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May 2015

SEVENTH FRAMEWORK PROGRAMME

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Validation Phase Meeting Special!

Welcome to this special edition of the FRAILOMIC newsletter! In this edition we report on the validation phase meeting held in Getafe, Spain on 19 January 2015. This meeting marks an important milestone for the FRAILOMIC project. It seemed appropriate to mark the occasion with a newsletter that could serve to update all members of the FRAILOMIC family on this event, and summarise some of the key outcomes. Please read on and enjoy hearing about all the pivotal developments at this meeting.

I would also ask you all once again to keep us informed of any news that you would like to share with all our FRAILOMIC colleagues. If you would consider writing a short article for the newsletter please email us with details. We would be delighted to help you with preparing your contribution and increasing your visibility within the consortium.

By Anna Durrance-Bagale – anna.durrance@niche.org.uk
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Validation Phase Meeting

19 January 2015 - Getafe, Spain

By Anna Durrance-Bagale, on behalf of Niche Science & Technology
(with thanks to our fantastic co-ordinator, Mónica Ballesteros, for sharing the minutes taken during the meeting)

The objective of this meeting was to provide each of the partner organisations with the opportunity to discuss processing and handling of biological samples involved in the validation phase of the project.

Professor Leocadio Rodriguez Mañas opened the meeting by welcoming everyone and giving the participants an update on the status of the project. Professor Mañas described how during 2014 the exploratory phase biological samples had been sent to the various laboratories. In addition, he reported how the study database had been populated with epidemiological and clinical data from the various cohorts. These two achievements in themselves represent significant progress in project implementation but Professor Mañas went on to report that assorted markers that form the basis of the sub-studies were being measured. He was delighted to report that, in short, the delivery of the pre-analysis stage of the exploratory phase is on target.

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Participants included

Leocadio Rodriguez Mañas and José Antonio Carnicero Carreno
Hospital Universitario de Getafe

Mónica Ballesteros, Mariam El Assar de la Fuente and José Maria Sánchez Puelles
Fundación de Investigación Biomédica Getafe

Fernando Rodríguez Artalejo
Universidad Autónoma de Madrid

Angelo Scuteri
Sardinia Cohort

David Gómez Cabrero
YouHealth

Somnath Chatterji
World Health Organization [WHO]

Francisco José Garcia Garcia
Hospital Virgen del Valle

Giuseppe Lippi
Azienda Ospedaliero-Universitaria di Parma

Alan Sinclair
Diabetes Frail, UK

The Harmonisation Process

David Gómez Cabrero gave an illuminating presentation describing the methodological aspects of the harmonisation process that represents a critical aspect of the FRAILOMIC project. The harmonisation process serves to control for differences in the data for the many variables (for example, frailty and Activities of Daily Living terms) that were derived from the various cohorts studied in our project. The process of harmonisation serves to provide coherence to measurements made at different sites during different studies, possibly with different scales, units and/or methodologies. It is easy to see how this was a Herculean task.

Cohorts in the Exploratory Phase

- InCHIANTI
- 3C
- ETES
- AMI

In the first phase, variable selection, the variables that are to be analysed were identified. Criteria for selecting variables included those data that:

- Provided useful information for the purposes of our research
- Complied with the required quality criteria
- Had an acceptable rate of missing data
- Were present in at least two of the four cohorts

In the second phase, the following criteria were used to obtain definitions for each variable:

1. A variable and measurement was selected: for example, age in years.
2. A variable was selected and units of measurement required harmonisation: for example, height in cm or m.
3. A variable was selected but both variable and measurements had to be harmonised: for example, smoking data.

The following summarises the results of this harmonisation process.

continued...

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Conclusions for each harmonised variable

Frailty criteria

- This variable will be handled criterion by criterion (Fried criteria)
- Combinations of several frailty criteria will be investigated
- The incidence of disability will be defined in each cohort
- The pre-frail concept will be used in the secondary analysis. The initial analysis will compare frail vs. non-frail (robust plus pre-frail)

Mini Mental State Examination

- The score for each item (30 items in total) and the overall score will be included
- The InChianti and ETES cohorts have recorded information about 30 items. The other cohorts will also be asked for this information
- In the validation phase (new cohorts) the score for each item will be included
- Education level in all cohorts will be included if available
- MMSE scores will be analysed adjusted by education level and age
- Potential associations with education will be checked and variables that are not associated with education will be identified

Center for Epidemiological Studies Depression Scale

- This variable will be handled as binary (depression: yes or no)
- For each database the definition will be independently defined but these will be documented
- All data will be investigated to discover any shared variables
- Potential associations with education will be checked and variables that are not associated with education will be identified

Conclusions for each harmonised variable

continued...

