Work And Budget Plan

BM1206 Grant Agreement Period 4

01/05/2016 to 29/04/2017

Section I: Action Profile

Action General Information

Action Code	BM1206	MC Chair	Dr Sergi Castellvi-Bel
Action Title	BM1206 - Cooperation Studies on Inherited Susceptibility to Colorectal Cancer		
MOU	BM1206-MoU	Draft MOU	oc-2012-1-11711
CSO Approval Date	2012-11-21		
Action Start Date	2013-04-30	Action End Date	2017-04-29
Science Officer	Dr Inga Dadeshidze	Administrative Officer	Ms Jeannette Nchung Oru

Participating COST Member Countries and Cooperating State:

	ITC		Non-ITC		Total
Cost Countries having accepted the MOU	Number	9	Number	13	22
	% of all ITCs	40.91%	% of all non-ITCs	59.09%	
Number of MC Members	14		18		32

Country and Acceptance Date		
AT 07/01/2013	IE 13/01/2014	RS 28/02/2014
HR 06/03/2014	IL 29/05/2013	ES 28/11/2012
CY 17/06/2013	IT 14/02/2013	SE 07/02/2013
CZ 06/06/2013	MT 12/03/2013	TR 07/05/2013
FI 17/12/2012	NL 21/01/2013	UK 28/11/2012
FR 14/06/2013	NO 22/10/2013	MK 27/02/2013
DE 17/01/2013	PT 11/01/2013	
EL 10/04/2014	RO 07/06/2013	

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International cooperation

	NNC	IPC	Specific Organisation	Total
Number of entities formally approved to join Action	0	1	0	1
Number of countries	0	1	0	1

Working Groups

	WG Title	WG Leader	Number of Members
WG1	Genetic Association Studies	Prof Ian Tomlinson	112
WG2	Functional Genomics	Dr JOSE LUIS GOMEZ-SKARMETA	50
WG3	Next Generation Sequencing	Dr Tom van Wezel	98
WG4	Statistical Modelling	Dr Albert Tenesa	115

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Section II: MoU objectives and Grant Agreement Period Goals and Activities

Action Objectives from MoU

Aim/primary Objective	The main objective of the Action is to comprehensively understand the impact of inherited susceptibility in CRC for profiling individual disease risk and performing early screening and treatment monitoring. By doing so, new molecular biomarkers will be implemented and validated for personalized CRC medicine.
Secondary objectives	• Identification of new CRC susceptibility variants: A polygenic model of inherited susceptibility to CRC implies the co-inheritance of multiple risk variants. So far, 20 common, low-penetrance genetic variants for CRC susceptibility have been identified by GWAS. This Action will permit to boost sample size and statistical power (participating cohorts sum up more than 50,000 cases and 50,000 controls) and, therefore, it is very likely that additional genetic variants linked to CRC will be identified. Large-scale meta-analyses of existing and newly generated GWAS data will be performed and replication of initial GWAS findings in additional cohorts will be used to robustly confirm those genetic variants that participate in CRC susceptibility. • Functional links for CRC susceptibility variants: Most GWAS variants are unlikely to alter protein function and fine mapping and functional studies will be used to identify a correlated functional variant. The identification of the functional variation that causes increased CRC risk may lead to the development of new means of preventing the disease. However, the journey from the associated polymorphism to functional variant is not simple and will require additional work. In order to perform an initial search for readily identifiable functional variants, fine mapping in the regions close to each disease-associated single nucleotide polymorphism (SNP) or copy number variant (CNV) should be undertaken, enriching for variants in strong linkage disequilibrium (LD) with that SNP/CNV and with possible functional effects. Basic functional work should also be performed, such as assessing the levels of mRNAs and proteins in each region in patients of known genotypes, as well as more complex studies such as chromatin mapping, gene reporter and allele-specific expression experiments. • Genetic variants involved in CRC survival and treatment toxicity: CRC genetic susceptibility variants could also act as biomarkers for CRC survival and treatment response. For instance, inherited genetic variants can modulate the pharmacokinetics/pharmacodynamics of drugs used in CRC treatment by substantially affecting individual response and toxicity to chemotherapy. Therefore, GWAS data will be analyzed regarding CRC survival and treatment toxicity in order to identify genetic variants linked to differential prognosis and adverse drug reactions. • Genetic variants enriched in CRC subgroups: The impact of CRC susceptibility genetic variation will not be universally generic and some of the risk variants will impact preferentially on CRC subtypes, such as early-onset or microsatellite-unstable CRC

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(MSI+ CRC). If some of the CRC genetic susceptibility variants appear to be associated with some clinical and familial features, it could have potential important implications for screening and surveillance strategies for this disease.

