



Version 21/04/2016

COST Action FA1201

Epigenetics and Periconception Environment - Periconception environment as an epigenomic lever for optimising food production and health in livestock

FINAL ACHIEVEMENT REPORT (04/10/2012 – 03/10/2016)

This report on the full lifetime of the Action is submitted by the MC Chair on behalf of the Management Committee.

Confidentiality: This report, other than section II.D, is non-confidential. Section II.D is confidential to the Management Committee and the COST Association (including the Committee of Senior Officials, Scientific Committee and Administration).

Executive summary of the Achievement Report:

Parental stress before, during and after conception (i.e. 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 were planned to be determined in livestock in order to optimize their health and productivity. This COST Action planned to identify stressors and molecules which induced, modulated or removed epigenetic marks on genes that are relevant for different applications in farm animals.

Our objectives were to:

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.

We achieved these objectives by discussing these topics at our conferences and workshops and as material output we published several review papers on the topic, as well as a Research Front entitled **Epigenetics and Periconception environment** in Reproduction, Fertility and Development (Editors: Ann Van Soom and Alireza Fazeli), and a book entitled **Periconception in Physiology and Medicine** (Editors: Alireza Fazeli and William V. Holt), which is in press by Elsevier.

Public engagement activities were 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. We communicated via organized Weeks and Nights of Science at our universities, and we were able to raise awareness and had an impact on young students of secondary schools. We used our website (<http://cost-epiconcept.eu/>;) to inform scientists and public and we produced a facebook page (<https://www.facebook.com/Epiconcept-COST-Action-1381626895453232/?fref=ts>) to interact with scientists, stakeholders and artificial insemination industry to improve breeding and gamete/embryo handling. We informed different companies and invited them in our workshops and courses, to hear about the possible impact of gamete and embryo handling on later life. A success story of our action was to manage to convince and include stakeholders like CRV in new research EU-projects on this topic.



COST is supported by
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Horizon 2020

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I. Achievement Report
I.A. COST Action Profile

Objective/ Aim
 Parental stress before, during and after conception (i.e. the periconception period) induces epigenetic changes in gametes and embryos. Such epigenetic changes may adversely affect the future health, development, productivity and fertility of offspring. While there is increasing evidence for this in agricultural species, most of the current knowledge is derived 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. Research on epigenetic control of development is being performed by different groups in the EU, but efforts need to be coordinated in order to avoid duplication, set targets and guidance for future research and to standardise protocols in this field through a large collaborative EU network. These goals can only be achieved under a COST programme.

Details				
MoU:	25/06/2012	Start of Action:	04/10/2012	
CSO approval date:	07/06/2012	End of Action:	03/10/2016	

COST Member Countries and Cooperating State having accepted the MoU

Parties							
Country	Date	Country	Date	Country	Date	Country	Date
Austria	16/07/2012	Belgium	13/06/2012	Bosnia and Herzegovina	29/04/2014	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	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	Serbia	13/10/2014	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	fYR Macedonia	28/06/2012				

Total: 30

Intentions to Accept the MoU
 0"

Other participants:

Institution Name	Country
Facultad Cs Bioquimicas y Farmaceuticas, UNR	Argentina

Contacts

Chair/ Vice Chair

Position	Name	Contact details	Country	Date of PhD	Gender
Chair:	Prof Ann VAN SOOM	Ghent University Salisburylaan 133 9820 Merelbeke Belgium ann.vansoom@ugent.be	Belgium	1996	F

Vice Chair:	Prof. Alireza Fazeli	University of Sheffield Level 4, Jessop Wing, Tree Root WalkS10 2SF Sheffield United Kingdom a.fazeli@sheffield.ac.uk	United Kingdom	1996	M
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Working Group Leaders

WG#	WG Title	WG Leader	Country	Date of PhD	Gender	Number of participants
1	Epigenomic Tools	Dr Trudee Fair	Ireland		F	20
2	Periconception Environment	Prof Kevin Sinclair	UK		M	40
3	Cross-Species Epigenetics, Gametogenesis and Embryogenesis	Dr Amos Tandler	Israel		M	40
4	Public, Periconception and Epigenome	Prof Tiziana Brevini	Italy	1994	F	20

Other positions if applicable (STSM Coordinator, WG Vice Leader, Task Force Leader...)

Position	Name	Country	Date of PhD	Gender
WG1 Vice Leader	Prof Alfonso Gutierrez-Adan	Spain		M
WG2 Vice Leader	Dr Anne Navarrette-Santos	Germany	2001	F
WG3 Vice Leader	Dr. Pascale Chavatte-Palmer	France		F
WG4 Vice Leader	Prof Anita Franczak	Poland		F
STSM Coordinator	Dr. Christine Aurich	Austria		F
STSM Deputy	Dr. Elin Kjorsvik	Norway		F

Action website:	www.cost-epiconcept.eu / http://www.cost.eu/COST_Actions/fa/FA1201?
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I.B. Achievement of MoU objectives and deliverables and additional outputs

