

COST

Domain Committee Food and Agriculture

COST Action FA1201

Start Date 01 February 2013

Epigenetics and Periconception Environment

MONITORING PROGRESS REPORT

Reporting Period: *from 01 February 2013 to 01 June 2014*

This Report is presented to the relevant Domain Committee.
It contains three parts:

- I. Management Report*** prepared by the COST Office/Grant Holder
- II. Scientific Report*** prepared by the Chair of the Management Committee of the Action
- III. Previous versions of the Scientific Report; i.e., part II of past reporting periods***

The report is a 'cumulative' report, ie it is updated annually and covers the entire period of the Action.

Confidentiality: the documents will be made available to the public via the COST Action web page except for chapter *II.D. Self evaluation*.

Based on the monitoring results, the COST Office will decide on the following year's budget allocation.

Executive Summary (max 250 words):

Parental stress before, during and after conception (ie the periconception period) induces epigenetic changes in gametes and embryos. Such epigenetic changes may adversely affect the future health, development, productivity and fertility of those offspring. While there is increasing evidence for this in agricultural species, most of this knowledge derives from epidemiological studies in humans and controlled studies in laboratory animals. In this COST Action, time frames and mechanisms during which the gametes and early embryo are susceptible to epigenetic modifications will be determined in livestock in order to optimize their health and productivity. This COST Action will identify stressors and molecules which induce, modulate or remove epigenetic marks on genes that are relevant for different applications in farm animals. Public engagement activities are planned during the COST Action to inform the general public on the importance of the epigenome via the periconception environment in future food production, health and welfare.

I. Management Report prepared by the COST Office/Grant Holder



I.A. COST Action Fact Sheet

COST Action FA1201 – Epigenetics and Periconception Environment

Domain Food and Agriculture

Action details:

CSO Approval: 07 June 2012

End date: 03 October 2016

Entry into force: 04 October 2012

Extension:

Objectives

1. Develop an epigenomic toolbox for large scale screening of epigenetic changes in gametes and embryos.
2. Define the factors that can influence the epigenetic profile during the periconceptional period of gametes and embryos.
3. Define the time-window during which most epigenetic changes take place
4. Define the range of the optimal periconception environments to ensure healthy offspring.
5. Compare the susceptibility of different species (livestock, poultry, fish) and different model systems (*in vivo* vs *in vitro*) to epigenetic disturbances.
6. Interact with stakeholders and artificial insemination industry to improve breeding and gamete/embryo handling.

Parties: List of countries and date of acceptance

Austria	16/07/2012
Belgium	13/06/2012
Bulgaria	26/09/2012
Croatia	27/08/2012
Czech Republic	25/04/2013
Denmark	04/07/2012
Estonia	20/06/2012
Finland	29/08/2012
France	19/09/2012
Macedonia	28/06/2012
Germany	06/07/2012
Greece	29/08/2012
Hungary	25/06/2012
Ireland	04/07/2012
Israel	27/06/2012
Italy	01/08/2012
Lithuania	03/10/2012
Netherlands	17/07/2012
Norway	30/08/2012
Poland	06/07/2012
Portugal	21/08/2012
Romania	05/03/2013
Slovakia	02/09/2012
Spain	25/06/2012
Sweden	20/09/2012
Switzerland	16/07/2012
Turkey	27/07/2012
United Kingdom	14/06/2012

Intentions to accept: *(List of countries and date)*

Argentina	01/04/2014

Other participants: *(Institution Name, Country, Town)*

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Action Web site: www.cost-epiconcept.eu

Grant Holder Representative: Alireza Fazeli, United Kingdom (a.fazeli@sheffield.ac.uk)

Working Groups: *(List of WGs and names and affiliations of participants)*

Working Group 1 – Epigenomic Tools

Lead – Dr Trudee Fair, Ireland
Deputy – Dr Alfonso Gutierrez, Spain

Working Group 2 – Periconception Environment

Lead – Prof Kevin Sinclair, United Kingdom
Deputy – Dr Anne Navarrette-Santos, Germany

