NucSys Newsletter,

Issue No. 3. – The Journeys Issue

April 2007

If I was going there, I wouldn't start from here….

This is an English phrase, or joke, about the difficulty of getting travel directions from local people. One of the major aims of the NucSys network is to provide the right directions to our ESRs so they develop into some of the leading scientists within Europe. That necessarily includes advice and insight from the lead scientists within the network on the right career choices. Reflecting the above statement, all advice is subjective and has personal bias.

One way around this bias is to seek and reflect continually on advice and insight from multiple individuals, both senior scientists and peers. From the noise, constant themes emerge.

We have the very good fortune in science to be able to use this reflection to continue our intellectual and professional development throughout our careers; this is most definitely not true in the overwhelming majority of careers.

Over the lifetime of the network (which was actually 'born' mid 2005) there has already been a lot of development in its members. For example several of our PI's have been promoted and assumed more responsibility at their host institutes, others now have joint affiliations; for example Carsten Carlberg (Universities of Kuopio and Luxembourg) and Hans Westerhoff (Free University Amsterdam and The University of Manchester) and I will shortly move to Roswell Park Cancer Inst., in the US.

These developments are the end process of much more subtle ongoing daily and weekly developments. In fact, around the network, what appears constant is actually only constant development. I have no doubt that through the course of the remaining 30 months of the network there will be further movements, and developments.

This issue will focus on these career developments, or journeys, and will look at the signposts and evolving destinations. This is a very important issue to the whole Marie Curie training scheme and was recently highlighted in *Nature*[1]

The long and winding road

To illustrate the unpredictable way in which career paths travel, I spoke recently to Bob Goodenow, Ph.D., who is the Chief Business Officer at a new venture capital-funded company called 'Syndax Pharmaceuticals', in San Diego

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[1] Researchers without frontiers, by Vanessa Díaz & Guggi Kofod, Nature Volume 446 Number 7134. http://www.nature.com/naturejobs/2007/070322/full/nj7134-466b.html

M J C *Outline your career path*
BG "I received a bachelor's degree in biochemistry from the University of California at Berkeley and then went to Stanford University Medical Center to get a Ph.D. in Biophysics with Henry Kaplan, MD. Henry pioneered basic research in radiation and cancer around the treatment of Hodgkin's lymphoma. I went to CALTECH to do a post-doctoral fellowship under Lee Hood, M.D. Ph.D. to learn molecular biology and immunology (i.e., cloning and studying class I MHC genes). I was on the faculty at UC Berkeley for 8 years where I continued to work in immunology and expanded into tumor immunology. At that point, I wanted to do something more applied and looked around in academia, but decided to enter industry to learn drug development. I took an industry position with Baxter Biotech where I launched and led R&D for several business initiatives in immunotherapy and gene therapy. This was mostly a "bench to clinic" experience where I had to identify and in-license new exciting opportunities that would expand the company's profile in several strategic areas. I then moved from Baxter to Aventis Corporate Marketing at the launch of Taxotere and help build the oncology franchise. I had to liaise between Sales and R&D to expand market indications and bring new products into the portfolio. Ultimately, I moved into business development at Aventis and really rounded out my skills. In 2001, I decided to apply my craft in a small biotechnology company and moved to Inovio, a small biotechnology firm in San Diego, developing drug-device combinations for cancer therapy and DNA vaccination. As head of Corporate Development, I was responsible for business development, patents, legal affairs and commercialization. In 2007, I moved to Syndax as Chief Business Officer. I've been fortunate to be able to apply my technical skills to influence some business in a lot of different ways. It is certainly challenging, rewarding but fun. I like to learn new things and I've never been disappointed"

MJC *What could academia learn from industry and vice versa?*

BG "In my simplistic view, the scientific community's directed by perceptions regarding the next "burning" question. The latter determines what get's funded so the scientist needs to focus on key questions that will take science to the next level in an incremental fashion. In industry, technology does focus on the frontiers but is more directed because of the commercial focus. From a career standpoint, the distinction in my mind is that academicians are by definition more individualistic. In industry, it's all about the business strategy and teamwork. While an academician is shaped by developments in the field, a scientist in industry can find himself impacted by commercial forces.

That can be difficult to appreciate and learn in transitioning from one to the other. I often meet a lot of people who are more theoretical in their approach and philosophy. I don't think that's as appropriate for industry as it is for academia. My advice to students is that if you're not going to stay in academia then be prepared to be flexible, evolve and grow!"