MoU objectives

MoU objective	Achieved Yes/ Partially/ No	Evidence of (partial) achievement
<p>Develop an epigenomic toolbox including next generation sequencing technologies and bioinformatics: due to rapid changes in molecular tools these techniques will allow for large scale screening of epigenetic changes in gametes and embryos.</p>	Yes	<p>We have published detailed papers on staining methods to detect changes in methylation see Pubmed links : https://www.ncbi.nlm.nih.gov/pubmed/?term=heras+van+soom+staining and https://www.ncbi.nlm.nih.gov/pubmed/?term=beaujean+n+review</p> <p>We have organized two training schools on NGS and bioinformatics in Murcia, Spain in 2015 and 2016.</p> <p>We have published an opinion paper on the importance of the genome and epigenome to inform scientists and public about the importance hereof. https://www.ncbi.nlm.nih.gov/pubmed/?term=van+soom+a+epigenome</p>
<p>Define the factors that can influence the epigenetic profile during the periconceptional period : these factors can be physical stressors like cold or heat, high pressure, nutritional status of the animal, maternal health or sickness, feed supplements or deficiencies, pharmaceuticals , endocrine factors, culture media....</p>	Yes	<p>We have published a review paper on this topic to define these areas in production animals https://www.ncbi.nlm.nih.gov/pubmed/27439952</p> <p>We are in the process of publishing a book entitled Periconception in Physiology and Medicine (Editors: Alireza Fazeli and William V. Holt), which is in press by Elsevier.</p> <p>Book covers the following: From the early days of discovery about the basics of the fertilization process, scientists have known that early events happening during conception play a major part in the creation of new offspring. However, until nearly a decade ago we thought these events were just concerned with the conception and nothing to do with lifelong health and welfare, or wellbeing of the offspring. This idea was supported by the widespread use of IVF, both in humans and livestock, and the fact that majority of IVF babies looked healthy. However, early indications from IVF in sheep and cattle suggested that the embryo culture conditions employed in the laboratory could result in unusually large and unhealthy offspring. These observations sounded alarm bells and stimulated research into the impacts of in vivo and in vitro conditions on the health of embryos and offspring.</p> <p>Nevertheless, thanks to the success of IVF, where fertilization takes place in a milieu that mainly consists of a balanced salt media with the right pH and temperature, many scientists assumed that the Fallopian tubes, or oviducts, are inert and passive organs that only provide an immediate milieu for fertilization and early development. However, the recent advances in the physiology and medicine of the periconception</p>

		<p>period have shown that this view is inaccurate. It is true that the immediate impacts of the periconception period in physiology and medicine influence the success of conception and fertility among mammalian species. However, we are also learning that this milieu has long lasting effect on our health and future development into and during adulthood. Furthermore with the advances in epigenetics we are learning that the periconception period also affects our epigenetic profile at adulthood and sets the scene for our future health and welfare.</p> <p>In this book we will try to provide a collection of timely reviews by experts in the field. The book will provide a good introduction for those new to the field as well as those who have worked in this field for some time, but not have been able to up to date themselves with recent advances in the field.</p> <p>After a review of the current knowledge in this field, the attention of the book is focused on short term and long term effects of periconception period on an individual, both from a physiological and medical perspective. Finally we have dedicated several parts of the book to the examination of the potential mechanisms involved in controlling periconception period</p>
<p>Define the timeframe at which most epigenetic changes take place: spermatogenesis takes 2 months in most livestock; oocyte and follicular development takes 3-4 months; fertilization that remodels parental chromatin takes a few hours; and embryogenesis, including development of the germline (the precursors of sperm and eggs) which undergoes epigenetic reprogramming during the first</p>	<p>YES</p>	<p>Objective 3 / Publications listed in Research Front Epigenetics and Periconception environment http://www.publish.csiro.au/rd/content/ResearchFronts?id=1283)</p>

months of pregnancy.		
Define the range of optimal periconception environments that ensure healthy offspring : based on experimental data a definition will be made for each species studied.	Partial	Not all species have been covered, there is no compiled paper but details on different species are available in the proceedings of different workshops and conferences see http://cost-epiconcept.eu/index.html
Compare the susceptibility of different species (livestock, poultry, fish) and different model systems (<i>in vivo</i> vs <i>in vitro</i>) to epigenetic disturbances	Yes	This has been achieved in the different papers listed on the website http://cost-epiconcept.eu/index.html
Interact with stakeholders and the artificial insemination industry to discuss the extent to which information generated can be integrated in the implementation of genetic schemes and in the adaptation of gamete and embryo production protocols (i.e. semen collection, cryopreservation of semen and	Yes	Several partner organizations which are stakeholders (CRV, IVI, Alice, ...) are involved in ongoing EU project (Rep Biotech) see link http://www.um.es/rep-biotech/partners.php and there is another EU project in preparation with a focus on epigenetics, with similar partners involved

embryos, superovulation, IVF...)		
Inform the scientific community and the public, especially people involved in animal production, about altering the epigenome via the periconception environment.	Yes	<p>We have informed CRV, an important breeding company via our workshops and our ongoing collaboration. We have informed the general public via science nights and weeks of science. We have informed animal breeders via general television (in reportage on dog cloning http://nieuws.vtm.be/buitenland/212069-nederlands-koppel-laathond-klonen)</p> <p>I have inspired other researchers for writing an overview paper on epigenetics and animal breeding which was quite identical to and probably based on the presentation I gave in the training school in Murcia in 2015 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4585102/</p>

MoU deliverables

MoU deliverable	Delivered Yes/ Partially/ No	Evidence of (partial) delivery
WG1 Deliverables		For each deliverable insert evidence of (partial) achievement including hyperlink to enable assessment (by the Action Rapporteur) of the achievement and access by end users
To organise focused Workshops called “Epigenomic toolbox”, one at year 1 focusing on Next Generation Sequencing and one at year 3; focusing on techniques to analyse proteins (proteomics).	Yes	See Website http://cost-epiconcept.eu/meetings.html Annual conference 2013 Turkey Annual conference 2015 Crete
To organise focused Workshops called “Epigenetic dynamics and highlights”, one at year 2 on the	Yes	See website http://cost-epiconcept.eu/meetings.html Workshop 2013 Spain Workshop 2014 Spain

