	EUROPEAN COMMISSION **RESEARCH AND INNOVATION DG**	**Final Report**

Project No: 222883

Project Acronym: MEIOsys

Project Full Name: Systematic analysis of factors controlling meiotic recombination in higher plants

Final Report

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Project coordinator name:

Dr. Susan Armstrong

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THE UNIVERSITY OF BIRMINGHAM

Final Report

PROJECT FINAL REPORT

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Project acronym:	MEIOsys
Project title:	Systematic analysis of factors controlling meiotic recombination in higher plants
Funding Scheme:	FP7-CP-IP
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4.1 Final publishable summary report

Executive Summary

Crops have played a major role in meeting human food demands for the last ten millennia. Today plants are at the heart of a European food industry with an annual turnover of more than a trillion Euros. Intensive breeding has boosted plant yield, quality and resistance to stress but current predictions suggest that over the next 50 years population growth and climate change will result in the need to produce more food than has been generated in the past 10,000 yrs. To achieve this we will need to adopt ever-more novel approaches to crop plant breeding, including developing crops matched to individual world populations.

We have found that application of genomics in combination with systems biology has provided a powerful strategy that will enable the factors that control meiotic recombination to be elucidated. Armed with this knowledge it will be possible to predicatively modify meiotic recombination in crop species to allow the breeding of new lines with novel combinations of alleles. Our aim to maximise the amount of genetic variability that is accessible to plant breeders and will enable the development of novel, improved cultivars that will in turn sustain an adequate food supply for the 21st century

Summary description of project context and objectives

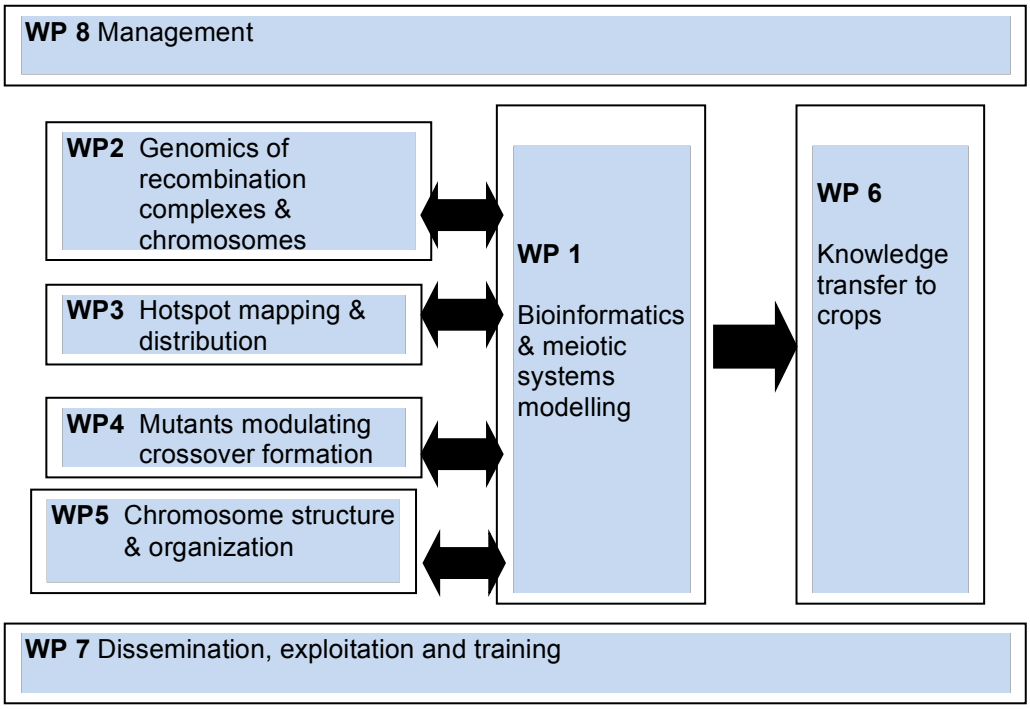
Meiosis is a specialized cell division used by both plants and animals to produce gametes (sperm and eggs) for reproduction. Meiosis ensures that the correct number of chromosomes is passed on from generation to generation. It also recombines, or mixes the versions of genes (alleles) inherited from the previous generation. This creates new combinations of genetic variants which can be used by plant breeders to develop new varieties. In many crop species, for example the cereals, recombination is skewed to the ends of the chromosomes and this restricts the ability of the breeder to produce improved varieties because many useful genes in the central portion of the chromosomes are rarely involved in the recombination pathway.