Instrumental Activities of Daily Living/Activities of Daily Living

- Both sets of data will be handled as binary and in aggregate form
- In ADL six variables will be considered, including incontinence

Lifestyle

- A coffee consumption variable will be included in the analysis
- In the validation phase (new cohorts), information on whether the coffee is regular or decaffeinated will be included. Whether this information is available in the existing cohorts will be ascertained
- The alcohol consumption variable will be standardised
- The smoking variable will be standardised by number of cigarettes/day

Consumption of medications

- The consumption of drugs will be analysed according to pharmacological groups
- Cohorts in which drug ATC classification has not been recorded will be asked to provide any available information. Whether it is possible to organise drugs into better high-level groups (for example, diabetes medication) will be investigated

Clinical information

- Data on systolic and diastolic blood pressure will be checked in the ETES cohort

Diagnosis of disease comorbidity

- The definition of ischaemic heart disease will be checked (using data from the InChianti cohort), and definitions of angina, myocardial infarction and heart failure will be refined

continued...

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- Chronic obstructive pulmonary disease will be included if it is available in the cohort data
- Self-reported disease will be identified to allow an analysis of disease comorbidity
- The definition of diabetes will be checked
- Data on visual loss/impairment and neurological dysfunction will be checked

Biological data

- Laboratories will provide information on haematimetric techniques and how biological samples were handled
- The International System of Units for biological samples will be reviewed
- Professor Lippi will provide a list with the basic data (glucose, uric acid, cholesterol, FT4, TSH, CPR, glycosylated haemoglobin, creatinine etc) to be determined in the biological samples
- Cardiovascular laboratory biomarkers will be checked

Others

- Self-reported health status, physical activity and diet will be included in the analysis
- YouHealth is to write a strategic plan for the statistical analysis. This will involve a meeting (face-to-face or virtual) between YouHealth, the study co-ordinator's team and the work package leaders of the validation phase (Dr Chatterji and Professor Rodriguez Artalejo). This will take place after the initial analysis but before too much time has been expended to allow YouHealth to gain valuable information for the analysis

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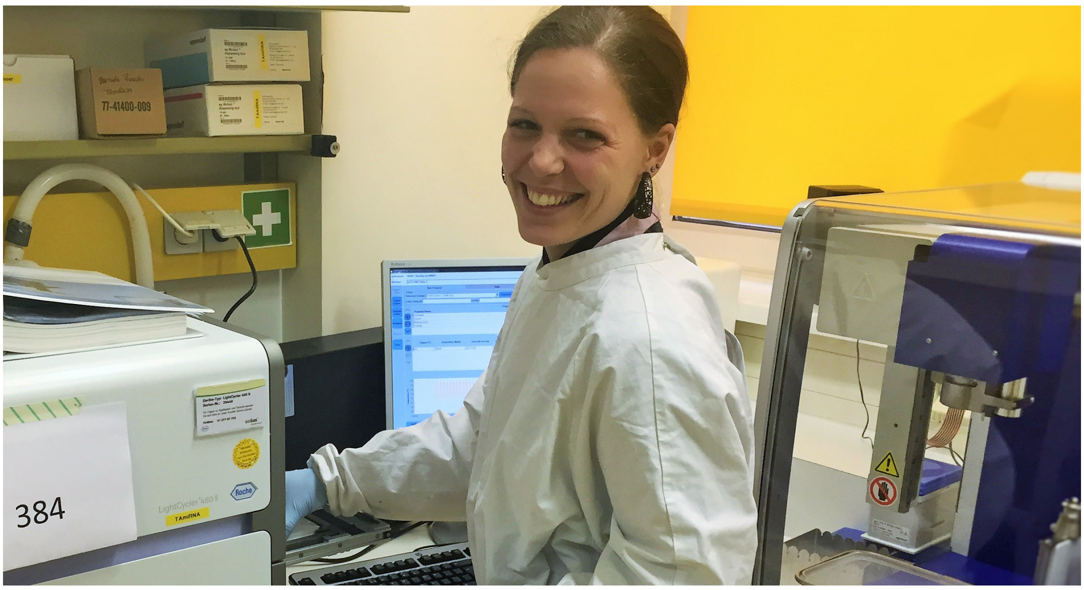
Partner News

Evercyte has concluded the analysis of blood-circulating microRNAs as part of the FRAILOMIC project. Amazingly, the Evercyte team have analysed over 430 samples from the Toledo Cohort (ETES) and 317 samples from the InChianti Cohort. They performed a parallel analysis of 91 distinct microRNA species and five quality control analytes for each sample.