- New predisposition genes for CRC in families with unknown genetic basis: Next generation sequencing will be useful to identify new CRC predisposition genes in selected high-risk and early-onset families with unknown genetic basis from the participating cohorts.
- Interactions between CRC susceptibility variants and environment: CRC risk is undoubtedly determined by complex interactions between genetic and lifestyle/dietary risk factors. Epidemiological studies have established several dietary risk factors for colorectal neoplasia; these include low vegetable and high red meat consumption and micronutrient deficiency and excessive alcohol intake. CRC genetic susceptibility variants are thus likely to interact with these environmental lifestyle risk factors to modify risk and they should be incorporated into models of predisposition.
- High risk CRC profile of inherited variants by statistical modelling: Besides gene-environment interactions, it is also entirely conceivable that epistatic interactions between CRC genetic susceptibility variants may exist. A high-risk CRC profile using mentioned parameters could be developed using data from all participating cohorts and be very useful as a molecular tool for personalized CRC medicine.

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Grant Agreement Period

Grant Agreement Period Start Date	01/05/2016	Grant Agreement Period End Date	29/04/2017

Grant Agreement Period Goals

Number	Grant Agreement Period Goal	MoU Objective(s) it relates to
GAPG 1	Identification of new CRC genetic susceptibility variants	Aim/Primary objective Secondary objective 1
GAPG 2	Identification of new adenoma genetic susceptibility variants	Aim/Primary objective Secondary objective 1 Secondary objective 4
GAPG 3	Meta-analysis of CRC genome-wide association studies (GWAS)	Aim/Primary objective Secondary objective 1
GAPG 4	Fine-mapping of CRC genetic susceptibility variants	Aim/Primary objective Secondary objective 2
GAPG 5	Fine-mapping of adenoma genetic susceptibility variants	Aim/Primary objective Secondary objective 2 Secondary objective 4
GAPG 6	Functional links for CRC genetic susceptibility variants	Aim/Primary objective Secondary objective 2
GAPG 7	Functional links for adenoma genetic susceptibility variants	Aim/Primary objective Secondary objective 2 Secondary objective 4
GAPG 8	Genotype-phenotype correlation of CRC genetic susceptibility variants with patient survival and treatment response	Aim/Primary objective Secondary objective 3
GAPG 9	Genotype-phenotype correlation of CRC genetic susceptibility variants with CRC subgroups	Aim/Primary objective Secondary objective 4
GAPG 10	Identification of new predisposition genes for familial CRC	Aim/Primary objective Secondary objective 5
GAPG 11	Identification of new predisposition genes for serrated polyposis syndrome	Aim/Primary objective Secondary objective 5
GAPG 12	Identification of new predisposition genes for multiple adenoma/polyposis	Aim/Primary objective Secondary objective 5
GAPG 13	Functional characterization of new candidate predisposition genes for CRC	Aim/Primary objective Secondary objective 2 Secondary objective 5

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GAPG 14	Functional characterization of new candidate predisposition genes for serrated polyposis syndrome	Aim/Primary objective Secondary objective 2 Secondary objective 5
GAPG 15	Functional characterization of new candidate predisposition genes for multiple adenoma/polyposis	Aim/Primary objective Secondary objective 2 Secondary objective 5
GAPG 16	Meta-analysis of next generation sequencing data	Aim/Primary objective Secondary objective 5
GAPG 17	Consortium database compiling clinical, tumoral, molecular, genotyping and sequencing data	Aim/Primary objective Secondary objective 1 Secondary objective 2 Secondary objective 3 Secondary objective 4 Secondary objective 5 Secondary objective 6 Secondary objective 7
GAPG 18	Epistatic interaction between CRC/adenoma genetic susceptibility variants	Aim/Primary objective Secondary objective 6 Secondary objective 7
GAPG 19	Gene-environment interaction for CRC/adenoma genetic susceptibility variants	Aim/Primary objective Secondary objective 6 Secondary objective 7

