understand where the process went wrong.

Gilles Laverny. Technically speaking, my major difficulty is the detection of a small peptide by Western Blot in the seminal fluid and these for many reason. First the viscosity of the fluid lead to some migration problem and in a second time, was difficult to find a good antibody and the good positive control. Well, so far I have just resolved the positive control problem by culturing dendritic cell, and detect the peptide in the supernatant. I have finally found a supplier for the native peptide form, which will permit me to add an other positive control. Others difficulties was presented to me but without all these problems, scientific life will become monotone.

Viola Wöckel. It took us about 6 months to figure out and refine a proper query from our Vitamin D₃ MicroArray. We finally made some decisions on which genes to focus on and tested them via various RT-PCR. The outcome was not

fulfilling! Out of 14 genes we could at least verify 2 genes. One of the genes is PTGS1 which is very well studied in our field and on the other one we planning to do further analysis. Although these results were kind of unexpected but we learned that our 1,5 fold query gave nice bioinformatic results but it was hard to verify them. To solve the problem we loosen the restrictions we made in our query and focus on genes which are more than 2 fold regulated.

Sebastiano Battaglia. I'm now half way through my PhD and I reckon a difficult thing is to let experiments work at the first time. Also, even when they work finely at the beginning it happened that after few months something unpredictable happens and the nice band is not there anymore or the film developed is a total mess or my controls are not the same anymore.

One of the things I learned is that cooperation and modesty are the best allied for a researcher...especially when we are students and have to learn everything. If I see that I'm simply unable to solve a problem that's bugging me there is no reason or "personal pride" in banging my head against a wall and try worthlessly to do work it out by myself.

I've personally seen that a simply chat with someone else, even in front of a nice drink(s), can help to solve almost everything; taking it calmly and being proactive with other people turned out to be the best way of doing that.

Network news.

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



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

Papers

Degenhardt T., Saramäki A., Malinen M., Rieck M., Väisänen S., Huotari A., Herzig KH., Müller M. and Carlberg C. Three members of the pyruvate dehydrogenase kinase gene family are direct targets of the peroxisome proliferators-activated receptor α (2007) *J Mol Biol* 372: 341-355

Heinäniemi M., Uski JO., **Degenhardt T.** and Carlberg C. Meta-analysis of primary target genes of peroxisome proliferator-activated receptors (2007) *Genome Biol.* 8: R147



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

Meeting abstracts

British Association for Cancer Research, Special Conference on

'Diet and Cancer; Susceptibility, prevention and therapy'

June 18/19, Nottingham, UK

Regulation of members of the sirtuin gene family by peroxisome proliferator-activated receptors

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



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

Meeting abstracts

British Association for Cancer Research, Special Conference on

‘Diet and Cancer; Susceptibility, prevention and therapy’

June 18/19, Nottingham, UK

Epigenetic corruption of fatty acid and bile acid signalling in urologic cancers

(Poster prize awarded)



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

Meeting abstracts

The role of akr1c3 on cell survival and differentiation

British Association for Cancer Research, Special Conference on

‘Diet and Cancer; Susceptibility, prevention and therapy’

June 18/19, Nottingham, UK

The Diet and Cancer meeting in Nottingham focused mainly on epidemiological studies that try to find correlations between diet and other daily habits and the incidence of cancer. Some speakers also brought to discussion the chemopreventive effects of some dietary compounds like vitamin D, polyphenols, fibre, etc. It was quite interesting to understand the basis behind some of this population studies even if sometimes the mathematical deductions were somehow hard to follow. The poster session was also very productive.

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



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

Meeting abstracts

ECTS conference 2007 (European Calcified Tissue Society)

New insights into Peroxisome proliferator-activated receptor γ action: Stimulation of human osteoblast differentiation

FEBS course “From molecules to life” 2007

Human osteoblasts as a model to study Peroxisome proliferator-activated receptor γ signalling during differentiation and proliferation using integrative systems-biology approaches



ESR 6: Viola Wöckel (1/07 to 12/09)

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



ESR7: Ellen Wiedemann (9/06 to 8/09)

Team 5, Prof. Westerhoff and Drs. Bruggeman & Bakker, Vrije Universiteit Amsterdam, The Netherlands

ESR8: Katja Rybakova, (7/06 to 6/09)



Papers

Systems Biology towards Life *in silico*: mathematics of the control of living cells. (2007). Journal of Mathematical Biology, Special issue; editor: Luigi Preziosi (In press)

Hans V. Westerhoff, **Alexey Kolodkin**, Stephen J. Wilkinson, **Frank J. Bruggeman**, Klaas Krab, Jacky L. Snoep, Riaan Conradie, Jan H. van Schuppen, Hanna Hardin, **Barbara M.**

Bakker, Martijn J. Moné, **Katja Rybakova**, Marco Eijken & **Hans (J. P.) van Leeuwen**

ESR9: Alexey Kolodkin. (7/06 to 6/09).