	1	2	3	4	5	6	7	8	9	10	11	12
A	hsa-miR-96-5p	hsa-miR-96-5p	hsa-miR-500a-5p	hsa-miR-500a-5p	hsa-miR-7-5p	hsa-miR-7-5p	hsa-miR-642a-5p	hsa-miR-642a-5p	hsa-miR-200b-3p	hsa-miR-200b-3p	hsa-miR-92a-3p	hsa-miR-92a-3p
B	hsa-miR-96-5p	hsa-miR-96-5p	hsa-miR-500a-5p	hsa-miR-500a-5p	hsa-miR-7-5p	hsa-miR-7-5p	hsa-miR-642a-5p	hsa-miR-642a-5p	hsa-miR-200b-3p	hsa-miR-200b-3p	hsa-miR-92a-3p	hsa-miR-92a-3p
C	hsa-miR-221-3p	hsa-miR-221-3p	hsa-miR-495-3p	hsa-miR-495-3p	hsa-miR-487b	hsa-miR-487b	hsa-miR-486-5p	hsa-miR-486-5p	hsa-miR-454-3p	hsa-miR-454-3p	hsa-miR-451a	hsa-miR-451a
D	hsa-miR-221-3p	hsa-miR-221-3p	hsa-miR-495-3p	hsa-miR-495-3p	hsa-miR-487b	hsa-miR-487b	hsa-miR-486-5p	hsa-miR-486-5p	hsa-miR-454-3p	hsa-miR-454-3p	hsa-miR-451a	hsa-miR-451a
E	hsa-miR-376a-5p	hsa-miR-376a-5p	hsa-miR-369-3p	hsa-miR-369-3p	hsa-miR-196b-5p	hsa-miR-196b-5p	hsa-miR-342-5p	hsa-miR-342-5p	hsa-miR-195-5p	hsa-miR-195-5p	hsa-miR-328	hsa-miR-328
F	hsa-miR-376a-5p	hsa-miR-376a-5p	hsa-miR-369-3p	hsa-miR-369-3p	hsa-miR-196b-5p	hsa-miR-196b-5p	hsa-miR-342-5p	hsa-miR-342-5p	hsa-miR-195-5p	hsa-miR-195-5p	hsa-miR-328	hsa-miR-328
G	hsa-miR-29a-3p	hsa-miR-29a-3p	hsa-miR-27a-3p	hsa-miR-27a-3p	hsa-miR-193b-3p	hsa-miR-193b-3p	hsa-miR-24-3p	hsa-miR-24-3p	Cel-miR-39-3p CP	Cel-miR-39-3p CP	hsa-miR-192-5p	hsa-miR-192-5p
H	hsa-miR-29a-3p	hsa-miR-29a-3p	hsa-miR-27a-3p	hsa-miR-27a-3p	hsa-miR-193b-3p	hsa-miR-193b-3p	hsa-miR-24-3p	hsa-miR-24-3p	Cel-miR-39-3p CP	Cel-miR-39-3p CP	hsa-miR-192-5p	hsa-miR-192-5p
I	hsa-miR-18a-5p	hsa-miR-18a-5p	hsa-miR-215	hsa-miR-215	hsa-miR-21-5p	hsa-miR-21-5p	hsa-miR-20a-5p	hsa-miR-20a-5p	hsa-miR-208a	hsa-miR-208a	hsa-miR-205-5p	hsa-miR-205-5p
J	hsa-miR-18a-5p	hsa-miR-18a-5p	hsa-miR-215	hsa-miR-215	hsa-miR-21-5p	hsa-miR-21-5p	hsa-miR-20a-5p	hsa-miR-20a-5p	hsa-miR-208a	hsa-miR-208a	hsa-miR-205-5p	hsa-miR-205-5p
K	hsa-miR-181a-5p	hsa-miR-181a-5p	hsa-miR-17-5p	hsa-miR-17-5p	UniSp2 CP	UniSp2 CP	hsa-miR-29b-3p	hsa-miR-29b-3p	hsa-miR-155-5p	hsa-miR-155-5p	hsa-miR-154-5p	hsa-miR-154-5p
L	hsa-miR-181a-5p	hsa-miR-181a-5p	hsa-miR-17-5p	hsa-miR-17-5p	UniSp2 CP	UniSp2 CP	hsa-miR-29b-3p	hsa-miR-29b-3p	hsa-miR-155-5p	hsa-miR-155-5p	hsa-miR-154-5p	hsa-miR-154-5p
M	hsa-miR-223-3p	hsa-miR-223-3p	hsa-miR-143-3p	hsa-miR-143-3p	hsa-miR-942	hsa-miR-942	hsa-miR-140-5p	hsa-miR-140-5p	hsa-miR-377-3p	hsa-miR-377-3p	hsa-miR-30e-3p	hsa-miR-30e-3p
N	hsa-miR-223-3p	hsa-miR-223-3p	hsa-miR-143-3p	hsa-miR-143-3p	hsa-miR-942	hsa-miR-942	hsa-miR-140-5p	hsa-miR-140-5p	hsa-miR-377-3p	hsa-miR-377-3p	hsa-miR-30e-3p	hsa-miR-30e-3p
O	hsa-miR-126-3p	hsa-miR-126-3p	hsa-miR-125b-5p	hsa-miR-125b-5p	hsa-miR-34a-5p	hsa-miR-34a-5p	hsa-miR-124-3p	hsa-miR-124-3p	hsa-miR-499a-5p	hsa-miR-499a-5p	hsa-miR-10b-5p	hsa-miR-10b-5p
P	hsa-miR-126-3p	hsa-miR-126-3p	hsa-miR-125b-5p	hsa-miR-125b-5p	hsa-miR-34a-5p	hsa-miR-34a-5p	hsa-miR-124-3p	hsa-miR-124-3p	hsa-miR-499a-5p	hsa-miR-499a-5p	hsa-miR-10b-5p	hsa-miR-10b-5p