Food security will become increasingly important in the near future due to the challenges of the increasing global demand for food together with the effects of climate change. Because of this we need to generate and identify the most appropriate combinations of alleles to successfully breed the new crops that will ensure maintenance of the food supply.

Our overall goal has been to improve our understanding of the control of meiotic recombination in the higher plants, as this is the process that underpins plant breeding and the generation of new varieties. Our starting point is the model plant *Arabidopsis thaliana* (the wall cress) as it is well suited to investigate meiosis through the development of novel approaches in genomics and systems biology.

Our knowledge from Arabidopsis has been translated and assessed by experiments aimed at altering meiotic recombination in the crop species; brassicas and the distantly related cereal barley.

In MEIOsys we have broken our work into 6 linked work packages (WPs). WPs 2-5 use *A. thaliana* and B*rassica oleracea* (WP2) whereas WP1 and WP6 also use barley and brassicas. The WPs are; bioinformatics and meiotic systems modelling (WP1); genomics of meiotic protein complexes (WP2); analysis of meiotic proteins function and crossover distribution (WP3); analysis of mutants modulating crossover formation (WP4); chromosome structure and structure organisation (WP5); knowledge transfer to crops (WP6); findings from these WPs are disseminated to scientists, interested parties and members of the public (WP7).



The overall aim of MEIOSys is to combine genomics with systems biology to provide a powerful strategy that will enable the factors that control meiotic recombination to be elucidated. Armed with this knowledge we have modified meiotic recombination in crop species to allow the breeding of new lines with novel combinations of alleles.

MEIOsys has an objective-based strategy based on 4 specific interdependent objectives (SO) that have been achieved during our project.

Our objectives for the program were as follows:

SO1. to identify genes and their cognate proteins that underpin meiotic recombination and its control through a combination of bioinformatics and genomic approaches.

SO2. to determine the functional role of novel meiotic proteins and their interactions with the components of the recombination machinery.

SO3. to investigate the pattern of recombination hotspot distribution and establish its interrelationship with chromosome organisation to establish a comprehensive model of the gene/protein networks that control the frequency and distribution of meiotic crossovers in plants.

SO4. to validate predications arising from the model in *Arabidopsis* and selected crops.

During our program we have made considerable progress in understanding the meiotic process in the model plant *A. thaliana*. Our results have advanced the knowledge on regulation of meiosis in this species **SO1, SO2, SO3**.

We are making excellent progress in our aim to transfer our understanding of meiotic recombination to crop species. Currently we are translating information from *A. thaliana* to alter crossover distribution and frequency in the crops species *Brassica rapa* (turnip) and barley, **SO4**.

We have combined our experience with our partners both industrial and members of the project RECBREED, in order to develop a new ITN network COMREC (LEAD UoB), that commenced on April 2014. Our network will provide training for the next generation of scientists to work with plant breeders, with the goal of providing a set of tools for plant breeding.

Description of main S & T results/foregrounds

MEIOsys results /foregrounds

WP 1 All of the deliverables/milestones have been accomplished. The central database (IMP, UoV, UoB, JHI and CNR) has been set up for the compilation and exchange of data in Arabidopsis, Brassica and barley (***WP1***). We have integrated the existing knowledge on recombination from literature and publically available database resources, and datasets generated within the scope of this project. In addition, innovative approaches for genetic network visualisation and gene function prediction have been carried out. Our database is currently only available for our partners and we propose keeping this data for our group for the next twelve months only.

We have discussed that we need to have a secure site for all of our data once the project has finished at our annual meeting in Naples, and we are in negotiation with Graham King, a member of our external committee, who is curating the international brassica database (University of Southern Cross, Australia http://scu.edu.au/scps/index.php/71) for long term storage of our data.

We will enter into discussions with the SME Keygene company, who have indicated that they would be interested in our databases.

WP2 results

This has proved to be the most labour intensive and complex WP and has turned out to be pivotal and from which many of our successes have been; The efforts of ***WP2*** were central to the success of the MEIOsys project as both ***WP1*** and ***WP3*** depended on input from ***WP2.***

The aim of ***WP2*** was to utilize genomics approaches to identify (novel) meiotic protein complexes and thereby generated a list of candidate genes involved in meiotic progression (***WP1)***. Additionally, we aimed at obtaining information on protein-protein interactions and meiotic protein complexes (***WP1)***. Two major, complementary approaches have been implemented:

(I) The proteomic approach aimed at identifying novel interaction partners of known meiotic proteins via co-immune precipitation or at identifying targets of DNA repair kinases utilizing mass-spectrometry (MS). This strategy has produced a large number of publications with high impact (see the following section) and has enhanced the work submitted by IMP, Vienna.