<p>dynamics of epigenetic modifications in living cells, gametes and embryos by means of fluorescence labeling and time-lapse microscopy, and one at year 4, to instruct on the determination of DNA methylation by means of enrichment for sequences with epigenetic modifications</p>		
<p>To deliver a technical publication on how to demonstrate epigenetic changes in samples with low cell numbers, derived from the four workshops</p>	<p>Partial ly</p>	<p>We did not make the publication, but gave this information at the training schools. Please see below website link to training school for further information.</p>
<p>To organise an inter-disciplinary Training School on “Epigenomic tools” in year 3.</p>	<p>Yes</p>	<p>We organized two training schools in Murcia Spain in 2015 http://www.um.es/actualidad/agenda/ficha.php?id=199621 http://www.ssr.org/event/2015/feb/epiconcept-training-school-epigenetics-reproductive-biology in 2016 http://eventos.um.es/event_detail/1936/detail/epiconcept-training-school-in-epigenetics-in-reproductive-biology.html http://www.campusmarenostrom.es/assets//images/formularios/subir_ima genes_aqui/pdfs/informative-sheet-2016-final-SCB.pdf</p>
<p>WG2 Deliverables</p>		
<p>To organise a focused section, called “Epigenetic modulators”</p>	<p>Yes</p>	<p>Programme at website : http://cost-epiconcept.eu/Epiconcept%20Conference%202013-Programme%20V1.4.pdf Annual conference 2013 Turkey</p>

<p>during the Annual Conference, at year 1, that will focus on factors influencing the epigenetic profile at periconception</p>		
<p>To deliver a document summarizing the most important epigenetic modulators during periconception, resulting from the Annual Conference at year 1.</p>	<p>Partially</p>	<p>This will be addressed in the book on periconception</p> <p>Publications within COST from WG2 Gürke J, Schindler M, Pendzialek M, Thieme R, Grybel KJ, Heller R, Spengler K7, Fleming T, Fischer B, Navarrete Santos A. (2016) Maternal diabetes promotes mTORC1 downstream signalling in rabbit preimplantation embryos. Reproduction. 2016 May;151(5):465-76. doi: 10.1530/REP-15-0523. Epub 2016 Feb 1.</p> <p>Project within COST from WG2 Bilateral Project 50021754, PPP DAAD Germany/ Slovakia - “Hormonal dysregulation in a diabetic pregnancy”, Dr. Anne Navarrete Santos and Dr. Stefan Cikos, 2015-2017</p>
<p>To organise a focused section, called “Epigenetic time frames” during the Annual Conference, at year 2, that will focus on developmental periods during which the epigenetic profile can be altered.</p>	<p>Yes</p>	<p>Workshop Dubrovnik Croatia : http://cost-epiconcept.eu/Programme-Workshop%202015%20V8.pdf</p> <p>Annual conference 2014 Spain: http://cost-epiconcept.eu/Programme-Conference%202014%20V1.15.pdf</p>
<p>To deliver a document summarizing the most important periods during periconception, resulting from the Annual Conference of year 2.</p>	<p>Yes</p>	<p>Review paper Sinclair WG 2 leader https://www.ncbi.nlm.nih.gov/pubmed/27439952</p>
<p>To organise a focused section, called</p>	<p>Yes</p>	<p>Annual conference 2015 Crete http://cost-epiconcept.eu/Programme-Conference%202015.pdf</p>

<p>“Epigenetic disruptors ” during the Annual Conference, at year 3, that will focus on molecules or modulators which can confer epigenetic changes to DNA</p>		<p>Workshop 2016 Croatia http://cost-epiconcept.eu/Programme-Workshop%202016.pdf</p>
<p>To deliver a document summarising the most important epigenetic disruptors and how they can be applied during periconception, resulting from the Annual Conference of year 3.</p>	<p>Yes</p>	<p>Proceedings of the meeting http://cost-epiconcept.eu/Epiconcept%20Proceedings%20Workshop%202016.pdf</p>
<p>To organise a focused section, called “EpiConcept ” during the Annual Conference, at year 4, that will focus on defining the right periconception environment to ensure healthy offspring.</p>	<p>yes</p>	<p>Annual meeting 2016 http://cost-epiconcept.eu/Programme-Conference%202016.pdf</p>
<p>To deliver a document summarizing the range of the right periconception environments</p>	<p>Yes</p>	<p>Review paper Sinclair https://www.ncbi.nlm.nih.gov/pubmed/27439952</p>
<p>WG3 Deliverables</p>		