MJC *What's your biggest current career challenge?*

BG "My current biggest challenge is still strategic i.e., taking a "pleuripotent" technology or product and focusing on the most promising and successful therapeutic applications. It is less about execution than making all the right decisions that could make or break a company down the line. That can be tough as you need to have a "gut feeling" about the likelihood for success with an intimate knowledge of the target disease and its unmet needs".

MJC *If you could change one aspect of your career to date, what would you do differently?*

BG "I struggled a lot about whether or not to go to medical school. I'm still enamored with the notion of impacting medicine and that's why I left academia to work in industry. I think I quickly realized that I wanted to participate at a more global level and that's why I moved into business. But having been at a medical school, I picked up a lot about medicine so I can't say it's hampered me totally. I guess my message to young people is to let your abilities influence your choices but don't ignore the way you approach and look at things because that will become more and more important as you become settled in your career".

MJC *Our network is focused around applying systems biology tools to dissecting nuclear receptor signaling. What is your view of systems biology - is it either the Emperor's new clothes, or the dawn of a new biological era?*

BG "I guess I still grapple with what systems biology is, but I'm not an expert and scientists like Lee Hood can best articulate and advocate for it. I would say that if we were having this discussion 50 years ago we might be talking about physiology, endocrinology or cell biology as capturing the next higher level of organization in understanding complex systems. Then again, today's tools weren't available back then. If you really pressed me, I guess I'd call it more of a viewpoint or approach to thinking about a particular problem. I'm open to the idea that as an approach it may well be or become a "true" discipline for the way it will approach and synthesize problems in biology".

ESRs reflect on the first 12 months in the network

At the other end of the scale, several of our ESRs have now been in the network for approximately 12 months. I've asked Claudia Bruedigam and Tatjana Degenhardt to reflect on the first 12 months

MJC*. What appealed to you about the NucSys network?*

TD: I liked the idea of an interdisciplinary network which offers you a lot of different possibilities to address scientific questions differently, maybe more broad, and it opens your horizon to look at your own data and data of others with different eyes. You are not so limited in your possibilities than other PhD students that mainly work on their own, only using possibilities the own group offers, regarding methods the NucSys network offers much more than one research group can. Consortia, and the combination of different experts in the field of NRs offers the possibility of addressing bigger scientific questions than a normal research group due to a bigger budget and distinct expertise of the different groups.

CB. After I had graduated, I was looking for an international and interdisciplinary research program offering PhD student positions. The Marie Curie Fellows Association took my interest because it strongly supports mobility, which is absolutely necessary for interdisciplinary communication and exchange of knowledge in an international environment.

My special interest for the NucSys network was taken by its aim to integrate systems biology modeling concepts into experimental design and interpretation in human aging-related disease research. I believe that a systems-biological view on mammalian physiology will provide novel insights, and gain more knowledge out of data, which are already available in literature.

MJC. *What extra did you think doing a PhD this way would give you?*

TD. Surely it offers you more contact to other research groups and with that more possibilities for collaborations. Additionally it keeps you more open-minded towards other strategies and approaches. This way you learn more about the whole field of nuclear receptor research and you can put your own research into that bigger picture, which might offer a different understanding and evaluation of the importance your own research.

CB. I thought that doing my PhD as a Marie Curie Fellow would give me more opportunities to discuss my research in an international and interdisciplinary environment. This would give me the possibility to earn knowledge in various fields and hence broaden my scientific view. I also expected to develop further communication skills by discussing and working together with collaborators from the network.

MJC. *At the time you were recruited what did you think you wanted to do after this?*
TD. After achieving the PhD I would like to work in R&D for a pharmaceutical company.

CB. My vision was to stay in scientific research, preferably as a post-doc after this.

MJC. *Has this changed?*

TD. The aim itself has not changed but it has become more explicit. I would not restrict myself to only pharma research anymore.

CB. No

MJC. What's been the most stimulating in the last year?

TD. I think the most stimulating times were the 2 NucSys meetings in Kuopio and Rotterdam and especially also the FEBS advanced course in Gosau, and the Keystone Symposium in Steamboat Springs. It is very nice, interesting and helpful to discuss ideas, hypothesis and models with other students of the network, as well as with people outside the network. The meetings helped me and opened different approaches to reflect about my own research data as well as offering new ideas for possible research projects in the future.

CB. The most stimulating was the first NucSys meeting I attended in Kuopio in June last year.