Book Chapters

Functional biomimetics in tissue engineering: engineering emergent tissue functions in vitro through complexity and networks science (2007) Petros Lenas, Verónica Saravia, José-Luis Toca-Herrera, José-Luis Paternain, Laertis Ikononou, Joerg Mayer, Irmelin Probst, John Crawford, Christos John Vassilicos, Angel Moreno, Maria Dravaliari, **Alexey Kolodkin**, Antonio Novellino, Ana Guzmán-Aránguez, and Jesus Pintor

Biomimetics in Biophysics: Model systems, experimental techniques and computation. Editor: J.-L. Toca-Herrera, Senior consultant: Edwin Donath (Dept. Medical Biophysics, Leipzig University). (*In press*)

Papers

Systems Biology towards Life *in silico*: mathematics of the control of living cells. (2007). Journal of Mathematical Biology, Special issue; editor: Luigi Preziosi (In press)

Hans V. Westerhoff, **Alexey Kolodkin**, Stephen J. Wilkinson, **Frank J. Bruggeman**, Klaas Krab, Jacky L. Snoep, Riaan Conradie, Jan H. van Schuppen, Hanna Hardin, **Barbara M. Bakker**, Martijn J. Moné, **Katja**

Rybakova¹, Marco Eijken & **Hans (J. P.) van Leeuwen**

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



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

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



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

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



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

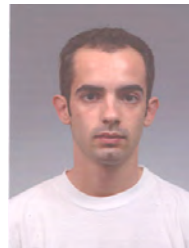
Team 9, Drs. Mazzatti & Mayes, Unilever R&D, United Kingdom

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



Mazzatti DJ, Karnik K, **Oita RC**, and Powell JR. Insulin resistance, chronic inflammation and the link with immunosenescence. In “Handbook on immunosenescence: basic understandings and clinical implications” edited by Dr Tamas Fulop, Dr Graham Pawelec, Dr Claudio Franceschi, and Dr Katsui Hirokawa. *To be published by Springer.*

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



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

Meetings Attended

4th European Course on Biotechnology Ethics - an interactive approach
Vilnius, Lithuania - 20-27 August

In this intensive course, we discussed many aspects related to Bioethics, including scientific integrity and fraud. It was a good exercise working with people with diverse views, like philosophers and theologians.

BioMed Conference on Inflammation and Chronic Disease
Barcelona, Spain - 25-27 June

In this conference, there were a multitude of good speakers, group leaders working in very diverse areas. I was able to contact with scientific work outside the cancer field, like diabetes, cardiovascular disease, etc.

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



ESR 15: Pedro Rocha, (09/06 to 08/09)

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



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

Meetings Attended

British Association for Cancer Research, Special Conference on

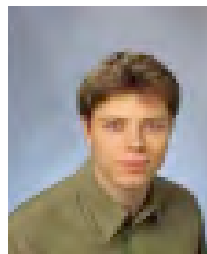
'Diet and Cancer: Susceptibility, prevention and therapy'

June 18/19, Nottingham, UK

Diet and cancer meeting in Nottingham:

High fat and meat diets have been shown to be associated with breast cancer. On the contrary, there is an inverse correlation between fish and fish oil consumption (as a proportion of animal fat) with breast cancer risk. This is probably due to the high level of vitamin D in the fish. Indeed, it has been demonstrated that $1\alpha, 25$ -dihydroxyvitamin D₃ has a protective role against breast cancer. The aim of my PhD is to determine the effect of Vitamin D treatment on VDR target gene expression, in malignant and non malignant breast epithelial cell lines. During this meeting I had a particularly interest in the presentation of Marjo Malinen (from Carsten Carlberg team). It was about her new paper about how HDACs are able to regulate the transcriptional response to $1\alpha, 25$ -dihydroxyvitamin D₃. Our work is close and we had a talk about a possible future collaboration and training for me in her lab in Kuopio to undertake CHIP assays. This meeting gave me a general overview of all the links between diet and cancer.