<p>To organise an interdisciplinary Workshop on “Epigenetics in vivo and in vitro – what is the difference?”, at year 1, that will focus on how to translate data from a model to the field</p>	<p>yes</p>	<p>Workshop 2013 Spain http://cost-epiconcept.eu/Programme-Workshop%202013%20V1.9.pdf</p>
<p>To organise an interdisciplinary Workshop on “Epigenetics and nutrition”, at year 2, that will focus on how nutritional guidelines can be used to drive epigenesis.</p>	<p>Yes</p>	<p>Workshop 2015 http://cost-epiconcept.eu/workshop_2015.html</p> <p>Workshop 2016 http://cost-epiconcept.eu/Programme-Workshop%202016.pdf</p>
<p>To organise an interdisciplinary Workshop on “Epigenetics and stress or disease”, at year 3, that will focus on how stress /pathology during gametogenesis and pregnancy can affect offspring health</p>	<p>Yes</p>	<p>Workshop 2016 http://cost-epiconcept.eu/Programme-Workshop%202016.pdf</p>
<p>To organise an interdisciplinary Workshop, called “Epigenetics in fish, poultry and livestock” during the Annual Conference, at</p>	<p>Yes</p>	<p>Workshop 2016 http://cost-epiconcept.eu/Programme-Workshop%202016.pdf</p> <p>proceedings http://cost-epiconcept.eu/Epiconcept%20Proceedings%20Workshop%202016.pdf</p>

year 4, that will deliver a document summarizing a comparative overview of epigenetic influences in different species.		
WG4 Deliverables		
To interact with the industry at the Annual Conference in a specialized practitioners forum to integrate the generated information in gamete and embryo production protocols and in animal breeding schemes	Yes	WG 4 had interactions at all annual meetings and workshops
To deliver a document based on these for a, to be put on the website		
To inform the scientific community and the general public, especially people involved in animal production, by establishing a website explaining the obtained achievements in lay terms	Yes	Facebook account https://www.facebook.com/Epiconcept-COST-Action-1381626895453232/?fref=hovercard Participation to the Researcher's night Organization of several Open Days for young students and the public. Dissemination evenings at Cultural Societies and organizations-School ambassadoring

Co-authored publications and FP7/ H2020 proposals



The co-authored publications and FP7/ H2020 proposals/ projects resulting from the Action are listed on the page following the “Additional outputs and achievements” section.

Additional outputs and achievements

Please describe any other outputs and achievements, focusing in particular on those that contribute to the COST mission of “COST enables break-through scientific developments leading to new concepts and products and thereby contributes to strengthen Europe’s research and innovation capacities.”

New projects were started such as :

EpiHealth: Collaborative EU FP7 project including several EpiConcept partners on “**Linking perturbed maternal environment during periconceptional development, due to diabetes, obesity or assisted reproductive technologies, and altered health during ageing**”. <http://epihealth.biotalentum.eu/>

EpiHealthNet: Marie Curie Initial Training Network, with several EpiConcept partners
<http://www.epihealthnet.org/>

REP Biotech : <http://www.um.es/rep-biotech/>

Bilateral Project 50021754, PPP DAAD Germany/ Slovakia - “Hormonal dysregulation in a diabetic pregnancy”, Dr. Anne Navarrete Santos and Dr. Stefan Cikos, 2015-2017



Co-authored publications and FP7/ H2020 proposals

Co-authored publications

This table contains the (up to) ten most significant co-authored publications resulting from the Action. All publications are on the topic of the Action, co-authored by at least two Action participants from two different countries participating in the Action.