I was very much looking forward to meet the NucSys partners, and happily surprised. I noticed that the different partners were very interested in the various research projects from the network. The discussions were lively, not only between the principal investigators but also between the PhD students. Overall, the very good organization of the meeting, and the open and friendly atmosphere made it easy to discuss scientific issues, and to exchange ideas for potential collaborations.

MJC. What's been the toughest aspect of the last year?

TD. The toughest aspect...probably the time where I had to think alone about how I want to construct my research project and to develop my own scientific ideas, always a little bit scared to miss certain controls or to mis-interpret my own data, because towards your own data you are not that objective. But that is probably a transition all of us have to go through at one point in our PhD studies.

CB. The toughest aspect of the last year was to define precise research questions which are of high impact for my field, and which can be answered with the technical expertise available. I earned knowledge within my field, and knowledge about the technical possibilities in a relatively short time frame. During scientific meetings and conferences I got so many ideas, but I sometimes later realized that it was too difficult or too laborious to follow them.

Network news.

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

ESR1: Tatjana Degenhardt, (3/06 to 2/09)

Attended meetings

1. 2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

The system of pyruvate dehydrogenase kinases and PPAR signaling

Poster presentation abstract published in abstract book

2. Keystone Symposia: Nuclear Receptors and metabolism Steamboat Springs, CO, USA March 27 - April 1, 2007

Three members of the pyruvate dehydrogenase kinase family are direct targets for PPARs

Poster presentation abstract published in abstract book

Meeting Summary

Keystone Symposium, Nuclear receptors and metabolism.

The most exciting current research on nuclear receptors and metabolism takes a systems approach, utilizing functional genomics, molecular biology, and bioinformatics to understand the role of nuclear receptors in physiology and in the pathophysiology of metabolic diseases such as obesity, diabetes,and metabolic syndrome. The major roadblocks to this research include the biological variation and technical precision of the state-of-art-measures of RNA, protein, and gene occupation by transcription factors, and the ability to accurately relate changes in nuclear receptor ligands and abundance to phenotypic changes. The goal of this meeting is to bring together investigators working on different nuclear receptors, and the regulation of different metabolic pathways, to present the latest and most exciting paradigmatic and technical breakthroughs.

My project for my PhD is based on mainly transcriptional regulation by PPARs, these 3 nuclear receptors play an important role controlling glucose and lipid homeostasis in the body. Misregulation is attributable to changes in the lipid profile, etc. in humans and mice. PPAR ligands, which modify their activity, are already in clinical use, e.g. rosiglitazone that is used to alter insulin senitivity in the patients. The pyruvate dehydrogenase kinases (PDKs) also occupy a strategic role in metabolism, because they regulate the activity of the pyruvate dehydrogenase complex, where nearly 50% of our daily food intake passes through. Once again, linking PPAR-dependent gene regulation tightly to metabolism.

The symposium gave me new insights of mainly metabolic processes that are controlled, not only by PPARs, also by other nuclear receptors and the tight link between gene regulation and phenotypic and disease outcomes. I also learned a lot about new functions of several nuclear receptors in new, formerly a bit ignored tissues.

Technically, you could see the progression away from single gene analysis that are attributable to a nuclear receptor more to whole pathways that are controlled and genome-wide analysis, including the challenges in performing such experiments as well as analyzing them, also using top-down systems biology approaches.

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)

Attended meetings

1. Differentiation Therapy, Paris (Versailles), France, Nov 2006,

Oral presentation, abstract published in abstract book

2. 2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

Poster presentation abstract published in abstract book

Meeting Summary

When during the first NucSys meeting in Kuopio I've heard about System Biology I was a bit confused: what can we really do with that, matching wet lab and math? Alexey and Katija in Rotterdam nicely explained how these two different, but complementary, fields can meet and support each other! I was then galvanized when I landed in Salzburg to finally take part to the 2nd FEBS Advanced Course in System Biology in Gosau; ideally, my aim was to apply what people would have explained to my experiment!

After the first talks I started to be a bit worried about the mathematical background requested; several speakers explained marvelous experiments involving algorithm, software or mathematical functions they developed during their studies, leaving a bit of bitter in my "dreams of glory"!

A huge effort was deposited in modeling yeast and bacterial mRNA production-digestion fluxes, protein-protein interactions, reverse engineering approaches to model cell cycle or "how to deal with the complexity of a "simple" eukaryotic cell", trying to explain in deep the mechanic of these biochemical functions with Ordinary Differential Equation with a lot of unknown parameters. Several scientists then modelled mammalian pathways involved in immunity, phenotypic cell functions, stress response or JAK/STAT signals.