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Section IV: Work and Budget Plan for the Grant Agreement Period

Work and Budget Plan Summary

A. COST Networking Tools	EUR
(1)Meetings	69,975.00
(2)Training Schools	18,240.00
(3)STSMs	8,400.00
(4)Dissemination	5,275.00
(5)Other Expenses Related to Scientific Activities	500.00
B. Total Science Expenditure(sum of(1) to (5))	102,390.00
C. FSAC(max. of 15% of B)	15,358.50
D. Total Expenditure(B+C)	117,748.50

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Meetings

Overview

Meeting Title	Meeting Type	Dates	Location	ITC	Total Cost(EUR)
October 2016 meeting	Management Committee Meeting, Working Group Meeting, Workshops/Conferences	20/10/2016 - 21/10/2016	Dubrovnik (Croatia)	Yes	30,000.00
February 2017 meeting	Management Committee Meeting, Working Group Meeting, Workshops/Conferences	08/02/2017 - 10/02/2017	Porto (Portugal)	Yes	39,975.00
				Total	69,975.00

Details

Meeting Type	Management Committee Meeting,Working Group Meeting,Workshops/Conferences		
Title of the Meeting	October 2016 meeting		
Grant Period Goal(s) it will address	Identification of new CRC genetic susceptibility variants,Identification of new adenoma genetic susceptibility variants,Meta-analysis of CRC genome-wide association studies (GWAS),Fine-mapping of CRC genetic susceptibility variants,Fine-mapping of adenoma genetic susceptibility variants,Functional links for CRC genetic susceptibility variants,Functional links for adenoma genetic susceptibility variants,Genotype-phenotype correlation of CRC genetic susceptibility variants with patient survival and treatment response,Genotype-phenotype correlation of CRC genetic susceptibility variants with CRC subgroups,Identification of new predisposition genes for familial CRC,Identification of new predisposition genes for serrated polyposis syndrome,Identification of new predisposition genes for multiple adenoma/polyposis,Functional characterization of new candidate predisposition genes for CRC,Functional characterization of new candidate predisposition genes for serrated polyposis syndrome,Functional characterization of new candidate predisposition genes for multiple adenoma/polyposis,Meta-analysis of next generation sequencing data,Consortium database compiling clinical, tumoral, molecular, genotyping and sequencing data,Epistatic interaction between CRC/adenoma genetic susceptibility variants,Gene-environment interaction for CRC/adenoma genetic susceptibility variants		
Description	Management Committee Meeting, Working Group Meeting, Workshops/Conferences. Co-located workshop, MC meeting and WG meeting in October 2016 focusing especially tumor somatic profiling		
Output(s)	Workshop dedicated to tumor somatic profiling in cancer, followed by our regular MC+WG meeting addressing everything going on in GAPG 1-19		
Location	Dubrovnik (Croatia)	ITC	Yes
Start Date	2016-10-20 13:00:00	End Date	2016-10-21 18:00:00

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Duration	2 days		
Number of expected total participants	40	Number of participants to be reimbursed from COST funds	40
Average reimbursement(per participant)(EUR)	695.00	Total Reimbursement costs (EUR)	27,800.00
Local Organiser Support (EUR)	2,200.00		
Total cost of the meeting (EUR)	30,000.00		