(II) (II) The yeast two-hybrid approach aimed at identifying novel binding partners of known plant meiotic proteins in a heterologous host and at verifying protein-protein interactions.

WP3 results

(i) To carry out a cytological analysis of predicted meiotic genes, in fact we found that was not the most productive way to approach this aspect of this WP< accordingly we modified the approach to this task, and have now have useful results.

(ii) The functional characterization of genes/proteins that modulate meiotic crossovers was successful and contributed to the publication of a major paper (see WP below).

(iii) Finally task 3.3 molecular analysis of Co hotspots was extremely successful, in reporting a method to achieve this type of analysis that has been replicated in a number of laboratories.

WP4 results

The aim of ***WP4*** was to identify novel genes controlling crossover frequency by conducting genetic suppressor screens with mutants deficient in crossover formation. A screen was performed on a total of 4000 lines. Twenty-six suppressors with very strong fertility and crossover restoration were found, corresponding to three complementation groups (consisting of 17, 8 and 1 mutant, respectively). All mutants are mono-locus and recessive. With genetic mapping and next generation sequencing, the three genes (and the corresponding mutations) have been identified and functionally characterized. Two patents have been applied for by INRA namely for FANCM and the third identified gene, FIDGETIN-L1, which limits crossover independently of FANCM. This leads to an amazing six fold increase of CO frequency in the double mutant compared to wild type. WP3 has been very successful, having identified and characterized the first three meiotic anti-crossover activities and has produced 2 patent applications.

WP5 results

This WP has been to investigate the role of chromosome organization on meiotic recombination, as such the main results show that there is a differential male/female recombination frequency in Arabidopsis, this result is reported in our annual report to our commercial partners.
(Task 5.3).

WP6 results

This WP is likely to produce results after the end of our project.

We decided to focus on genes that had been identified from our project at our meeting in Vienna, 2013,namely FANCM, PCH2 and ASY1. These genes were assessed by RNAi lines in Barley and from a tilling population in B. rapa

Potential impact and main dissemination activities and exploitation results

Table 1. Our output, results and exploitation from the MEIOsys project

Major Output and Results	Range of Applications	Expected Impact /Targeted User Group	Time - span	Responsible exploitation partners
1.Techniques and procedures for a systems biology approach to complex biological processes.	• Understanding basis of recombination networks • A systems biology approach has been developed as a powerful tool that may be applied to other basic biological processes.	Enhancing European research and esteem Extension of informatic approaches for use in other biological applications	4-5	UoB UNIVIE IMP INRA JHI
2 Inventory of recombination proteins	• We have produced an extensive database	Place EU in highly competitive global research area with our Meiotic research laboratories generally The company Key gene has indicated that it is interested in these results	5	UoB UNIVIE INRA CNRS UCM
3. ***Optimised system for modulating recombination in crop species***	• Increased variation in crop species	Use of techniques for range of crops in EU. Increased yields in crops New cultivars to cope with environmental challenges KWS and Riik –Zwann have already expressed an interest in our results; we will negotiate with them regarding their input in taking this work forward	4-10	UoB UNIVIE JHI CNR

In addition to the project-level major outputs and results listed in the table above we anticipate that we will provide: The methodology associated with modulating recombination in crop species will be provided to research laboratories and plant breeders

The end-users in the consortium will begin to make use of the project results following the close of the project. This additional time will be needed partly for the dissemination of results and partly for further research, development and validation work to tailor models to specific applications. The full potential for exploitation will be available approximately 5-7 years after project start, when plant breeders will use our protocols.

3.2.3 Additional dissemination activities

Further to the dissemination and exploitation activities mentioned in the preceding section, the following extra activities have also been carried out by the MEIOsys consortium:

A website for the MEIOsys project was created and continuously updated during the project period. The web-site consists of separate portals for public access and a restricted site for participants, including a site for data bases that has been developed.

Partners will continue to make efforts in disseminating information by continually presenting the findings (with the prior consent of the MEIOsys consortium) of the research through publications in international scientific journals and conferences. Our project has generated new knowledge and new technology that has been published in leading international journals, and has also been presented at academic conferences.

Two workshops have taken place, each in 4 days in length; the Madrid training workshop in February 2012, designed for our researchers and our final meeting in Naples in May 2014. With the exception of that related to the confidentiality of the project, non-confidential information given during training will be made available to the targeted groups. The target groups will include staff belonging to the partner organisations and to other potential users, who have been trained on project's methods, tools, and outcomes, and their implementation and use for industrial support.