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



ESR 17: Thomas Nittke, (04/06 to 03/09)

Papers

NUTRITIONAL CALCIUM MODULATES colonic EXPRESSION OF VITAMIN D RECEPTOR AND PREGNANE X RECEPTOR TARGET GENES **Thomas Nittke**, Stephan Selig, **Enikő Kallay**, **Heide S. Cross** (2007) *Molecular Nutrition & Food Research*, (in press)

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



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

Meetings Attended

5th SIICA (*Società Italiana di Immunologia, Immunologia Clinica ed Allergologia*) national Conference at Trieste from the 6th to 9th June 2007. During this meeting I was substituted Guiseppe Penna to make his oral presentation called “Exploiting the Anti-inflammatory potential of VDR Agonists in the treatment of Male Infertility”.

Report of the SIICA meeting.

After this meeting, in my point of view, 2 keys points was treated. first, the role of dendritic cells and/or T regulatory cells and more specifically the FoxP3+ cells in inflammatory disorder, then the regulation system existing between dendritic cells and NK cells. According to my personal research, the satellite synopsis about the diversity of TNF- α blocking agent was useful for a better understanding of inflammatory bowel disease and what expected the

clinician from a potential new therapy.

During the poster session, I got the opportunity to discuss with some researchers which focused on cathelicidin, a member of the antimicrobial family. This was really interesting for me because it's not so often that I can share some technical information concerning the detection of this small peptide and also discussing his potential role in the immune system regulation.

Group Publications 1/1/07 to 30/9/07

Bold = PI

Bold and underlined = ESR

1. Reichrath, J., Lehmann, B., **Carlberg, C.**, Varani, J. and Zouboulis, C.C. Vitamins as hormones. (2007) *Horm. Metab. Res.* **39**, 71-84.

2. **Carlberg, C.**, Dunlop, T.W., Saramäki, A., Sinkkonen, L., Matilainen, M. and Väisänen, S. Controlling the chromatin organization of vitamin D target genes by multiple vitamin D receptor binding sites (2007) *J. Steroid Biochem. Mol. Biol.* **103**, 338-343

3. Saavalainen, K., Tammi, M.I., Bowen, T., Schmitz, M.L. and **Carlberg, C.** Integration of the activation of the human *hyaluronan synthase 2* gene promoter by common cofactors of the transcription factors RAR and NF- κ B. (2007) *J. Biol. Chem.* **282**, 11530-11539

4. Turunen, M.M., Dunlop, T.W., **Carlberg, C.** and Väisänen, S. Selective use of multiple vitamin D response elements underlies the $1\alpha,25$ -dihydroxyvitamin D₃-mediated negative regulation of the human *CYP27B1* gene. (2007) *Nucl. Acids Res.* **35**, 2734-2747