Meeting Type	Management Committee Meeting,Working Group Meeting,Workshops/Conferences		
Title of the Meeting	February 2017 meeting		
Grant Period Goal(s) it will address	Identification of new CRC genetic susceptibility variants,Identification of new adenoma genetic susceptibility variants,Meta-analysis of CRC genome-wide association studies (GWAS),Fine-mapping of CRC genetic susceptibility variants,Fine-mapping of adenoma genetic susceptibility variants,Functional links for CRC genetic susceptibility variants,Functional links for adenoma genetic susceptibility variants,Genotype-phenotype correlation of CRC genetic susceptibility variants with patient survival and treatment response,Genotype-phenotype correlation of CRC genetic susceptibility variants with CRC subgroups,Identification of new predisposition genes for familial CRC,Identification of new predisposition genes for serrated polyposis syndrome,Identification of new predisposition genes for multiple adenoma/polyposis,Functional characterization of new candidate predisposition genes for CRC,Functional characterization of new candidate predisposition genes for serrated polyposis syndrome,Functional characterization of new candidate predisposition genes for multiple adenoma/polyposis,Meta-analysis of next generation sequencing data,Consortium database compiling clinical, tumoral, molecular, genotyping and sequencing data,Epistatic interaction between CRC/adenoma genetic susceptibility variants,Gene-environment interaction for CRC/adenoma genetic susceptibility variants		
Description	Management Committee Meeting, Working Group Meeting, Workshops/Conferences Co-located 1-day MC meeting and WG meeting, and 2-day international workshop in February 2017. The workshop has the tentative title “Translating colorectal cancer research”		
Output(s)	2-day international workshop with the tentative title “Translating colorectal cancer research” with some participants in our Action as speakers, preceded by a 1-day MC+WG meeting addressing everything going on in GAPG 1-19 and closing up our Action as final meeting		
Location	Porto (Portugal)	ITC	Yes
Start Date	2017-02-08 09:00:00	End Date	2017-02-10 18:00:00
Duration	3 days		
Number of expected total participants	60	Number of participants to be reimbursed from COST funds	55

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Average reimbursement(per participant)(EUR)	545.00	Total Reimbursement costs (EUR)	29,975.00
Local Organiser Support (EUR)	10,000.00		
Total cost of the meeting (EUR)	39,975.00		

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Training School

Overview

Title of the Training School	Dates	Location	ITC	Total Cost(EUR)
Introduction to genetic models: from C. elegans to mouse	04/07/2016 - 08/07/2016	Sevilla (Spain)	No	18,240.00
			Total	18,240.00

Details

Title of the Training School	Introduction to genetic models: from C. elegans to mouse		
Grant Period Goal(s) it will address	Fine-mapping of CRC genetic susceptibility variants,Fine-mapping of adenoma genetic susceptibility variants,Functional links for CRC genetic susceptibility variants,Functional links for adenoma genetic susceptibility variants,Functional characterization of new candidate predisposition genes for CRC,Functional characterization of new candidate predisposition genes for serrated polyposis syndrome,Functional characterization of new candidate predisposition genes for multiple adenoma/polyposis,Consortium database compiling clinical, tumoral, molecular, genotyping and sequencing data		
Description	This training school will introduce trainees into the use of animal models in functional genomics. It is very related to our WG2 (Functional Genomics) and it will include both theoretical and especially practical classes where trainees will spend most of their time on the lab performing the experiments with animal models. Trainers will be 10 members of the organizing group in Sevilla and they will not be paid for it. There will be 24 trainees from our Action and they will be reimbursed adjusting to their country of origin in the following manner: 450€ for ES participants 525€ for UK and NL participants 600€ for CZ participants 850€ for TR, MK and RS participants The total reimbursement grant is 13450€ but the system does not allow to set this number and automatically sets 13440€.		
Output(s)	It will be organized in a Functional Genomics platform (Aquatics vertebrate platform, https://www.upo.es/CABD/AquaticVertebratesPlatform/) in Seville located in the group of the WG2 leader (José Luis Gómez-Skarmeta) and trainers will be members of his group. This training school will be take place specifically for 24 participants from our COST Action, mostly junior researchers.		
Location	Sevilla (Spain)	ITC	No
Start Date	2016-07-04 09:00:00	End Date	2016-07-08 13:30:00
Number of trainers	10	Number of trainees	24
Number of trainers to be reimbursed	0	Number of trainees to be reimbursed	24
Average trainer Reimbursement(EUR)	0.00	Average reimbursement per trainee(EUR)	560.00
Total trainer Reimbursement(EUR)	0.00	Total trainee Grant(EUR)	13,440.00
Local Organiser Support (EUR)	4,800.00		

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Total cost of the Training School(EUR)	18,240.00