A very interesting talk was hold by Jaroslav Stark (Imperial College, London); they derived a mathematical function used to predict, starting from microarray data and supported by qRT-PCRs, which genes were directly regulated by p53.

This was the talk which better got close to what we are dealing with and several uplifting chats during the poster sessions supported the link between System Biology and molecular biology.

After those days I cannot say that I'm a system biologist but in the other hand I'm getting more familiar with concepts like "robustness" or "noise" and a bit more confident in developing with my own model; differential equations and algorithms are still far, and they will remain like this for awhile, but step by step I'll cope with them as well!

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

Attended meetings

2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

Poster presentation abstract published in abstract book

Developmental Biology, Marburg, - Gesellschaft für Entwicklungsbiologie

21 - 24 March 2007

Meeting Summary

In the Developmental Biology Meeting in Marburg, the speakers talked about their work in a huge variety of models - human cells, mouse, Drosophila, Tribolium and cnidarians. The most interesting subjects, in my point of view and concerning my own research, were related to stem cell differentiation (adult and embryonic stem cells) and the importance of the niche environment, the asymmetric cell division and the polarization as forms of regulating the balance between proliferation and differentiation. It was important (and surprising) to understand how these strategies occur and it's importance. Also a few speakers had very good communication skills and got me following talks about subjects I wasn't that much interested (like axis determination in Drosophila and cnidarians). The social environment was also very relaxing.

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

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

Attended meetings

Dutch society for calcium and bone metabolism 2006 9-10/11/2006

Wetenschapsdagen Goes 11-12/01/2007 Goes, The Netherlands

Poster presentation abstract published in abstract book

2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

Poster presentation abstract published in abstract book

ESR 6: Viola Woeckel (1/07 – 12/09)

Attended meetings

Wetenschapsdagen Goes 11-12/01/2007 Goes, The Netherlands

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)

Attended meetings

BTK meeting: Systems Biology:Redefining BioThermoKinetics, Trakai, Lithuania, September 14-17, 2006

Poster presentation abstract published in abstract book

2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

Poster presentation abstract published in abstract book

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

Attended meetings

BTK meeting: Systems Biology:Redefining BioThermoKinetics, Trakai, Lithuania, September 14-17, 2006

Poster presentation abstract published in abstract book

BioSysBio: Systems biology, bioinformatics, synthetic biology, Manchester, UK, January 11-13, 2007

Poster presentation abstract published in abstract book

Winter school on System Biology for Medical Application, Puerto de la Cruz, Tenerife, Spain, February 27-March 2, 2007

Poster presentation abstract published in abstract book

2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

Poster presentation abstract published in abstract book

Meeting Summary (by Alexey and Katja)

Biothermokinetic (BTK) meeting in Trakai.

Almost 7 months have passed after Biothermokinetic (BTK) meeting in Trakai. But the river of time washes out only the mud from the memory undamaging diamonds of really important and great events.

Now I am opening the book of BTK proceedings and read the date: September 14th- 17th, 2006. It was like yesterday. Again, like in September's days full of sun on the shore of beautiful lake with medieval castle, my attention was captured by the strange cover of book. Picture of tissue,.. and formulas drawn like ancient scripts on the walls of a Stone Age cave …And I listen again the voice of Hans Westerhoff explaining what does mean the picture on the cover of proceedings in the contest of redefining of Biothermokinetics to System Biology.

I am thinking for a while how well this picture symbolises the emergence of my understanding of what is systems biology, and turn several pages forward. Now I can read names and topics of presentation…Jan-Hendrik Hofmeyr, opening lecture: Bottom-up systems biology: from enzyme and pathway to cell…- I was very glad to realize that the biggest part of this concepts considered to be new is already familiar by M.Sc. courses I took in Amsterdam, …Jurgen Haanstra with control and regulation of gene expression in Trypanosoma brucei…- I was proud that such a bright speaker is my colleague with whom we are sharing the same room…Further and further trough names and topics… Already before the meeting, when I was reading a program I could recognise many of these names as famous scientists. I have met them in many publications, but still these names were just a combination of sounds. During the meeting name turned out to be a real people. With him we have discussed model expansion on the board during the cruise on Trakai lake, and she was dancing so nice in the restaurant in Vilnius…Amazing. They all are real people. They seat with me around the table in a Medieval castle. They are joking, talking and between coffee breaks and dinner building the castle of science.

