NucSys Newsletter,

Issue No. 2. – The training issue

October 2006

The main focus of this Newsletter is to highlight the key features of the training programme. Currently PhD training standards amongst EC member states are different, with variation in time spent registered and undertaking research (between 3 and 5 years), the level of formal taught courses and the number of published papers.

The European Credit transfer system is central to ESR training in NucSys.

The NucSys network aims to apply a harmonized training standard to all the ESRs built around the concept of the European Credit Transfers (ECTS).

The network will use the Finnish system as a guide where a PhD would be made up of 60 ECTS, with each ECT being made up of 20 hours of student's time, and aim to deliver, ultimately, 3 or 4 papers. In practice it is most likely that the 60 ECTS will contain components from courses attended prior to entry to the Network, and others in the write-up period after the 36 month research contract has finished; for example relevant Masters courses and specialist workshops.

There are difficulties in applying these standards, even within our network, and so Mieke Verstuyf (KUL) and Heide Cross (WIE) will oversee the development of individual training plans of all ESRs and co-ordinate training opportunities within the network.

To accumulate ECTS the network has provided four core courses, which all ESRs are expected to attend, with each course being worth 5 ECTS. To accumulate the remaining 40 ECTS, these core course will be complimented by

- winter and summer NucSys meeting: 1 ECT each (2 ECTS per year x 3 year = 6 ECTS)
- Conferences (for example a congress of 4-5 days): 2 ECTS
- Oral presentation on a congress: 1 ECT
- Poster presentation: 0.5 ECT
- Workshop of 2 days: 1 ECT
- Publication first author: 2 ECTS
- Publication co-author: 1 ECT
- Departmental seminars: 1 ECT
- Local courses (academic writing, general cell biology course, biosafety laboratory animals, bioinformatics)

Four core courses are provided for ESRs

1. Systems Biology, Lead: Hans Westerhoff (VU). 10-16th of March 2007. Gasuo, Austria

Second FEBS Advanced Course on Systems Biology: From Molecules To Life. This is a follow up of the highly successful

first Advanced Lecture Course on Systems Biology, which was held in March 2005. The deadline for application is 20th of November (http://www.febssysbio.net/)

2. **Physiomics**, Lead: Heinrich Schrewe (MAX). Mouse embryonic stem cell culture training course 07-12 May 2007 and May 2008, Berlin, Germany.

Courses in ES technology to be held at the Max Planck-Institute. This cutting edge week-long course is very focussed on the practical aspects of murine transgenic approaches and therefore only 9 students can take part per session. The deadline for registration is 31/12/2007, contact schrewe@molgen.mpg.de

3. Metabolomics, Leads: Moray J. Campbell, Chris M. Bunce (BIR) and Nick Plant (UniS). June 13-19 2007. Birmingham, UK

This workshop is a combination of educational lectures in metabolomics from leaders in the field, 'hands-on' practical demonstrations and research seminars, and includes the annual summer school meeting of the network. Importantly a vital component of this meeting will be a 2 day international meeting on Diet and Cancer. Contact m.j.campbell@bham.ac.uk

4. Transcriptomics, theory and practice, Lead: Carsten Carlberg (KUO). These courses run annually in October and have a range of flexible options to tailor the taught component to match the specific ESR research project. Contact carsten.carlberg@uni.lu

Esatblish a career development plan (CDP).

Training within the NucSys network is flexible and reflects the need of ESR to build on shared, core components to develop and pursue specialist interests. Central to monitoring this development is the generation of a CDP for each ESR.

A form to guide and log the development of the CDP is available at the NucSys website (http://www.uku.fi/nucsys/). The form includes sections to address core courses attended, specialist workshops, and the possibility of identifying what other training needs are possible and where these may be met (both within NucSys and more generally).

Network Recruitment.