WP8 is designed to improve the training of our researchers in the various activities that each participant is able to offer. We have developed both cytogenetic and molecular tools to study *Arabidopsis* meiosis, and have already exchanged researchers for training in these techniques. MEIOsys will improve the training of researchers.

Linking MEIOsys dissemination to International Conferences, partners, such as UNIVIE and UCM have experience of the successful organisation of International Conferences on Meiosis. They will continue to be involved in these events in the following years. MEIOsys partners will use these conference series as opportunities to disseminate the project's information. Key partners of the project are also involved in organising other major international conferences, which will help, greatly, the project's dissemination.

The MEIOsys project will be also disseminated at other local events in the participating EU countries (e.g. seminars, workshops and conferences across the EU)**.** Partners will make efforts to participate in these events.

Other dissemination activities, also at our final Naples meeting focused on "Gender Issues". The purpose of this activity was to attract academic both female and male, and encourage their involvement in the research and applications of the results from the project, the implementation of the Meiosis methods and tools in their activities.

4.1 Report on societal implications

ETHICS

1. Did your project undergo an Ethics Review (and/or Screening)?	Not applicable
If Yes: have you described the progress of compliance with the relevant Ethics Review/Screening Requirements in the frame of the periodic/final reports?	Not applicable

2. Please indicate whether your project involved any of the following issues:

RESEARCH ON HUMANS

Did the project involve children?	Not applicable
Did the project involve patients?	Not applicable
Did the project involve persons not able to consent?	Not applicable
Did the project involve adult healthy volunteers?	Not applicable
Did the project involve Human genetic material?	Not applicable
Did the project involve Human biological samples?	Not applicable
Did the project involve Human data collection?	Not applicable

RESEARCH ON HUMAN EMBRYO/FOETUS

Did the project involve Human Embryos?	Not applicable
Did the project involve Human Fetal Tissue / Cells?	Not applicable
Did the project involve Human Embryonic Stem Cells (hESCs)?	Not applicable
Did the project on human Embryonic Stem Cells involve cells in culture?	Not applicable
Did the project on human Embryonic Stem Cells involve the derivation of cells from Embryos?	Not applicable

PRIVACY

Did the project involve processing of genetic information or personal data (eg. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?	Not applicable
Did the project involve tracking the location or observation of people?	Not applicable

RESEARCH ON ANIMALS

Did the project involve research on animals?	Not applicable
Were those animals transgenic small laboratory animals?	Not applicable
Were those animals transgenic farm animals?	Not applicable
Were those animals cloned farm animals?	Not applicable
Were those animals non-human primates?	Not applicable

RESEARCH INVOLVING DEVELOPING COUNTRIES

Did the project involve the use of local resources (genetic, animal, plant etc)?	Yes - plant
Was the project of benefit to local community (capacity building, access to healthcare, education etc)?	Not applicable

DUAL USE

Research having direct military use	Not applicable
Research having potential for terrorist abuse	Not applicable

WORKFORCE STATISTICS

3. Workforce statistics for the project: Please indicate in the table below the number of people who worked on the project (on a headcount basis).

Type of Position	Number of Women	Number of Men
Scientific Coordinator	1	1
Work package leaders	3	5
Experienced researchers (i.e. PhD	11	7
PhD student	5	6
Other	7	2

4. How many additional researchers (in companies and universities) were recruited specifically for this project?	4
Of which, indicate the number of men:	2

5. Did you carry out specific Gender Equality Actions under the project?	We have considered whether sex and gender are relevant to the objectives and methodology of the project and considered that these are not specifically gender orientated. We did however devise a Gender Action Plan as it is recognised that participation of women both in research and academic posts in Plant Genetics is still low. We have actively encouraged participation of both genders in the context of this project. The women involved in this project are experienced researchers and leaders in their scientific fields and we have allocated the responsibility and lead for 3 of our work- packages to women (WP 5, 7, 8). **Athena SWAN Charter** The Athena SWAN Charter promotes and rewards good employment practice in the recruitment, retention and progression of female academics in STEMM. The Charter was founded in 2005 by the Royal Society and the Scientific Women's Academic Network (SWAN) to address the sector-wide issues of female under-representation in STEMM – particularly at senior level – and the high loss rate of women in STEMM. The University joined the Charter in March 2011. The Schools of Chemistry, Civil Engineering and Mathematics and the School of Biosciences have achieved Bronze Athena SWAN Charter awards in the April 2013 round of awards, announced in September 2013. The awards recognise the commitment made by those Schools to improving the recruitment, retention and progression of female academics in STEMM. Further reference can be found by visiting: https://intranet.birmingham.ac.uk/collaboration/equality/documents/UoBirmingham-Biosciences-April-2013-APPLICATION