5. Seuter, S., Väisänen, S., Rådmark, O., **Carlberg, C.** and Steinhilber, D. Functional characterization of vitamin D responding regions in the human 5-*lipoxxygenase* gene. (2007) *Biochim. Biophys. Acta* **1771**, 864-872
6. Heinäniemi, M., Uski, J.O., **Degenhardt, T.** and **Carlberg, C.** Meta-analysis of primary target genes of peroxisome proliferator-activated receptors. (2007) *Genome Biol.* **8**, R147
7. Rakhshandehroo, M., Sanderson, L.M, Matilainen, M., Stienstra, R., **Carlberg, C.**, de Groot, P.J., **Müller, M.** and **Kersten, S.** Comprehensive analysis of PPAR α -dependent regulation of hepatic metabolism by expression profiling. (2007). *PPAR Res.* **2007**, 26839
8. Lee, S.S., Crabb, S.J., Janghra, N., **Carlberg, C.**, Williams, A.C., Cutress, R.I., Packham, G. and Hague, A. Subcellular localization of BAG-1 and its regulation of vitamin D receptor-mediated transactivation and involucrin expression in oral keratinocytes: implications for oral carcinogenesis. (2007) *Exp. Cell. Res.* **313**, 3222-3238
9. **Degenhardt, T.**, Saramäki, A., Malinen, M., Rieck, M., Huotari, A., Herzig, K.-H., Müller, R. and **Carlberg, C.** Three members of the human pyruvate dehydrogenase kinase family are direct targets of the peroxisome proliferator-activated receptor β/δ . (2007). *J. Mol. Biol.* **372**, 341-355
10. **Carlberg, C.** and Seuter, S. The vitamin D receptor. (2007) *Dermatol. Clin.* **25**, 515-523
11. Botter SM, van Osch GJ, Waarsing JH, van der Linden JC, Verhaar JA, Pols HA, **van Leeuwen JP**, Weinans H. Cartilage damage pattern in relation to subchondral plate thickness in a collagenase-induced model of osteoarthritis. *Osteoarthritis Cartilage.* 2007 in press
12. Stolk L, van Meurs JB, Jhamai M, Arp PP, **van Leeuwen JP**, Hofman A, de Jong FH, Pols HA, **Uitterlinden AG.** The catechol-O-methyltransferase Met158 low-activity allele and association with nonvertebral fracture risk in elderly men. *J. Clin. Endocrinol Metab.* 2007 92:3206-12.
13. Eijken M, Swagemakers S, Koedam M, Steenbergen C, Derkx P, **Uitterlinden AG**, van der Spek PJ, Visser JA, de Jong FH, Pols HA, **van Leeuwen JP.** The activin A-follistatin system: potent regulator of human extracellular matrix mineralization. *FASEB J.* 2007 21:2949-60
14. de Mos M, Koevoet WJ, Jahr H, Verstegen MM, Heijboer MP, Kops N, van **Leeuwen JP**, Weinans H, Verhaar JA, van Osch GJ. Intrinsic differentiation potential of adolescent human tendon tissue: an in-vitro cell differentiation study. *BMC Musculoskelet Disord.* 2007 8:16
15. Fang Y, van Meurs JB, Rivadeneira F, van Schoor NM, **van Leeuwen JP**, Lips P, Pols HA, **Uitterlinden AG.** Vitamin D receptor gene haplotype is associated with body height and bone size. *J. Clin. Endocrinol. Metab.* 2007 92:1491-501
16. Westbroek I, Waarsing JH, **van Leeuwen JP**, Waldum H, Reseland JE,

- Weinans H, Syversen U, Gustafsson BI. Long-term fluoxetine administration does not result in major changes in bone architecture and strength in growing rats. *J. Cell. Biochem.* 2007; 101:360-8
17. **Bruggeman FJ**, Hornberg JJ, Boogerd FC, **Westerhoff HV**. Introduction to systems biology. *EXS.* 2007; 97:1-19
- 18: Hornberg JJ, **Bruggeman FJ**, **Bakker BM**, **Westerhoff HV**. Metabolic control analysis to identify optimal drug targets. *Prog Drug Res.* 2007; 64:171, 173-89
19. Daran-Lapujade P, Rossell S, van Gulik WM, Lutтик MA, de Groot MJ, Slijper M, Heck AJ, Daran JM, de Winde JH, **Westerhoff HV**, Pronk JT, Bakker BM. The fluxes through glycolytic enzymes in *Saccharomyces cerevisiae* are predominantly regulated at posttranscriptional levels. *Proc Natl Acad Sci U S A.* 2007; 104:15753-8
20. Rossell S, Lindenbergh A, van der Weijden CC, Kruckeberg AL, van Eunen K, **Westerhoff HV**, **Bakker BM**. Mixed and diverse metabolic and gene-expression regulation of the glycolytic and fermentative pathways in response to a HXK2 deletion in *Saccharomyces cerevisiae*. *FEMS Yeast Res.* 2007 in press
21. **Westerhoff HV**. Systems biology: new paradigms for cell biology and drug design. *Ernst Schering Res Found Workshop.* 2007; 61:45-67
22. **Kersten S.** (2007) PPARs and lipoprotein metabolism. *PPAR research.* In press
23. Lichtenstein L, Berbee JFP, van Dijk SJ, Willems van Dijk K, Bensadoun A, Kema, IP, Voshol PJ, **Müller M**, Rensen PCN, **Kersten S** (2007) Angptl4 upregulates cholesterol synthesis in liver by inhibiting LPL- and HL-dependent remnant uptake. *Arterioscler. Thromb. Vasc. Biol.* In press
24. Joosen AM, **Kersten S**, Bakker AK, Westerterp K. (2007) The PPAR γ ligand rosiglitazone influences triacylglycerol metabolism in non-obese males, without increasing the transcriptional activity of PPAR γ in the subcutaneous adipose tissue. *Br. J. Nutr.* In press
25. Rakhshandehroo M, Sanderson L, Zhu W, de Groot P, **Müller M**, **Kersten S.** (2007) Global analysis of gene expression by PPARs in liver: Identification of triglyceride hydrolysis as novel PPAR dependent pathway. *PPAR research.* In press
26. Bunger M, Hooiveld GJ, **Kersten S**, **Müller M.** (2007) Exploration of PPAR functions by microarray technology-A paradigm for nutrigenomics. *Biochim. Biophys. Acta.* In press
27. Duval C, **Müller M**, **Kersten S.** (2007) PPARs and dyslipidemia. *Biochim. Biophys. Acta.* In press
28. Bünge M, van den Bosch H, van der Meijde J, **Kersten S**, Hooiveld G, **Müller M.** (2007) Genome-wide analysis of PPAR α activation in murine small intestine. *Physiol. Genom.* In press
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30. van den Bosch HM, Bünge M, de Groot PJ, van der Meijde J, Hooiveld GJEJ, **Müller M.** Gene expression of transporters and phase I/II metabolic enzymes in murine small intestine during fasting *BMC Genomics* 2007, 8:267