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

ESR1: Tatjana Degenhardt, (04/2006 to 03-2009)

ESR2: to be recruited during 2006

Team 2, Dr. Moray J. Campbell, Dr. Chris Bunce, University of Birmingham, UK

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

ESR4: Pedro Velica, Microbiology and Genetics Degree, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal. 1 year Leonardo Da Vinci research training period, Imperial College London, UK. (9/06 to 8/09)

Team 3, Dr. Johannes P.T.M. van Leeuwen, Erasmus University Medical Centre, Rotterdam The Netherlands

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

ESR 6: to be recruited during 2006

Team 4, Prof. Peter Goldfarb, Prof. Gordon Gibson, Dr. Nick Plant, University of Surrey, United Kingdom

ESR7: Ellen Wiedemann, MSc degree in Biochemistry, University of Bayreuth, Germany. (9/06 to 8/09)

Team 5, Prof. Hans V. Westerhoff, Dr. Barbara M. Bakker, Vrije Universiteit Amsterdam, The Netherlands

ESR8: Katja Rybakova, Master of Science in Biochemistry, Moscow State University, Moscow, Russia

ESR9: Alexey Kolodkin. BSc Department of Biology, Irkutsk State University, Russia and M.Sc in Chemical Engineering at University of Rovira i Virgili, Spain.

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

ESR 10: Anastasia Georgiadi. MSc diploma: Health and Nutrition/ Molecular Nutrition (specialization). Greece. (08/06 to 07/09)

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

ESR 11: Marcin Buler Master of Biology, University of Warsaw, Poland 1/07 to 12/09

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

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

Team 9, Dr. Andrew Mayes, Unilever R&D, United Kingdom

ESR13: to be recruited during 2006

Team 10, Prof. Alberto Muñoz, Dr. José M. González-Sancho, Instituto de Investigaciones Biomédicas, Spain

ESR 14: Fabio Pires, MSc Nutrition Sciences, Faculty of Nutrition and Food Sciences, University of Porto, Portugal. (10/06 to 09/09)

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

ESR 15: Pedro Rocha, Microbiology and Genetics Degree, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal. 1 year Leonardo Da Vinci research training period, Max-Planck Institute for Molecular Biology, Berlin, Germany. (09/06 to 08/09)

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

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

Team 13, Prof. Heide S. Cross, Prof. Eniko Kallay, Prof. Therese Thalhammer, Medical University of Vienna, Austria

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

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

ESR 18: Gilles Laverny, Pharmacology (MSc) University Louis Pasteur, Strasbourg (10/06 to 09/09)

Group Publications 1/1/06 to 31/3/06

1. **Carlberg C**, Dunlop TW. The impact of chromatin organization of vitamin D target genes. Anticancer Res. 2006 Jul-Aug;26(4A):2637-45..

2. **Carlberg C**, Molnar F. Detailed molecular understanding of agonistic and antagonistic vitamin D receptor ligands. Curr Top Med Chem. 2006;6(12):1243-53.

3. Sorg BL, Klan N, Seuter S, Dishart D, Radmark O, Habenicht A, **Carlberg C**, Werz O, Steinhilber D. Analysis of the 5-lipoxygenase promoter and characterization of a vitamin D receptor binding site. Biochim Biophys Acta. 2006 Jul;1761(7):686-97.

4. Molnar F, Perakyla M, Carlberg C. Vitamin D receptor agonists specifically modulate the volume of the ligand-binding pocket. J Biol Chem. 2006 Apr 14;281(15):10516-26.

5. Abedin SA, Banwell CM, **Colston KW**, **Carlberg C**, **Campbell MJ**. Epigenetic corruption of VDR signalling in malignancy. Anticancer Res. 2006 Jul-Aug;26(4A):2557-66.

6. **Campbell MJ**, **Adorini L**. The vitamin D receptor as a therapeutic target. Expert Opin Ther Targets. 2006 Oct;10(5):735-48.

7: **Colston KW**, Lowe LC, Mansi JL, **Campbell MJ**. Vitamin D status and

breast cancer risk. Anticancer Res. 2006 Jul-Aug;26(4A):2573-80.

8: Banwell CM, MacCartney DP, Guy M, Miles AE, Uskokovic MR, Mansi J, Stewart PM, O'Neill LP, Turner BM, **Colston KW**, **Campbell MJ**. Altered nuclear receptor corepressor expression attenuates vitamin D receptor signaling in breast cancer cells. Clin Cancer Res. 2006 Apr 1;12(7 Pt 1):2004-13.