6. Which of the following actions did you carry out and how effective were they?	
Design and implement an equal opportunity policy	Already in place within each partner institution
Set targets to achieve a gender balance in the workforce	Already in place within each partner institution
Organise conferences and workshops on gender	Already in place within each partner institution
Actions to improve work-life balance	Flexible working hours and working from home for female members of the consortium with children.
Other:	See Athena Swan Charter above and at: https://intranet.birmingham.ac.uk/collaboration/equality/documents/UoBirmingham-Biosciences-April-2013-APPLICATION

7. Was there a gender dimension associated with the research content - i.e. wherever people were the focus of the research as, for example, consumers, users, patients or in trials, was the issue of gender considered and addressed?	Not applicable
If yes, please specify:	Not applicable

SYNERGIES WITH SCIENCE EDUCATION

8. Did your project involve working with students and/or school pupils (e.g. open days, participation in science festivals and events, prizes/competitions or joint projects)?	Yes
If yes, please specify:	(1) Sexual Plant Reproduction Open Day at Bristol University and outreach event aimed at general public and children in July 2011. (2) Outreach event at Think Tank, Birmingham in June 2014 aimed at primary and secondary school children involving interactive plant DNA extraction experiments.

9. Did the project generate any science education material (e.g. kits, websites, explanatory booklets, DVDs)?	(1) Project website with public-facing section: www.meiosys.org. (2) MEIOsys banners - both public and scientific based explaining project theory and objectives.

INTERDISCIPLINARITY

10. Which disciplines (see list below) are involved in your project?	
Main discipline:	Meiotic recombination research
Associated discipline:	Bioinformatic modeling
Associated discipline:	Mass Spectrophotometry (MS)

ENGAGING WITH CIVIL SOCIETY AND POLICY MAKERS

11a. Did your project engage with societal actors beyond the research community?	No
11b. If yes, did you engage with citizens (citizens' panels / juries) or organised civil society (NGOs, patients' groups etc.)?	Not applicable
11c. In doing so, did your project involve actors whose role is mainly to organise the dialogue with citizens and organised civil society (e.g. professional mediator; communication company, science museums)?	Not applicable
12. Did you engage with government / public bodies or policy makers (including international organisations)	Not applicable
13a. Will the project generate outputs (expertise or scientific advice) which could be used by policy makers?	Not applicable

USE AND DISSEMINATION

14. How many articles were published/accepted for publication in peer-reviewed journals?	26
To how many of these is open access provided?	24
How many of these are published in open access journals?	24
How many of these are published in open repositories?	24
To how many of these is open access not provided?	2

Please check all applicable reasons for not providing open access:

publisher's licensing agreement would not permit publishing in a repository	No
no suitable repository available	No
no suitable open access journal available	Yes
no funds available to publish in an open access journal	No
lack of time and resources	No
lack of information on open access	No
If other - please specify	
15. How many new patent applications ('priority filings') have been made? ("Technologically unique": multiple applications for the same invention in different jurisdictions should be counted as just one application of grant).	1: Mercier, R. and W. Crismani (2013). Increase in meiotic recombination in plants by inhibiting the fancm protein, Google Patents.
16. Indicate how many of the following Intellectual Property Rights were applied for (give number in each box).	Not applicable
Trademark	0
Registered design	0
Other	0
17. How many spin-off companies were created / are planned as a direct result of the project?	Not applicable
Indicate the approximate number of additional jobs in these companies:	Not applicable
18. Please indicate whether your project has a potential impact on employment, in comparison with the situation before your project:	Not applicable
19. For your project partnership please estimate the employment effect resulting directly from your participation in Full Time Equivalent (FTE = one person working fulltime for a year) jobs:	0

MEDIA AND COMMUNICATION TO THE GENERAL PUBLIC

20. As part of the project, were any of the beneficiaries professionals in communication or media relations?	Not applicable
21. As part of the project, have any beneficiaries received professional media / communication training / advice to improve communication with the general public?	Not applicable

22. Which of the following have been used to communicate information about your project to the general public, or have resulted from your project?	
Press Release	Yes
Media briefing	Yes
TV coverage / report	No
Radio coverage / report	No
Brochures /posters / flyers	Yes
DVD /Film /Multimedia	No
Coverage in specialist press	Yes
Coverage in general (non-specialist) press	No
Coverage in national press	No
Coverage in international press	No
Website for the general public / internet	Yes
Event targeting general public (festival, conference, exhibition, science café)	Yes

23. In which languages are the information products for the general public produced?	
Language of the coordinator	Yes
Other language(s)	No
English	Yes

Attachments	
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