Working Group 3 – Cross-Species Epigenetics, Gametogenesis and Embryogenesis

Lead – Dr Amos Tandler, Israel
Deputy – Prof Pascale Chavatte-Palmer, France

Working Group 4 – Public, Periconception and Epigenome

Lead – Prof Tiziana Brevini, Italy
Deputy – Prof Anita Franczak

I.B. Management Committee member list

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I.C. Overview activities and expenditure

2013-2014 Budget

Category	Total
	EUR
Action Budget	244000
Remaining Action Commitment	60000
Action Expense	184000

Conferences

Title	Date	Place	Cost	Total
			EUR	EUR
Conference 2013	2013-04-24 – 2013-04-25	Antalya, Turkey, TY	69344	
				69344

Workshops

Title	Date	Place	Cost	Total
			EUR	EUR
Workshop 2013	2013-10-14 – 2013-10-14	Sant Feliu de Guixols; Spain	48227	
				48227

Short Term Scientific Missions

Beneficiary	Date	Place		Cost	Total
		From	To		
Action Members	2013-02-01 – 2013-06-01	Guest	Host	31424	
					31424

Schools

Title	Date	Place	Cost	Total
			EUR	EUR
				0

Dissemination

Title	Date	Place	Cost	Total
			EUR	EUR
Website Maintenance	2013-05-03	Sheffield, United Kingdom, GB	1125	
Publicity Leaflet	2014-09-28		1500	
				2625

General Support Grants

Beneficiary	Date	Cost	Total
		EUR	EUR
			0

II. Scientific Report prepared by the Chair of the Management Committee of the Action, describing results achieved during the Action operation in this period, in no more than 3 pages (the report is “cumulative”). All items listed in Sections A, B, and C, below, must be addressed.

Additional documentation such as extended scientific reports, proceedings of workshops, seminars or conferences may be provided separately as an annex to this report, and should be referenced in the report.

II.A. Innovative networking

Innovative knowledge resulting from COST networking through the Action.

- We have shown that fertilization with heat stressed sperm cause changes in de-methylation of paternal pronuclei of bovine zygotes (Rahman et al., *Reprod Fertil Dev* doi10.1071/RD13218)
- We have developed a new staining for methylation: Heras S, Forier K, Rombouts K, Braeckmans K, Van Soom A (2014) DNA counterstaining for methylation and hydroxymethylation immunostaining in bovine zygotes. *Analytical biochemistry* in press

Significant scientific breakthroughs as part of the COST Action. (Specific examples)

- We have developed a new protocol for the direct epigenetic conversion of one cell type into another avoiding a stable pluripotent state and the use of any gene transfection (Pennarossa G, Maffei S, Campagnol M, Tarantini L, Gandolfi F, Brevini TA. Brief demethylation step allows the conversion of adult human skin fibroblasts into insulin-secreting cells. *Proc Natl Acad Sci U S A*. 2013 May 28;110(22):8948-53. doi: 10.1073/pnas.1220637110).

Tangible medium term socio-economic impacts achieved or expected. (Specific examples)