9. 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, AG 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.

10. T Nijenhuis, BCJ van der Eerden, U Zügel, A Steinmeyer, H Weinans, JGJ Hoenderop, **JPTM van Leeuwen**, RJM Bindels (2006) The novel vitamin D analog ZK191784 as an intestine-specific vitamin D antagonist. FASEB J first published on August 25, 2006 as doi:10.1096/fj.05-5155fje.

11. SM Botter, GJ van Osch, JH Waarsing, J Day, JA Verhaar, HA Pols, **JPTM van Leeuwen**, H Weinans. (2006) Quantification of subchondral bone changes in a murine osteoarthritis model using micro-CT. Biorheology. 43(3-4):379-388

12. **AG Uitterlinden**, SH Ralston, ML Brandi, AH Carey, D Grinberg, BL Langdahl, P Lips, R Lorenc, B Obermayer-Pietsch, J Reeve, DM Reid, A Amidei, A Bassiti, M Bustamante, LB Husted, A Diez-Perez, H Dobnig, AM Dunning, A Enjuanes, A Fahrleitner-Pammer, Y Fang, E Karczmarewicz, M Kruk, **JPTM van Leeuwen**, C Mavilia, JB van Meurs, J Mangion, FE McGuigan, HA Pols, W Renner, F Rivadeneira, NM van Schoor, S Scollen, RE Sherlock, JP Ioannidis; APOSS Investigators; EPOS Investigators; EPOLOS Investigators; FAMOS Investigators; LASA Investigators; Rotterdam Study Investigators; GENOMOS Study. (2006) The association between common vitamin D receptor gene variations and osteoporosis: a participant-level meta-analysis. Ann Intern Med. 145(4):255-264.

13. M van Driel, M Koedam, CJ Buurman, M Roelse, F Weyts, H Chiba, **AG Uitterlinden**, HAP Pols, **JPTM. van Leeuwen** (2006) Evidence that both 1α,25-dihydroxyvitamin D_3 and 24-hydroxylated D_3 enhance human osteoblast differentiation and mineralization. J Cell Biochem, Jun 1.

14. JH Jansen, H Jahr, JA Verhaar, HA Pols, H Chiba, H Weinans, **JPTM van Leeuwen**. (2006) Stretch-induced modulation of matrix metalloproteinases in mineralizing osteoblasts via extracellular signal-regulated kinase-1/2. J Orthop Res. 24(7):1480-1488.

15. M van Abel, S Huybers, JG Hoenderop, AW van der Kemp, **JPTM van Leeuwen**, RJ Bindels. (2006) Age-dependent alterations in Ca2+ homeostasis: role of TRPV5 and TRPV6. Am J Physiol Renal Physiol. 2006 May 16;

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17. Lewis DF, Ito Y, **Goldfarb PS**. Investigating human P450s involved in drug metabolism via homology with high-resolution P450 crystal structures of the CYP2C subfamily. Curr Drug Metab. 2006 Aug;7(6):589-98.

18. **Gibson GG**, Phillips A, Aouabdi S, Plant K, **Plant N**. Transcriptional regulation of the human pregnane-X receptor.Drug Metab Rev. 2006;38(1-2):31-49.

19. Plant KE, Everett DM, **Gibson G**, Lyon J, **Plant NJ**. Transcriptomic and phylogenetic analysis of Kpna genes: a family of nuclear import factors modulated in xenobiotic-mediated liver growth. Pharmacogenet Genomics. 2006 Sep;16(9):647-58.

20. **Plant N.** Use of reporter genes to measure xenobiotic-mediated activation of CYP gene transcription. Methods Mol Biol. 2006;320:343-54.

21. Snoep JL, **Westerhoff HV**, Rohwer JM, Hofmeyr JH. Is there an optimal ribosome concentration for maximal protein production? Syst Biol (Stevenage). 2006 Sep;153(5):398-400.

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23. Conradie R, **Westerhoff HV**, Rohwer JM, Hofmeyr JH, Snoep JL. Summation theorems for flux and concentration control coefficients of dynamic systems. Syst Biol (Stevenage). 2006 Sep;153(5):314-7.