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

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

Attended meetings

2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

Poster presentation abstract published in abstract book

N W O days for Nutrition in the Netherlands (October 2006).

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

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

Gene regulation analysis and ChIP-on-chip Workshops, Espoo 14-15/02/2007

FEBS Advanced Lecture Course on "Systems Biology - From Molecules to Life", Gosau 10-16/03/2007

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

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

2nd FEBS Advance Course on System Biology; from molecules to life. Gosau – Austria – 10th, 16th March 2007

Poster presentation abstract published in abstract book

XIth BELACT meeting 24.11.07

6th annual VIB MicroArray Usergroup meeting in Leuven 13-15.11.06

Meeting Summary

This meeting offered a good opportunity to get familiar with the different suppliers of MicroArray platforms and with different technologies (Array CGH, miRNA Array). The meeting started with a general introduction to MicroArray technology and basic statistics. The remaining talks were given by people that are highly involved in the work with MicroArrays. There was no poster session during this meeting.

It was remarkable to see how many different platforms you can use to get your data. The majority of speakers agreed that the Affymetrix platform is the best to use. A central statement during the meeting was that the used technology gets cheaper over time and that this fact should be used to run more experiments to make statistical analysis afterwards possible and more reliable. This is an important remark also for people involved in Systems biology. Moreover, it should be taken into account that changes in transcriptional regulation, as detected by microarray analysis, are not always reflected by changes in protein levels. Therefore, microarray data should rather be considered as a starting point for further research. The Array CGH technology I consider to be very interesting, because it is relatively easy to detect changes in chromosome copy number at high resolution level. This technique may prove very useful for the detection of DNA aberrations in a wide variety of clinical samples (e.g. cancer, hereditary diseases).

The meeting was a nice opportunity for networking and to hear about improvements in MicroArray technology and related topics.

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

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

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

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

Attended meetings

14th United European Gastroenterology Week. Berlin, Germany, 2006.

Oral and poster presentation, abstract published in abstract book

Meeting Summary The 14th United Europpean Gastroenterology Week (UEGW) was held in Berlin. It was an opportunity to participate again in this congerence that I already knew from Prague 2004. The Berlin UEGW 2006 was a huge conference: 9.955 people registered from 103 countries attended UEGW. It featured 114 sessions and 2.729 abstracts were submitted. I presented 2 oral communications and one poster, concerning genetic susceptibility to celiac disease and colon cancer, respectively. I was very glad because I had the chance to watch the speech made by the recently nobel prize awarded, Dr. Barry Marshall. Also, this conference provided very exciting lectures, like the one made by Dr JeanMarie Houghton about bone marrow derived stem cells in the development of gastric cancer (published on Science).

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

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

***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 1/10/06 to 31/3/07

Bold = PI

Bold = ESR

1. **Degenhardt, T.,** Matilainen M., Herzig, K.-H., Dunlop, T.W. and **Carlberg, C.** The insulin-like growth factor binding protein 1 gene is a primary target of peroxisome proliferator activated receptors. (2006). J. Biol. Chem. 281, 39607–39619

2. Turunen, M.M., Dunlop, T.W., **Carlberg, C.** and Väisänen, S. Selective use of mutiple vitamin D response elements underlies the 1α,25-dihydroxyvitamin D3-mediated negative regulation of the human CYP27B1 gene. (2007) Nucl. Acids Res. *in press*

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-κB. (2007) J. Biol. Chem. 282, *in press*

4. Seuter, S., Väisänen, S., Rådmark, O., **Carlberg, C.** and Steinhilber, D. Functional characterization of vitamin D responding regions in the human 5-lipoxygenase gene. (2007) Biochim. Biophys. Acta *in press*

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

6. **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

7. **Carlberg, C.** and Seuter, S. Vitamin D receptor. (2007) Derm. Clinics. *in press*

8. Anderson MR, Harrison R, Atherfold P, **Campbell MJ**, Darnton SJ, Obszynska J, Jankowski JAZ. (2006). Met receptor signalling in esophageal adenocarcinoma: evidence for effects on cell biology and patient survival. *Clinical Cancer Research* Oct 15;12(20):5936-43.