- We have informed veterinarians about Epiconcept at a one day meeting (24 October 2012) (Van Soom, BE).
- We have informed secondary school children about Epiconcept at a two day meeting (Week of Science) (22-23 november 2012)(Ann Van Soom-Ghent University, Belgium)
<http://www.wetenschapsweek.be/indexiker/search.asp?action=detail&id=1224&orgid=261>
- Ann Van Soom has taught in an Epigenetics course in Murcia (Spain) in collaboration with Prof. Pilar Coy: “What is epigenetics and how can it be studied” (3rd June 2013)
- Ann Van Soom has taught in a Biotechnology course in Bari (Italy) in collaboration with Professor Elena Del’Aquila: “What is epigenetics and how can it be studied” (12 December 2013)
- Two lectures about the scientific topic of the COST action Epiconcept within “Seniorenkolleg” MLU, Halle Germany (<http://www.seniorenkolleg.uni-halle.de/>) and “Kinderuni” MLU, Halle (<http://www.kinderuni.uni-halle.de/>) held by Dr. Navarrete Santos (Halle, Germany)
- Alfonso Gutierrez-Adan has taught in an Epigenetics course in Murcia (Spain) in collaboration with Prof. Pilar Coy: “Epigenetic mechanisms involved in embryonic development” (5th June 2013)
- As invited speaker Alfonso Gutierrez-Adan has thanked and informed about Epiconcept in 39th Annual Conference of the International Embryo Transfer Society (IETS), Hanover, Germany, January 19-23, 2013; 11th Annual transgenic technology meeting 2013 (TT2013). International Society for Transgenic Technologies (ISTT), February 28-March 2, 2013, Guangzhou/Canton, P.R. China; CARD-CNB MOUSE SPERM AND EMBRYO CRYOPRESERVATION workshop. Spanish National Centre for Biotechnology (CNB-CSIC), Madrid, Spain, 7 - 11 October 2013.
- The MC of Larvanet (FA0801) was informed of Epiconcept at its last meeting in November 2012, in Rome, Italy (Amos Tandler, Israel)
- We have informed the public about Epiconcept during a Polish one day meeting called “Night of Biologists”, Olsztyn, Poland, 2013 Jan 11 (poster presentation) (PL) (Anita Franczak)
- We have informed all Departments of Biology in Poland about Epiconcept FA1201 (PL).
- We have informed the public about Epiconcept during an Italian one day meeting called “Meet-me-tonight”, Milan, Italy, 28 September 2012 (<http://www.meetmetonight.it/>) (IT) (Tiziana Brevini and F Gandolfi)
- COST to COST networking at Food for Feed Conference, 19 February 2013 (IT)
- Open day, 21 February 2013 (IT- Milan)
- High School Ambassador, 15 March 2013 (IT-Milan)

- Bernard Roelen (NL) has taught and informed about EpiConcept at the Faculty of Biology of the University of Lisbon (Portugal) (host Gabriela Rodrigues), (28 Jan-1 Feb 2013).
- Unimi Open day, 17 February 2014 (IT-Milan)
- High School Ambassador, 14 March 2014 (IT-Milan)
- We have informed the public about Epiconcept during an Italian one day meeting called “Meet-me-tonight”, Milan, Italy, 27 September 2013 (<http://www.meetmetonight.it/>) (IT) (Tiziana Brevini and F Gandolfi).
- Tiziana A.L. Brevini informed the scientific public about our Epiconcept Action during the Cell Transplantation Society (CTS) meeting in Milan (July 2013).
- We have informed the public about Epiconcept at a one night meeting called “ScientificaMente”, 31 January 2014.
- We have promoted our action at Unistem Day, Europe united by Science on 14 March 2014 (<http://users2.unimi.it/unistem/index.php/unistemday2014>)

Spin off of new EC RTD Framework Programme proposals/projects. (List)

- Project EpiHealth (FP-7 N°278418): Linking perturbed maternal environment during periconceptional development, due to diabetes, obesity or assisted reproductive technologies, and altered health during ageing. Coordinator : Prof. Andras Dinnyes, all members are partner of COST EpiConcept, links: http://ec.europa.eu/research/health/medical-research/human-development-and-ageing/projects/epihealth_en.html; <http://epihealth.biotalentum.eu/>
- Marie Curie Initial Training Networks (EpiHealthNet) (EU, FP7 2012 – 2016) Coordinator: Prof. Andras Dinnyes, all partners are part of COST EpiConcept

II.B. Inter-disciplinary networking

Additional knowledge obtained from working with other disciplines within the COST framework. (Specific examples)