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31. Schepens W, Van Haver D, Vandewalle M, **Bouillon R**, **Verstuyf A**, De Clercq PJ. Synthesis of Spiro[4.5]decane CF-Ring Analogues of 1alpha,25-Dihydroxyvitamin D(3). Org Lett. 2006 Sep 14;8(19):4247-50.

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41. Aust S, Brucker B, Graf J, Klimpfinger M, **Thalhammer T.** Melatonin modulates acid/base transport in human pancreatic carcinoma cells. Cell Physiol Biochem. 2006;18(1-3):91-102.

42. **Cross HS**, Lipkin M, **Kallay E**. Nutrients regulate the colonic vitamin D system in mice: relevance for human colon malignancy. J. Nutr. 136: 561-4, 2006.

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44. **Cross HS.** Commentary: from epidemiology to molecular biology – vitamin D and colorectal cancer prevention. Int J Epidemiol 35: 225-7, 2006.

45. Maggi M, Crescioli C, Morelli A, Colli E, **Adorini L**. Pre-clinical evidence and clinical translation of benign prostatic hyperplasia treatment by the vitamin D receptor agonist BXL-628 (Elocalcitol).J Endocrinol Invest. 2006 Jul-Aug;29(7):665-74.

46. Penna G, Mondaini N, Amuchastegui S, Degli Innocenti S, Carini M, Giubilei G, Fibbi B, Colli E, Maggi M, **Adorini L**. Seminal Plasma Cytokines and Chemokines in Prostate Inflammation: Interleukin 8 as a Predictive Biomarker in Chronic Prostatitis/Chronic Pelvic Pain Syndrome and Benign Prostatic Hyperplasia. Eur Urol. 2006 Jul 28;

47. **Adorini L**, Daniel KC, Penna G. Vitamin D receptor agonists, cancer and the immune system: an intricate relationship. Curr Top Med Chem. 2006;6(12):1297-301.

48. Uskokovic MR, Manchand P, Marczak S, Maehr H, Jankowski P, **Adorini L**, Reddy GS. C-20 cyclopropyl vitamin D3 analogs. Curr Top Med Chem. 2006;6(12):1289-96.

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G, Maggi M, Baldi E. The vitamin D analogue BXL-628 inhibits growth factor-stimulated proliferation and invasion of DU145 prostate cancer cells. J Cancer Res Clin Oncol. 2006 Jun;132(6):408-16.

Patents

1. "Vitamin D3 in Chronic Prostatitis"

Inventors: Giuseppe PENNA; **Luciano ADORINI**

Application Date and No.: 30/09/2005 - PCT/EP2005/054965

Published on: 06/04/2006

2. "1,25-DIHYDROXY,20-CYCLOPROPYL, 26,27-ALKYL/HALOAKYL VITAMIN D3 COMPOUNDS AND USES THEREOF"

Inventors: Stanislaw MARCZAK; Giuseppe PENNA; **Luciano ADORINI**; Milan Radoje USKOKOVIC; Enrico COLLI

Application Date and No.: 23/09/2005 - PCT/US2005/034213

Published on: 06/04/2006

3. "Compound and use in treatment (BXL-628 in BPH)"

Inventors: ADORINI Luciano; COLLI Enrico

Granted in: Belgium (04/07/2006)
France (28/04/2006)
Portugal (19/07/2006)

Landmark or provocative papers published by other groups in the same period

Important papers:

1. Bookout A. L., Jeong Y., Downes M., Yu R. T., Evans R. M. and Mangelsdorf D. J. (2006) Anatomical profiling of nuclear receptor expression reveals a hierarchical transcriptional network. *Cell* 126, 789-799

Yang X., Downes M., Yu R. T., Bookout A. L., He W., Straume M., Mangelsdorf D. J. and Evans R. M. (2006) Nuclear receptor expression links the circadian clock to metabolism. *Cell* 126, 801-810.

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Systems Biology, Incorporated? http://www.nature.com/nbt/journal/v24/n9/pdf/nbt0906-1055.pdf