NO	Bibliographic data (including: Title, Authors, Title of the periodical or the series, Issue number or volume, Publisher, Year of publication, Relevant pages)	Main author	Number of authors	Action participants listed among the authors (Name, country and role ¹)	WGs involved in publication	Date of submission (must be after Action start date)	Expected date of publication (if not already published)	Persistent link to publicly available version of the paper (if available) or the abstract	Is/Will open access ² provided to this publication?	Is/ will COST be cited/ acknowledged in the publication?	Are/ will COST funds (be) implicated in this publication	Relevance to H2020 Societal Challenges ³ ?	Is it peer-reviewed?	Was the added value of the Action Networking necessary for the publication	Impact Factor (if applicable)
1	Epigenetics and periconception environment: an introduction A. Van Soom ^{A C} and A. Fazeli ^{UK} <i>Reproduction, Fertility and Development</i> 27(5) iii-v http://dx.doi.org/10.1071/RDv27n5_IN	Van Soom A	2	Van Soom BE Fazeli UK	WG1234		3 june 1015	http://www.publish.csiro.au/view/journals/dsp_journal_fulltext.cfm?nid=44&f=RDv27n5_IN	No	Yes	No	Health, demographic change and wellbeing	No	Yes	2.4
2	Epigenetic processes in the male germline Alan M. O'Doherty ^{A C} and Paul A. McGettigan <i>Reproduction, Fertility and Development</i> 27(5) 725-738 http://dx.doi.org/10.1071/RD14167	O'Doherty	2	O Doherty Ireland	WG1-2	20 may 2014	9 september 2014	http://www.publish.csiro.au/view/journals/dsp_journal_fulltext.cfm?nid=44&f=RD14167	No	Yes	No	Health, demographic change and wellbeing	Yes	Yes	2.4
3	DNA methylation reprogramming during oogenesis and interference by reproductive technologies: Studies in mouse and bovine models Ellen Anckaert and Trudee Fair <i>Reproduction, Fertility and Development</i> 27(5) 739-754 http://dx.doi.org/10.1071/RD14333	Fair	2	Fair Ireland WG leader Anckaert Belgium Member	WG1-2	8 september 2014	15 may 2015	http://www.publish.csiro.au/view/journals/dsp_journal_fulltext.cfm?nid=44&f=RD14333	No	Yes	No	Health, demographic change and wellbeing	Yes	Yes	2.4
4	Determinants of valid measurements of global changes in 5'-methylcytosine and 5'-hydroxymethylcytosine by immunolocalisation in the early embryo J. Salvaing ^A , Y. Li ^B , N. Beaujean ^{A C} and C. O'Neill ^{B C} <i>Reproduction, Fertility and Development</i> 27(5) 755-764 http://dx.doi.org/10.1071/RD14136	Beaujean	3	Salvaing and Beaujean France-Participant O'Neill Australia-participant	WG1	24 april 2014	29 october 2014	http://www.publish.csiro.au/nid/44/paper/RD14136.htm	No	Yes	No	Health, demographic change and wellbeing	Yes	Yes	2.4
5	Why we should not select the faster embryo: lessons from mice and cattle Alfonso Gutierrez-Adan ^A , Carlee R. White ^{C D E} , Ann Van Soom ^B and Mellissa R. W. Mann ^{C D E F} <i>Reproduction, Fertility and Development</i> 27(5) 765-775 http://dx.doi.org/10.1071/RD14216	Mann	4	Gutierrez Adan Spain MC Ann Van Soom Belgium Chair	WG2	18 june 2014	11 september 2014	http://www.publish.csiro.au/view/journals/dsp_journal_fulltext.cfm?nid=44&f=RD14216	No	Yes	No	Food security	Yes	Yes	2.4
6	Phenotype switching through epigenetic conversion T. A. L. Brevini ^{A B} , G. Pennarossa ^A , S. Maffei ^A and F. Gandolfi ^A <i>Reproduction, Fertility and Development</i> 27(5) 776-783 http://dx.doi.org/10.1071/RD14246	Brevini	4	Italy	WG4	10 july 2014	5 march 2015	http://www.publish.csiro.au/nid/44/paper/RD14246.htm	No	Yes	No	Health, demographic change and wellbeing	Yes	Yes	2.4
7	Relationship between genome and epigenome--challenges and requirements for future research. Almouzni G, Altucci L, Amati B, Ashley N, Baulcombe D, Beaujean N, Bock C, Bongcam-Rudloff E, Bousquet J, Braun S, Bressac-de Paillerets B, Bussemakers M, Clarke L, Conesa A, Estivill X, Fazeli A, Grgurević N, Gut I, Heijmans BT, Hermouet S, Houwing-Duistermaat J, Iacobucci J, Ilaš J, Kandimalla R, Krauss-Etschmann S, Lasko P, Lehmann S, Lindroth A, Majdić G, Marcotte E, Martinelli G, Martinet N, Meyer E, Miceli C, Mills K, Moreno-Villanueva M, Morvan G, Nickel D, Niesler B, Nowacki M, Nowak J, Ossowski S, Pelizzola M, Pochet R, Potočník U, Radwanska M, Raes J, Rattray M, Robinson MD, Roelen B, Sauer S, Schinzer D, Slagboom E, Spector T, Stunnenberg HG, Tiligada E, Torres-Padilla ME, Tsonaka R, Van Soom A, Vidaković M, Widschwendter M ¹ . <i>BMC Genomics</i> . 2014 Jun 18;15:487. doi: 10.1186/1471-2164-15-487. 18	None	Several	many	WG1-4		18 june 2014	http://www.ncbi.nlm.nih.gov/pubmed/24942464	Yes	Yes	No	Health, demographic change and wellbeing	Yes	Yes	2.4
8	Local activation of uterine Toll-like receptor 2 and 2/6 decreases embryo implantation and affects uterine receptivity in mice. Sanchez-Lopez JA, Caballero I, Montazeri M, Maslehat N, Elliott S, Fernandez-Gonzalez R, Calle A, Gutierrez-Adan A, Fazeli A: <i>Biology of reproduction</i> 2014, 90(4):87.	Sanchez-Lopez JA	9	A Gutierrez-Adan (Spain): MC; A Fazeli (UK): Vice-Chairman; Sanchez-Lopez JA (UK):	1	02/11/2013		http://www.bioreprod.org/content/90/4/87.short	yes	yes	yes	Food Security...	Yes	yes	3.5



				STSM Recipient											
9	Interaction between differential gene expression profile and phenotype in bovine blastocysts originating from oocytes exposed to elevated non-esterified fatty acid concentrations Van Hoeck V, Rizos D, Gutierrez-Adan A, Pintelon I, Jorssen E, Dufort I, Sirard MA, Verlaet A, Hermans N, Bols PE et al.: <i>Reprod Fertil Dev</i> 2013.	Van Hoeck V	11	A Gutierrez-Adan (Spain): MC; D Rizos (Spain): MC substitute; LMR Leroy (Belgium) : MC	1	13/08/2013	http://www.publish.csiro.au/?act=view_file&file_id=RD13263.pdf	yes	Yes	Yes	Food Security...	Yes	Yes	2.4	
10	Lactation-induced changes in metabolic status and follicular-fluid metabolomic profile in postpartum dairy cows Forde N, O'Gorman A, Whelan H, Duffy P, O'Hara L, Kelly AK, Havlicek V, Besenfelder U, Brennan L, Lonergan P. <i>Reprod Fertil Dev.</i> 2015 Jun 15. doi: 10.1071/RD14348	Forde	10	Lonergan (Ireland) MC Besenfelder (Austria) MC	WG1 and 2	17/09/2014	http://www.publish.csiro.au/index.cfm?paper=RD14348	Yes	yes	yes	Food security	yes	yes	2.4	

FP7/ H2020 Proposals and projects

This table contains FP7/ H2020 proposals/ projects spinning off from Action activities and including in the proposing consortium at least three Action participants from at least three different countries participating in the Action.