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32. Abass K, Reponen P, Turpeinen M, Jalonen J, **Pelkonen O**. Characterization of diuron N-demethylation by mammalian hepatic microsomes and cDNA-expressed human cytochrome P450 enzymes. *Drug Metab. Dispos.* 2007; 9:1634-41
33. Tolonen A, Petsalo A, Turpeinen M, Uusitalo J, **Pelkonen O**. In vitro interaction cocktail assay for nine major cytochrome P450 enzymes with 13 probe reactions and a single LC/MSMS run: analytical validation and testing with monoclonal anti-CYP antibodies. *J. Mass Spectrom.* 2007; 42:960-6
34. Arpiainen S, Lamsa V, Pelkonen O, Yim SH, Gonzalez FJ, **Hakkola J**. Aryl hydrocarbon receptor nuclear translocator and upstream stimulatory factor regulate Cytochrome P450 2a5 transcription through a common E-box site. *J. Mol. Biol.* 2007; 369:640-5
35. Volotinen M, Turpeinen M, Tolonen A, Uusitalo J, Maenpää J, **Pelkonen O**. Timolol metabolism in human liver microsomes is mediated principally by CYP2D6. *Drug Metab. Dispos.* 2007; 35:1135-41
36. **Pelkonen O**. Metabolism and pharmacokinetics in children and the elderly. *Expert Opin. Drug Metab. Toxicol.* 2007; 3:147-8
37. Turpeinen M, Koivuviita N, Tolonen A, Reponen P, Lundgren S, Miettunen J, Metsarinne K, Rane A, **Pelkonen O**, Laine K. Effect of renal impairment on the pharmacokinetics of bupropion and its metabolites. *Br. J. Clin. Pharmacol.* 2007; 64:165-73
38. Korhonen LE, Turpeinen M, Rahnasto M, Wittekindt C, Poso A, **Pelkonen O**, Raunio H, Juvonen RO. New potent and selective cytochrome P450 2B6 (CYP2B6) inhibitors based on three-dimensional quantitative structure-activity relationship (3D-QSAR) analysis. *Br. J. Pharmacol.* 2007; 150:932-42
39. Biggs JS, Wan J, Cutler NS, **Hakkola J**, Uusimäki P, Raunio H, Yost GS. Transcription factor binding to a putative double E-box motif represses CYP3A4 expression in human lung cells. *Mol. Pharmacol.* 2007; 72:514-25
40. Abu-Bakar A, Lamsa V, Arpiainen S, Moore MR, Lang MA, **Hakkola J**. Regulation of CYP2A5 gene by the transcription factor nuclear factor (erythroid-derived 2)-like 2. *Drug Metab. Dispos.* 2007; 35:78
41. Rahi M, Heikkinen T, Hartter S, **Hakkola J**, Hakala K, Wallerman O, Wadelius M, Wadelius C, Laine K. Placental transfer of quetiapine in relation to P-glycoprotein activity. *J. Psychopharmacol.* 2007; 21:751-756
42. Moilanen AM, **Hakkola J**, Vaarala MH, Kauppila S, Hirvikoski P, Vuoristo JT, Edwards RJ, Paavonen TK. Characterization of androgen-regulated expression of CYP3A5 in human prostate. *Carcinogenesis* 2007; 28:916-21
43. **Mazzatti DJ**, Malavolta M, White AJ, Costarelli L, Giacconi R, Muti E, Cipriano C, Powell JR, and Mocchegiani E. Differential effects of in vitro zinc treatment on gene expression in

peripheral blood mononuclear cells derived from young and elderly individuals. 2007; *Rejuvenation Research*, In press