- Ignacio Caballero Posadas (ESR from UK) represented our COST Action at a TRANS COST meeting in Amsterdam, the Netherlands on 29 november 2012. His report will appear in the newsletter.
- Ann Van Soom, Alireza Fazeli as chair and vice chair and ESRs Nathalie Beaujean, Georgios MICHAILDIS and Bernard Roelen attended a workshop on 14-15 Feb.2013 in Brussels, Belgium, where COST Actions met with the FP7 consortia and high level policy makers. The field of interest was epigenetics as there are several consortia in FP7 dealing with various aspects of epigenetics. This was informative for all of us and ended in new contacts e.g with Sasa Jenko, who attended our first Annual meeting in Antalya, Turkey 24-25 april 2013
- A COST Workshop on Genomics and Epigenetics held in Brussels in February has been helpful for networking and establishing collaborations. As a result, Bernard Roelen (NL) and Ann Van Soom (BE) were invited as a speaker on the COST meeting on Developmental Origins of Chronic Lung Disease in Munich from 13-15 June 2013 (Host S. Krauss_Etschmann).
- In addition as a result of the workshop Bernard Roelen (NL) was invited as a speaker at an IDEAL satellite meeting in Oxford (UK) Sept 12-13 (Host Tobias Uller).
- Bernard Roelen (NL) is member of the Executive Board of the Dutch Society for Developmental Biology (new contacts for EPICONCEPT)
- Ann Van Soom, Fulvio Gandolfi and Pascale Chavatte-Palmer are members of the Board of Governors of IETS (new contacts for EPICONCEPT)
- Jo Leroy, Dimitrios Rizos and Urban Besenfelder are members of the Board of Governors of AETE (new contacts mainly with practice and industry)
- Tiziana A.L. Brevini represented our COST Action (FA1201) at Domain's Annual Progress Conference (APC) in Jerusalem (Israel), (July 2013).

Evaluation of whether the level of inter-disciplinarity is sufficient to potentially provide scientific impacts. (Specific examples)

- *Too early to say.*

Evaluation of whether the level of inter-disciplinarity is sufficient to potentially provide socio-economic impacts. (Specific examples)

- *Too early to say.*

II.C. New networking

Additional new members joining the Action during its life

Argentina has joined the Action.

Total number of individual participants involved in the Action work. (Number of participants. Give % of female and of Early Stage Researcher participants)

Total number of participants is 351.

The gender distribution is 50% male (175) and 50% female (176) in all Action Members (351).

The gender distribution is 46% male (24) and 54% female (28) in the Management Committee (52).

Involvement of Early Stage Researchers in the Action, in particular with respect to STSMs, networking activities, and Training Schools. In addition, justification should be provided if less than 4 STSMs were carried out during the year.

- See website EPICONCEPT <http://cost-epiconcept.eu/2013.html>
- 16 STSMs were awarded to ESR so far (8 females, 8 males)

Involvement of researchers from outside of COST Countries. (Number of participants from non-COST Countries approved by the CSO. Give % of such participants from countries with reciprocal agreements. Specify their contribution)

- We have very good contact with Canadian Researchers MA Sirard and CL Robert and their Embryogene research programme (see website <http://embryogene.ca>)
- They were invited at our Annual meeting to present their research but due to a strike of Lufthansa end of April 2013 they could not attend. They have made a presentation which was put on our website.
- Some of our members attended the Embryogenomics meeting in Canada 7-10 October 2013 (see programme <http://embryogenomics2013.fsa.ulaval.ca/en/program/wednesday-october-9/>)

Advancement and promotion of scientific knowledge through publications and other outreach activities. (Number of publications and other outreach activities that resulted from COST networking through the Action. Complete list should be given in an annex)