	13	14	15	16	17	18	19	20	21	22	23	24
A	hsa-miR-19a-3p	hsa-miR-19a-3p	hsa-miR-576-3p	hsa-miR-576-3p	hsa-miR-550a-5p	hsa-miR-550a-5p	hsa-miR-550a-3p	hsa-miR-550a-3p	hsa-miR-542-5p	hsa-miR-542-5p	hsa-miR-199b-5p	hsa-miR-199b-5p
B	hsa-miR-19a-3p	hsa-miR-19a-3p	hsa-miR-576-3p	hsa-miR-576-3p	hsa-miR-550a-5p	hsa-miR-550a-5p	hsa-miR-550a-3p	hsa-miR-550a-3p	hsa-miR-542-5p	hsa-miR-542-5p	hsa-miR-199b-5p	hsa-miR-199b-5p
C	hsa-miR-423-5p	hsa-miR-423-5p	hsa-miR-199a-5p	hsa-miR-199a-5p	hsa-miR-409-3p	hsa-miR-409-3p	hsa-miR-378a-5p	hsa-miR-378a-5p	hsa-miR-23a-3p	hsa-miR-23a-3p	hsa-miR-376c-3p	hsa-miR-376c-3p
D	hsa-miR-423-5p	hsa-miR-423-5p	hsa-miR-199a-5p	hsa-miR-199a-5p	hsa-miR-409-3p	hsa-miR-409-3p	hsa-miR-378a-5p	hsa-miR-378a-5p	hsa-miR-23a-3p	hsa-miR-23a-3p	hsa-miR-376c-3p	hsa-miR-376c-3p
E	hsa-miR-323a-3p	hsa-miR-323a-3p	hsa-miR-31-5p	hsa-miR-31-5p	hsa-miR-30e-5p	hsa-miR-30e-5p	hsa-miR-26b-5p	hsa-miR-26b-5p	hsa-miR-30a-5p	hsa-miR-30a-5p	hsa-miR-194-5p	hsa-miR-194-5p
F	hsa-miR-323a-3p	hsa-miR-323a-3p	hsa-miR-31-5p	hsa-miR-31-5p	hsa-miR-30e-5p	hsa-miR-30e-5p	hsa-miR-26b-5p	hsa-miR-26b-5p	hsa-miR-30a-5p	hsa-miR-30a-5p	hsa-miR-194-5p	hsa-miR-194-5p
G	hsa-miR-223-5p	hsa-miR-223-5p	hsa-miR-190a	hsa-miR-190a	UniSp5 CP	UniSp5 CP	hsa-miR-222-3p	hsa-miR-222-3p	hsa-miR-1908	hsa-miR-1908	hsa-miR-210	hsa-miR-210
H	hsa-miR-223-5p	hsa-miR-223-5p	hsa-miR-190a	hsa-miR-190a	UniSp5 CP	UniSp5 CP	hsa-miR-222-3p	hsa-miR-222-3p	hsa-miR-1908	hsa-miR-1908	hsa-miR-210	hsa-miR-210
I	hsa-miR-203a	hsa-miR-203a	hsa-miR-188-3p	hsa-miR-188-3p	hsa-miR-181c-5p	hsa-miR-181c-5p	hsa-miR-214-3p	hsa-miR-214-3p	hsa-miR-181c-3p	hsa-miR-181c-3p	hsa-miR-181a-3p	hsa-miR-181a-3p
J	hsa-miR-203a	hsa-miR-203a	hsa-miR-188-3p	hsa-miR-188-3p	hsa-miR-181c-5p	hsa-miR-181c-5p	hsa-miR-214-3p	hsa-miR-214-3p	hsa-miR-181c-3p	hsa-miR-181c-3p	hsa-miR-181a-3p	hsa-miR-181a-3p
K	UniSp4 CP	UniSp4 CP	hsa-miR-330-3p	hsa-miR-330-3p	hsa-miR-148a-3p	hsa-miR-148a-3p	hsa-miR-146b-5p	hsa-miR-146b-5p	UniSp3 IPC	UniSp3 IPC	hsa-miR-145-5p	hsa-miR-145-5p
L	UniSp4 CP	UniSp4 CP	hsa-miR-330-3p	hsa-miR-330-3p	hsa-miR-148a-3p	hsa-miR-148a-3p	hsa-miR-146b-5p	hsa-miR-146b-5p	UniSp3 IPC	UniSp3 IPC	hsa-miR-145-5p	hsa-miR-145-5p