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STSM

Number	4
Average cost per STSM(EUR)	2,100.00
Total cost(EUR)	8,400.00

How will the STSMs contribute to the achievement of the Grant Period Goals?
Identification of new CRC genetic susceptibility variants,Identification of new adenoma genetic susceptibility variants,Meta-analysis of CRC genome-wide association studies (GWAS),Fine-mapping of CRC genetic susceptibility variants,Fine-mapping of adenoma genetic susceptibility variants,Functional links for CRC genetic susceptibility variants,Functional links for adenoma genetic susceptibility variants,Genotype-phenotype correlation of CRC genetic susceptibility variants with patient survival and treatment response,Genotype-phenotype correlation of CRC genetic susceptibility variants with CRC subgroups,Identification of new predisposition genes for familial CRC,Identification of new predisposition genes for serrated polyposis syndrome,Identification of new predisposition genes for multiple adenoma/polyposis,Functional characterization of new candidate predisposition genes for CRC,Functional characterization of new candidate predisposition genes for serrated polyposis syndrome,Functional characterization of new candidate predisposition genes for multiple adenoma/polyposis,Meta-analysis of next generation sequencing data,Consortium database compiling clinical, tumoral, molecular, genotyping and sequencing data,Epistatic interaction between CRC/adenoma genetic susceptibility variants,Gene-environment interaction for CRC/adenoma genetic susceptibility variants Exchange Visits particularly intended for young scientists These Exchange Visits are aimed at strengthening the existing networks by allowing scientists to go to an institution or laboratory in another COST Country to foster collaboration, to learn a new technique or to take measurements using instruments and/or methods not available in their own institution/laboratory. They are particularly intended for young scientists. STSM will generally contribute to all GP goals (GAPG 1-19) and outputs will include those specific to the related goal.

Disseminations

Title	Type	Publisher/provider	Expected date of Release	Cost(EUR)
Open-access articles	Printed publication	Several open-access publishers	01/09/2016	4,275.00

How will this Dissemination contribute to the achievement of the Grant Period Goals?
Identification of new CRC genetic susceptibility variants,Identification of new adenoma genetic susceptibility variants,Meta-analysis of CRC genome-wide association studies (GWAS),Fine-mapping of CRC genetic susceptibility variants,Fine-mapping of adenoma genetic susceptibility variants,Functional links for CRC genetic susceptibility variants,Functional links for adenoma genetic susceptibility variants,Genotype-phenotype correlation of CRC genetic susceptibility variants with patient survival and treatment response,Genotype-phenotype correlation of CRC genetic susceptibility variants with CRC subgroups,Identification of new predisposition genes for familial CRC,Identification of new predisposition genes for serrated polyposis syndrome,Identification of new predisposition genes for multiple adenoma/polyposis,Functional characterization of new candidate predisposition genes for CRC,Functional characterization of new candidate predisposition genes for serrated polyposis syndrome,Functional characterization of new candidate predisposition genes for multiple adenoma/polyposis,Meta-analysis of next generation sequencing data,Consortium database compiling clinical, tumoral, molecular, genotyping

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and sequencing data,Epistatic interaction between CRC/adenoma genetic susceptibility variants,Gene-environment interaction for CRC/adenoma genetic susceptibility variants

Title	Type	Publisher/provider	Expected date of Release	Cost(EUR)
Dedicated website maintenance	Action Website	Antaviana, S.L.	01/05/2016	1,000.00

How will this Dissemination contribute to the achievement of the Grant Period Goals?	
Identification of new CRC genetic susceptibility variants,Identification of new adenoma genetic susceptibility variants,Meta-analysis of CRC genome-wide association studies (GWAS),Fine-mapping of CRC genetic susceptibility variants,Fine-mapping of adenoma genetic susceptibility variants,Functional links for CRC genetic susceptibility variants,Functional links for adenoma genetic susceptibility variants,Genotype-phenotype correlation of CRC genetic susceptibility variants with patient survival and treatment response,Genotype-phenotype correlation of CRC genetic susceptibility variants with CRC subgroups,Identification of new predisposition genes for familial CRC,Identification of new predisposition genes for serrated polyposis syndrome,Identification of new predisposition genes for multiple adenoma/polyposis,Functional characterization of new candidate predisposition genes for CRC,Functional characterization of new candidate predisposition genes for serrated polyposis syndrome,Functional characterization of new candidate predisposition genes for multiple adenoma/polyposis,Meta-analysis of next generation sequencing data,Consortium database compiling clinical, tumoral, molecular, genotyping and sequencing data,Epistatic interaction between CRC/adenoma genetic susceptibility variants,Gene-environment interaction for CRC/adenoma genetic susceptibility variants	
Total Disseminations	5,275.00

OERSA

Item	Cost(EUR)
Bank fees	500.00

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