Since the Action has just started the number of publications is still limited

1. Van Soom A, L. Vandaele, K. Goossens, S. Heras, E. Wydooghe, M.M. Kamal, M. Van Eetvelde, G. Opsomer, L. Peelman (2013) Epigenetics and the periconception environment in ruminants. Proceedings of the Belgian Royal Academies Of Medicine II; 1-23
2. Van Hoeck V, Leroy JLMR, Arias-Álvarez M, Rizos D, Gutierrez-Adan A, Schnorbusch K, Bols PEJ, Leese HJ & Sturmey RGS (2013) Oocyte developmental failure in response to elevated non-esterified fatty acid concentrations: mechanistic insights. *Reproduction* 145, 33-44
3. Rahman MB, Vandaele L, Rijsselaere T, El-Deen MS, Maes D, Shamsuddin M, Van Soom A. Bovine spermatozoa react to in vitro heat stress by activating the mitogen-activated protein kinase 14 signalling pathway. *Reprod Fertil Dev.* 2013 Jan 18. doi: 10.1071/RD12198
4. Franczak A., Wojciechowicz B., Kotwica G. Transcriptomic analysis of endometrium in pigs during early pregnancy and the estrous cycle. *Reprod. Biol.* 2013; 13: 229-237
5. Franczak A., Wojciechowicz B., Kolakowska J., Kotwica G. The effect of interleukin 1 β (IL1 β), interleukin 6 (IL6) and tumor necrosis factor α (TNF α) on estradiol-17 β (E2) release in the myometrium - the in vitro study on the pig model. *Theriogenology* 2014 Jan 15;81(2):266-74
6. Schindler M, Fischer S, Thieme R, Fischer B, Navarrete Santos A. cAMP-responsive element binding protein: a vital link in embryonic hormonal adaptation. *Endocrinology* 2013, 154: 2208-21
7. Schindler M, Pendzialek M, Navarrete Santos AI, Plösch T, Seyring S, Gürke J, Haucke E, Knelangen JM, Fischer F, Navarrete Santos An. (2014) Maternal diabetes leads to unphysiological high lipid accumulation in rabbit preimplantation embryos. *Endocrinology*. Jan15:en20131760 [Epub ahead of print]
8. Pennarossa G, Maffei S, Campagnol M, Tarantini L, Gandolfi F, Brevini TA. Brief demethylation step allows the conversion of adult human skin fibroblasts into insulin-secreting cells. *Proc Natl Acad Sci U S A.* 2013 May 28;110(22):8948-53. doi: 10.1073/pnas.1220637110
9. Brevini TAL, Pennarossa G, Maffei S, Campagnol M, Tarantini L, Gandolfi F. Epigenetic reprogramming of human skin fibroblasts into insulin secreting cells. *CellR4* 2013; 1(1): 110.
10. Pennarossa G., Maffei S., Campagnol M., Rahman M.M., Brevini T.A., Gandolfi F. (2013) Reprogramming of pig dermal fibroblast into insulin secreting cells by a brief exposure to 5-aza-

cytidine. Stem Cell Reviews And Reports, DOI 10.1007/s12015-013-9477-9.)

11. Pennarossa G., Maffei S., Gandolfi F., Brevini T.A., Gentle Makeover: Epigenetic Conversion of One Cell into Another. *CellR4* 2013; *CellR4* 2013; 1 (3): e526

Activities and projects with COST network colleagues

1. Epigenetics course in Murcia 3-7 June 2013 : Ann Van Soom (BE)-Pilar Coy (ES)
2. Biotechnology course in Bari -12 December 2013 : Ann Van Soom (BE) – Elena del'Aquila (IT)
3. Endocrine control of the equine oviduct – gene expression and immunofluorescence Summer 2013 : Ann Van Soom (BE) – Anita Franczak (PL)
4. Project AUF (l'Agence universitaire de la francophonie): « Protocoles non-hormonaux de la reproduction des chèvres et l'amélioration de la production laitière ; TROUPEAUF-REPROD », BECO-2011-75-U-56115FT110; partners from Croatia (Juraj Grizelj) and Macedonia (prof. Toni Dovenski)
5. Analysis of the gene expression and protein secretion in the bovine oviduct and uterus: Manuel Avilés (ES)-Stefan Bauersachs (GE).
6. Submission of research proposal in cooperation with MC Member Dr. Susanne Ulbrich from Germany to the Swiss State Secretariat for Education, Research and Innovation (SERI) in the frame of FA 1201 (Braunschweig and Bee, Switzerland).
7. Project with Christine Aurich (AU), from Vienna veterinary school, started after the Brussels meeting. There was one visit from their group to our lab at INRA Jouy en Josas (FR) and we will welcome an early stage researcher in the autumn. No STSM have been asked as we have decided to first try and get local funding. STSM will be asked if needed.
8. Submission of a research proposal in cooperation with MC Member Dr. Alireza Fazeli (England) to the National Science Center in Poland: "Epigenetic changes in embryos and reproductive system of pigs affected by restricted diet" (A Franzack, PL)
9. One visit of Kamila Zglejc, PhD student from University of Warmia and Mazury in Olsztyn, Poland is planned in summer 2014 in prof. Alireza Fazeli laboratory (England) – the activity will be granted by Erasmus + programme (supervisor A. Franczak, PL)
10. One visit of Marcin Martyniak, PhD student from University of Warmia and Mazury in Olsztyn, Poland is planned in summer 2014 in prof. Ann van Soom laboratory (Belgium) The activity will be granted by Erasmus + program, University of Warmia and Mazury in Olsztyn, Poland (supervisor A. Franczak, PL)