NO.	Title	Name and country of main proposer	Number of proposers	Action participants listed among the proposers (Name, country, role ³ in the Action)	Funding agency submitted to	Date submitted	Date results expected	Result	Call identifier	Relevance to H2020 Societal Challenges ⁴ ?	Was the added value of the Action Networking necessary for the proposal / project?
Projects											
1	REP-BIOTECH	Pilar Coy -Spain	5	Ann Van Soom -Belgium - Chair Pat Lonergan – Ireland – MC Karl Schellander – Germany – Member Mattioli- Italy- Member	Marie Skłodowska-Curie Actions (MSCA) Innovative Training Networks (ITN) H2020-MSCA-ITN-2015	January 2015	Result known	Approved May 2015	H2020-MSCA-ITN-2015	Health, demographic change and wellbeing Food security	Yes we got to know each other through this action
2	EpiHealth: "Linking perturbed maternal environment during periconceptual development, due to diabetes, obesity or assisted reproductive technologies, and altered health during ageing". http://epihealth.biotalentum.eu/	Andras Dinnyes-Hungary	7	Andras Dinnyes-Hungary- MC Member Judith Eckert, UK - MC Substitute Anne Navarrette-Santos, Germany, MC Member	EU FP7	Nov 2011	Result known	approved	HEALTH.2011.2.2-2 - Linking human development and ageing	Health, demographic change and wellbeing	Beneficial to develop ideas further during the project and for dissemination
3	EpiHealthNet	Andras Dinnyes-Hungary/The Netherlands	9	Andras Dinnyes-Hungary- MC Member Judith Eckert, UK - MC Substitute Anne Navarrette-Santos, Germany, MC Member	EU FP7	May 2013	Result known	approved	FP7-PEOPLE-2012-ITN - Marie-Curie Action: "Initial Training Networks"	Health, demographic change and wellbeing	Yes, to develop ideas further and train students during the

¹ MC Member/ MC Substitute/ MC Observer/ WG Member/ Training School Trainee/ STSM Recipient/ Other Action Participant

² Open Access is defined as free of charge access for anyone via Internet. Please answer "yes" if the open access to the publication is already established and also if the embargo period for open access is not yet over but you intend to establish open access afterwards.

³ H2020 Societal Challenges are "Health, demographic change and wellbeing"; "Food security, sustainable agriculture and forestry, marine and maritime and inland water research, and the Bioeconomy"; "Secure, clean and efficient energy"; "Smart, green and integrated transport"; "Climate action, environment, resource efficiency and raw materials"; "Europe in a changing world - inclusive, innovative and reflective societies"; "Secure societies - protecting freedom and security of Europe and its citizens"

				Tom Stout, The Netherlands, MC Member Bernard Roelen, The Netherlands, MC Member							project and for dissemination
Proposals											
	List FP7/ H2020 proposals submitted as a result of the Action in this section of the table										



I.C. Networking

Added value of the Networking			
We have met several new researchers through this network which were interested in epigenetic influences during periconception. By this network, some of us were invited as speakers at conferences (COST and others), some were invited to take part in a FP7 proposal, some of us started to collaborate on mutual publications. None of this would have happened without the COST Action.			
The table below shows the extent to which it would have been possible to achieve each of the Action's objectives without the Action networking.			
MoU objective	Possibility of achievement without Action networking		
Develop an epigenomic toolbox for large scale screening of epigenetic changes in gametes and embryos			Impossible
Define the factors that can influence the epigenetic profile during the periconceptual period of gametes and embryos.			Impossible
Define the time-window during which most epigenetic changes take place			Impossible
Define the range of the optimal periconception environments to ensure healthy offspring			Impossible
Compare the susceptibility of different species (livestock, poultry, fish) and different model systems (<i>in vivo</i> vs <i>in vitro</i>) to epigenetic disturbances			Impossible
Extent of the networking			
We have made contact with collaborators from many countries, which is obvious by our achievements such as the many STSMs, the Rep-Biotech project, the Research Front in Reprod Fertil Dev. It can be deduced from our website e.g; http://cost-epiconcept.eu/2014.html that STSMs were occurring between all participating countries including inclusiveness target countries such as Hungary, Poland, Portugal, and Slovakia. STSMs were dedicated to ESRs, and at each conference/Workshop we allowed ESRs to present their data, while taking into account gender balance			

I.D. Impacts

The impacts that have resulted, or might result from the Action are described in the following table.

Description of the impact	Type of impact ⁴	Timing of impact ⁵
More public awareness of environmental influences on human health .	Societal	In 5-10 years
Increased knowledge on epigenetic profile of pluripotent and differentiated cells	Societal and economic	In 5-10 years
Development of patient-based medicine	Economic	In 5-10 years

I.E Dissemination and exploitation of Action results

Describe the Action's dissemination and exploitation approach as well as all activities undertaken to ensure dissemination and exploitation of Action results and the effectiveness of these activities.			
Week of science and Night of research is an annual event that has been used by several participants of the COST-action to disseminate the results and the research topics of the Action.			
Item/ activity	Target audience	Result	Hyperlink
We have performed several scientific days on EPICONCEPT informing the public e.g. at Gent and Milan	Secondary school students	Very enthusiastic responses	Since these actions were performed hands-on, there is no hyperlink

⁴ Scientific/ technological, Economic, Societal

⁵ Achieved/ Foreseen within 2 years/ Foreseen 2-5 years/ Foreseen 5-10 years/ Foreseen 10+ years

Training school Murcia Epigenetics and Reproductive Biology 18-21 may 2015	PhD students	15 students got expertise in epigenetics and hands on experience	There was no hyperlink, only a mailing to all participants of the COST Action
Training school Murcia Epigenetics and Reproductive Biology 18-21 February 2016	PhD students	15 students got expertise in epigenetics and hands on experience	There was no hyperlink, only a mailing to all participants of the COST Action



I.F Action success(es)

COST regularly communicates the successes of Actions. What aspect(s) (outcomes and/ or impacts, rather than activities) of this Action is/ are the most suitable for communication?