44. Haase H, **Mazzatti DJ**, White A, Ibs KH, Engelhardt G, Hebel S, Powell JR, Rink L. Differential gene expression after zinc supplementation and deprivation in human leukocyte subsets. 2007 *Molecular Medicine*. In press

45. **Mazzatti DJ**, Karnik K, **Oita RC**, and Powell JR. Insulin resistance, chronic inflammation and the link with immunosenescence. In "Handbook on immunosenescence: basic understandings and clinical implications" edited by Dr Tamas Fulop, Dr Graham Pawelec, Dr Claudio Franceschi, and Dr Katsui Hirokawa. *To be published by Springer*

46. Verlinden L, Vanden Bempt I, Eelen G, Drijkoningen M, Verlinden I, Marchal K, Wolf-Peters C, Christiaens MR, Michiels L, **Bouillon R**, **Verstuyf A** The E2F-Regulated Gene Chk1 Is Highly Expressed in Triple-Negative Estrogen Receptor /Progesterone Receptor /HER-2 Breast Carcinomas. *Cancer Res.* 67:6574-6581, 2007

47. Sanchez-Abella L, Fernandez S, **Verstuyf A**, Verlinden L, Ferrero M, Gotor V: Synthesis and biological evaluation of new 6-s-cis locked 1,2,25-trihydroxyprevitamin D₃ analogues. *Bioorg. Med. Chem.* 15:4193-4202, 2007

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Gamble GD, **Bouillon R**, Reid IR Age-, gender-, and weight-related effects on levels of 25-hydroxyvitamin D are not mediated by vitamin D binding protein. *Clin. Endocrinol.(Oxf)* 67:259-264, 2007

50. Laura González-Santiago, Patricia Alfonso, Yajaira Suárez, Antonio Núñez, Luis F. García-Fernández, Enrique Alvarez, **Alberto Muñoz** and J. Ignacio Casal "Proteomic analysis of the resistance to Aplidin in human cancer cells". *J. Proteomic Res.*, 6, 1286-1294 (2007)

51. Óscar Aguilera, Cristina Peña, José Miguel García, María Jesús Larriba, Paloma Ordóñez-Morán, Diego Navarro, Antonio Barbáchano, Isabel López de Silanes, Esteban Ballestar, Mario F. Fraga, Manel Esteller, Carlos Gamallo, Félix Bonilla, **José Manuel González-Sancho** and **Alberto Muñoz** The Wnt antagonist *DICKKOPF-1* gene is induced by 1 α ,25-dihydroxyvitamin D₃ associated to the differentiation of human colon cancer cells. *Carcinogenesis*, In press (2007)

52. Lechner D, Manhardt T, Bajna E, Posner GH, **Cross HS**. A 24-phenylsulfone analog of vitamin D inhibits 1 α ,25-dihydroxyvitamin D₃ degradation in vitamin D metabolism-competent cells. *J Pharmacol. Exp. Ther.* 2007, 320: 1119-1126

53. Tempfer CB, Bentz EK, Leodolter S, Tscherne G, Reuss F, **Cross HS**, Huber JC. Phytoestrogens in clinical Practice: a review of the literature. *Fertility and Sterility* 2007, 87: 1243-49

54. Krugluger W, Brandstaetter A, **Kállay E**, Schueller J, Krexner E, Kriwanek S, Bonner E, **Cross HS**. Regulation of genes of the circadian clock in human colon cancer: reduced period-1 and dihydropyrimidine

dehydrogenase transcription correlates in high grade tumors. *Cancer Res.* 67:7917-22, 2007

55. **Cross HS.** Extra-renal vitamin D hydroxylase expression and activity in normal and malignant cells: Modification of expression by epigenetic mechanisms and dietary substances (calcium, folate, soy). *Nutrition Reviews* 65: S108-S113, 2007

56. **Nittke T,** Selig S, **Kallay S, Cross HS.** Nutritional calcium modulates colonic expression of vitamin D receptor and pregnane X receptor target genes. *Molecular Nutrition*, in print 2007

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