9. Townsend K, Trevino V, Falciani F, Stewart PM, Hewison M, **Campbell MJ** (2007). Identification of VDR responsive gene signatures in breast cancer cells. *Oncology*. 71:111-123

10. **Campbell MJ** (2007) Staying power. *Nature* 446 (7134): 468

11. Fang, JB van Meurs, F Rivadeneira, NM van Schoor, **JPTM van Leeuwen**, P Lips, HAP Pols , **AG Uitterlinden**. (2007) Vitamin D receptor gene haplotype is associated with body height and bone size. J Clin Endocrinol Metab. 2007 Jan 9;

12. I Westbroek, JH Waarsing, **JPTM van Leeuwen**, H Waldum, JE Reseland, H Weinans, U Syversen, BI Gustafssonl. (2007) Long-term fluoxetine administration does not result in major changes in bone architecture and strength in growing rats. J Cell Biochem. 2006 Dec 12;

13. M van Driel, M Koedam, CJ Buurman, M Hewison, H Chiba, **A G Uitterlinden**, HAP Pols, **JPTM van Leeuwen** (2006) Evidence for auto/paracrine actions of vitamin D in bone: 1a-hydroxylase expression and activity in human bone cells. FASEB J Express,20(13):2417-2419.

14. F Rivadeneira, JB van Meurs, J Kant, MC Zillikens, L Stolk, TJ Beck, P Arp, SC Schuit, A Hofman, JJ Houwing-Duistermaat, CM van Duijn, **JPTM van Leeuwen**, HAP Pols, **A G Uitterlinden**. (2006) Estrogen Receptor beta (ESR2) Polymorphisms in Interaction With Estrogen Receptor alpha (ESR1) and Insulin-Like Growth Factor I (IGF1) Variants Influence the Risk of Fracture in Postmenopausal Women. J Bone Miner Res 21(9):1443-56

15. **Plant, N,** ESTs and SNPs: What large scale sequencing projects can tell us about ADME Xenobiotica (2006) **36:** 860-876

16. **Plant, N.** The human cytochrome P450 3A sub-family: Transcriptional regulation, inter-individual variation and interaction networks. Biochimica et Biophysica Acta – General Subjects (2007) **1770:** 478-488.

17. Pushparajah, P., Umachandran, M., Plant, K., **Plant, N.** and Ioannides C. Evaluation of the precision-cut liver and lung slice systems for the study of induction of CYP1, epoxide hydrolase and glutathione S-transferase activities Toxicology (2007) **231:** 68-80

18. Rivero-Müller, A., De Vizcaya-Ruiz, A., **Plant, N.**, Ruiz, L. and Dobrota, M. Mixed chelate Copper Complex, Casiopeina IIgly, Binds and Degrades nucleic acids: A Mechanism of Cytotoxicity. Chemico-Biological Interactions (2007) **165:** 198-199

19. F.C. Boogerd, **F.J. Bruggeman**, J.-H.S. Hofmeyr and **H.V. Westerhoff**, Edited book: Systems Biology – Philosophical Foundations, 2007, Elsevier, Amsterdam The Netherlands.

20. F.C. Boogerd, **F.J. Bruggeman**, J.-H.S. Hofmeyr and **H.V. Westerhoff**, Towards philosophical foundations of Systems Biology: introduction, IN: Systems Biology – Philosophical Foundations, Eds Boogerd F.C., **Bruggeman F.J**., Hofmeyr J.-H.S. and **Westerhoff H.V.**, 2007, pp. 3-20, Elsevier, Amsterdam – The Netherlands.

21. F.C. Boogerd, **F.J. Bruggeman**, J.-H.S. Hofmeyr and **H.V. Westerhoff**, Afterthoughts as foundations for systems biology, IN: Systems Biology Philosophical Foundations, Eds Boogerd F.C., **Bruggeman F.J.**, Hofmeyr J.-H.S. and **Westerhoff H.V.**, 2007, pp. 321-336, Elsevier, Amsterdam, The Netherlands.

22. **F.J. Bruggeman,** S. Rossell, K. van Eunen, J. Bouwman, **H.V. Westerhoff** and **B. Bakker**. Systems Biology and the reconstruction of the Cell: from molecular components to integral function. IN: Subcellular Fractionation and Proteomics, Eds Bertrand E., and Faupel (2007) in press.

23. **F.J. Bruggeman**, J.J. Hornberg, F.C. Boogerd and **H.V. Westerhoff**, Introduction to Systems Biology, IN: Plant Systems Biology, Experientia Supplementum, Vol 97, S. Baginsky and A.R. Fernie Eds.2007, in press.

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