Description of the success story	Dimension of the success <ul style="list-style-type: none"> ■ Breakthrough: scientific, technological or socioeconomic ■ Policy implementation (specify which policy) ■ Capacity building
A seminal paper was published in PNAS by Pennarossa and others (group of Brevini and Gandolfi) (www.pnas.org/cgi/doi/10.1073/pnas.1220637110) describing a successful approach, involving epigenetic erasing, cell commitment and differentiation. This discovery has opened the way to a pre-clinical study for diabetes and to the request of a patent (property UniMi).	This is a scientific breakthrough for diabetes stem cell research. Similar approaches are being tested with embryos and gametes at present
We have published a Research Front in Reprod Fertil Dev dedicated to Epigenetics and Periconception. http://www.publish.csiro.au/nid/45/issue/7304.htm	This is an example of capacity building, making the scientific community aware of the problem
Expertscape, the prestigious web and search engine dedicated to the identification of the best scientific institutions and experts in different medicine areas, placed Brevini Tiziana fat the first place in research on reproduction and parthenogenesis (epigenetically asymmetric embryo) http://expertscape.com/ex/parthenogenesis	This is an example of capacity building

II. Management Report

II.A. Overview of expenditure

The table below summarises the Action’s expenditure throughout its four year life.

Unfortunately the E-Cost System does not allow the Grant holder to have access to summary data needed to fill this table.

GP start and end dates	(01/02/2013-18/08/2014)	(02/06/2014-30/07/2015)	(01/06/2015-20/06/2016)	(01/05/2016 - 03/12/2016)	
Grant Holder institution	The University of Sheffield (UK)	The University of Sheffield (UK)	The University of Sheffield (UK)	GH institution name (country code)	
Meetings	EUR 174,017.11	EUR 112,525.99	EUR 59,346.31	EUR 101,704.47	EUR 447,593.88
Training Schools	EUR -	EUR 16,538.09	EUR 14,299.43	EUR -	EUR 30,837.52
STSMs	EUR 34,022.00	EUR 23,420.00	EUR 13,000.00	EUR 4,000.00	EUR 74,442.00
Dissemination	EUR 2,625.00	EUR -	EUR -	EUR -	EUR 2,625.00
OERSA ¹	EUR -	EUR -	EUR -	EUR -	EUR -
Total Scientific Expenditure	EUR 210,664.11	EUR 152,484.08	EUR 86,645.74	EUR 105,704.47	EUR 555,498.40
FSAC ²	EUR 31,599.52	EUR 22,872.17	EUR 12,994.62	EUR 15,654.83	EUR 83,121.14
TOTAL	EUR 242,263.63	EUR 175,356.25	EUR 99,640.36	EUR 121,359.30	EUR 638,619.54

¹ OERSA = Other Expenses Related to Scientific Expenditure (e.g. bank charges)

² FSAC = Amount received by Grant Holder for Financial Scientific and Administrative Coordination

II.B. Budget and Participation management

II.B.1 Budget spent in relation to individuals/ institutions outside participating COST countries					
<i>STSMs from or to institutions from countries other than Participating COST countries</i>					
The table below describes the added value STSMs to approved institutions in IPC or NNC or Specific Organisations and any STSMs from an approved institution in an NNC to a participating COST country.					
Grantee		Host		Date	Topic and value added to the Action
Institution	Country	Institution	Country		
Add home institution and country		Add host institution and country		Date	Describe topic of the STSM and the added value to the Action
Add home institution and country		Add host institution and country		Date	Describe topic of the STSM and the added value to the Action
Add home institution and country		Add host institution and country		Date	Describe topic of the STSM and the added value to the Action
<i>Invited Speakers</i>					
The table below highlights the added value of Invited Speakers from COST countries that have not accepted the MoU and/ or non-participating NNC, IPC or Specific Organisations whose participation at a meeting or Training School was reimbursed by the Action.					
Participant name		Institution	Country	Event date	Topic and added value to the Action
Melissa Mann		University of Ontario	Canada	Conference 2013 2013-04-24	Susceptibility of Genomic Imprint Maintenance to Assisted Reproductive Technologies