M	hsa-miR-136-3p	hsa-miR-136-3p	hsa-miR-135a-5p	hsa-miR-135a-5p	hsa-miR-133a	hsa-miR-133a	hsa-miR-133b	hsa-miR-133b	hsa-miR-130a-3p	hsa-miR-130a-3p	hsa-miR-127-3p	hsa-miR-127-3p
N	hsa-miR-136-3p	hsa-miR-136-3p	hsa-miR-135a-5p	hsa-miR-135a-5p	hsa-miR-133a	hsa-miR-133a	hsa-miR-133b	hsa-miR-133b	hsa-miR-130a-3p	hsa-miR-130a-3p	hsa-miR-127-3p	hsa-miR-127-3p
O	hsa-miR-410	hsa-miR-410	hsa-miR-10a-5p	hsa-miR-10a-5p	hsa-miR-582-3p	hsa-miR-582-3p	hsa-miR-106b-5p	hsa-miR-106b-5p	hsa-miR-1	hsa-miR-1	hsa-miR-624-5p	hsa-miR-624-5p
P	hsa-miR-410	hsa-miR-410	hsa-miR-10a-5p	hsa-miR-10a-5p	hsa-miR-582-3p	hsa-miR-582-3p	hsa-miR-106b-5p	hsa-miR-106b-5p	hsa-miR-1	hsa-miR-1	hsa-miR-624-5p	hsa-miR-624-5p

This picture is of the Evercyte technician, Susanna, loading the final qPCR plate into the reader. As you can see from her smile, we are all happy about this event!



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Publications Update

The project leaders wanted to say 'well done everyone' in submitting your financial and scientific reports to the co-ordinating team – another milestone achieved!

Niche is continuing to work on the dissemination plan for the FRAILOMIC project. The first manuscript was submitted to the journal 'Gerontology' in early December. Peer review comments were received in early February, and a response was sent to the journal in early April. A second review manuscript is also being developed.

Professor Lippi has commented about the study in a 'Letter to the Editor' submitted to the journal 'Clinical Chemistry and Laboratory Medicine'. The article, entitled 'Laboratory biomarkers and frailty: presentation of the FRAILOMIC Initiative' explains why frailty needs to be addressed, how we can prevent or at least delay frailty, and describes the molecular and biochemical markers that will be measured during the FRAILOMIC project to help predictive, diagnostic and prognostic models. The letter was accepted for publication by the journal in late February.

If you have a manuscript, letter to the editor, abstract, or any other type of document that you would like the IPC to consider please do submit it to Anna. And remember that Niche is always here to help in any way we can.

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