The capacity of the Action members to raise research funds

- BE-IWT Grant-Sonia Heras Garcia : Epigenetic modifications induced by in vitro culture in bovine embryos: is there a benefit in dynamic versus static culture conditions –2011-2015 (Ann Van Soom-BE)
- EI- EmbryoGENE, Quebec competition, UCD Trudee Fair: Effect of superovulation and in vitro embryo production on the stability of the bovine methylome. April 2013 (EI)
- BE- Embryogene Quebec, project granted, UA, Jo Leroy: epigenetic modifications of Day 7 embryos originating from oocytes originating from NEFA exposed oocyte. November 2013 (BE)
- UK – BBSRC Grant reference: BB/K017810/1 Grant holder: Professor Kevin Sinclair, University of Nottingham/University of Edinburgh Grant title: Genetics of one-carbon metabolism in sheep in relation to productivity, fertility and health. AWARDED. Start September 2013.
- UK – BBSRC Grant reference: BB/L001314/1 Grant holder: Professor Kevin Sinclair, University of Nottingham. Effects on sperm function and sperm/seminal-plasma mediated programming of offspring health and wellbeing UNDER REVIEW. October 2013.
- IT- Netlips, Cariplo Foundation Grant 2012-2015 (T Brevini- F Gandolfi)
- BE-FWO postdoc grant – Katrien Smits - Maternal recognition of pregnancy in the horse: are miRNAs the secret messengers? (2013-2016) (A Van Soom-BE)

- BE-BOF Postdoc – Catharina De Schauwer- Bovine embryos, stem cells and epigenetic modifiers (2013-2017) (A Van Soom BE)
- BE- FWO project – Ann Van Soom BE- Chromosomal instability during early embryonic development: elucidating key mechanisms in a bovine model (2014-2018)
- Scientific project in Frame of FA 1201: Study of metabolic and epigenetic changes induced by adiponectin in mouse blastocyst by Bernd Fischer, Anne Navarrete Santos, Department Anatomy and Cell Biology, Martin Luther University Faculty of Medicine, Halle (Saale)(DE) and Juraj Koppel, Assoc. Prof. , DVM., DrSc. Slovak Academy of Sciences Institute of Animal Physiology, Dr Jan Burkus, Slovak Academy of Sciences, Kosice (SK)
- Grant NCN 2013-2015, Bartosz Wojciechowicz (PL) - grant holder, Anita Franczak(PL) – supervisor. Transcriptomic profile of uterine tissues and peripheral blood cells in pigs during maternal recognition of pregnancy.
- Grant NCN 2013-2015, Justyna Kołakowska(PL), PhD student - grant holder, Anita Franczak (PL) - supervisor. Analyses of proteome of the endometrium and embryos in pigs (*Sus scrofa domestica*)
- ES-AGL project- Alfonso Gutierrez-Adan- Origin of intrauterine alterations of epigenome: periconceptional factor modeling offspring phenotype variability (2013-2015) (Collaboration with C.Galli)
- European Foundation for the Study of Diabetes (EFSD) Grant – Tiziana A.L. Brevini- Translational research for the clinical use of insulin secreting cells generated by epigenetic conversion (2014-2015).

III. Previous scientific report(s)

Part II of past periods' reports are to be found here.