			- 2013-04-25	
Lior David	Hebrew University of Jerusalem	Israel	Conference 2013 2013-04-24 - 2013-04-25	Epigenetics in evolution – bridging the gap in timescales of adaptation
Amir Sagi	Ben Gurion University	Israel	Conference 2014 2014-10-01 - 2014-10-03	On sexual intervention and safety considerations in the use of RNAi in aquaculture
Peter Hatemi	Pennsylvania State University	United States	Conference 2014 2014-10-01 - 2014-10-03	Expression of epigenetic effects in identical twins
Hasan Khatib	University of Wisconsin-Madison	United States	Conference 2014 2014-10-01 - 2014-10-03	Genetics and epigenetics of early embryonic development and fertility in cattle
Charles Long	Texas A&M University	United States	Conference 2014 2014-10-01 - 2014-10-03	Are cloned animals in fact identical?
Moshe Szyf	McGill University	Canada	Workshop 2013 2013-10-14 - 2013-10-14	Epigenetic processes mediating genome adaptation to experience and exposure
Yoav Soen	Weizmann Institute of Science	Israel	Workshop 2013 2013-10-14 - 2013-10-14	Non-Mendelian Mechanisms of Inheritance of a Response to Toxic Stress
Amir Sagi	Ben Gurion University	Israel	Workshop 2013 2013-10-14 - 2013-10-14	Insulin-like androgenic hormones and monosex culture of prawns: The first implementation of RNA-interference in aquaculture
Christopher Ashwell	North Carolina State University	United States	Workshop 2013 2013-10-14 - 2013-10-14	Dietary conditioning in poultry by limiting specific nutrients early in life
Andreas Gnirke	Broad Institute of MIT and Harvard	United States	Workshop 2013 2013-10-14 - 2013-10-14	Genome-scale DNA-methylation analysis
Mary Goll	Memorial Sloan-Kettering Cancer Center	United States	Workshop 2013 2013-10-14 - 2013-10-14	Understanding heterochromatin establishment and maintenance in the zebrafish embryo
Claude Robert	Laval University	Canada	Workshop 2014 2014-05-07 - 2014-05-09	Integrating the DNA methylome and transcriptome to better define the long term impacts of assisted reproductive technologies
Yael Heifetz	Hebrew University of Jerusalem	Israel	Workshop 2015 2015-04-26 - 2015-04-29	Studying the periconception environment in Drosophila: a model organism to bridge unknown gaps
Louis Guillelte	Medical University of South Carolina	United States	Workshop 2015 2015-04-26 - 2015-04-29	From sentinel species to human health: the epigenetics of environmental health
Michael Skinner	Washington State University	United States	Conference 2016 2016-09-26- 2016-09-29	Environmentally induced epigenetic transgenerational inheritance of disease: ancestral ghosts in your genome

Brian Dixon	University of Waterloo	Canada	Conference 2016 2016-09-26- 2016-09-29	Epigenetic control of teleost fish immunity: an ocean of possibilities
Yoav Soen	Weizmann Institute of Science	Israel	Conference 2016 2016-09-26- 2016-09-29	Adaptation by natural improvisation
Moshe Szyf	McGill University	Canada	Workshop 2016 2016-05-18 - 2016-05-19	DNA methylation mediating between exposure and phenotype; therapeutic and diagnostic implications
Vadim Fraifeld	Ben Gurion University	Israel	Workshop 2016 2016-05-18 - 2016-05-19	Aging, longevity and late-onset diseases from the bird's eye view
Yoav Soen	Weizmann Institute of Science	Israel	Workshop 2016 2016-05-18 - 2016-05-19	Interactions between the gut microbiota and the host germline

<i>Dissemination meetings</i>					
The table below highlights the added value of Dissemination Meetings financed from Action funds.					
Participant name	Role	Country	Date	Location	Topic and added value to the Action
Add	Add	Add	Add	Add	Describe the speaker's topic and the added value to the Action

II.C. Participants

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Annex 1

Definitions:

COST Action Challenge (main aim)	“The research question addressed by the COST Action targeting scientific, technological, and / or socioeconomic problems”
COST Action Innovation	“The creation and / or development of new or improved concepts, products, processes, services, and / or technologies that are made available to markets, governments and society”
COST Action objectives	“COST Action objectives are the results that an Action needs to achieve in order to respond to meet its challenge. These are SMART (Specific, Measurable, Achievable, Relevant, Timely) and twofold: research coordination objectives and capacity building objectives.”
COST Action research coordination objectives	“Achieving these objectives turns COST Actions from initially scattered teams into one transnational team and leverages the existing funded research. These objectives entail the distribution of tasks, sharing of knowledge and know-how, and the creation of synergies among Action participants to achieve specific outputs.”
COST Action capacity building objectives	“Achieving these objectives entail building critical mass to drive scientific progress, thereby strengthening the European Research Area. They can be achieved by the delivery of specific outputs and / or through network features or types and levels of participation.”
COST Action networking activities	“any activities organised by the COST Action (whether or not directly funded by COST) in order to achieve research coordination and capacity building objectives.”
COST Action networking tools	“instruments through which eligible activities can be funded”
COST Action outputs	“direct results from the COST Action activities. These can be codified knowledge, tacit knowledge, technology, and societal applications.”
COST Action impact	“the short- to long-term scientific, technological, and / or socioeconomic changes produced by a COST Action, directly or indirectly, intended or unintended.”
COST Action deliverable	“a distinct, expected and tangible output of the Action, meaningful in terms of the Action’s overall objectives such as a report, a document, a technical diagram, a software etc. Action deliverables are used to measure its progress and success.”
COST Action milestones	“Control points in the Action that help to chart progress. They are also needed at intermediary points so that, if problems have arisen, corrective measures can be taken. A milestone may be a critical decision point in the Action where, for example, the MC must decide which of several technologies to adopt for further development (e.g. core group and MC meetings, mid-term reviews)”
Inclusiveness Target Country (ITC):	Current COST Member Countries targeted by the COST inclusiveness Policy (“Inclusiveness Target Countries” (ITC)): EU 13 (Bulgaria, Cyprus, Czech Republic, Estonia, Croatia, Hungary, Lithuania, Latvia, Malta, Poland, Romania, Slovenia, Slovakia), EU candidate countries (the former Yugoslav Republic of Macedonia, Montenegro, Republic of Serbia, Turkey) and potential EU candidate countries (Bosnia and Herzegovina). In addition, to comply with the EC criteria for ‘Spreading Excellence and Widening Participation’, Portugal and Luxemburg are included.