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Welcome to the latest issue of the FRAILOMIC newsletter!

In the UK we have a saying that you wait hours for a bus and then two come along at once. Well, it seems that in this case FRAILOMIC newsletters are like buses!

Please read on and enjoy hearing about all the recent developments for this project. I would also ask you to keep us informed of any news that you would like to share with all our FRAILOMIC colleagues. If you would like to engage in writing a short article for the newsletters please email us with details. We would be more than happy to help you with anything you may need to prepare it.

In this issue...

- Mallorca Meeting Updates

Annual Meeting

3-4 November 2014

By Anna Durrance-Bagale, on behalf of Niche Science & Technology

I really enjoyed meeting everyone at the FRAILOMIC meeting in November, particularly as I have been in contact with many of you about publications since taking over from Sev, so putting faces to names and shaking hands was useful.

I even enjoyed the weather on Tuesday, when it felt as if the roof of the building might be ripped off before lunch! I have summarised what I think were the main 'take home messages' from the meeting, which served as an opportunity for us to update each other on the project achievements and advances we made during 2014. The full minutes of the meeting have been emailed out to everyone, but please do let us know if you haven't received a copy and we will ensure that these are sent to you. In addition, the minutes and slide presentations from the meeting have also been disseminated to all partners. Please let us know if you haven't received a copy.

Day 1

Professor Leo Rodriguez Mañas from SERMAS started the meeting by sharing with everyone the sad news that Magali González-Colaço Harmand was leaving the consortium. Mónica Ballesteros, a clinical epidemiologist who is studying for a PhD in Public Health at Universitat Autònoma de Barcelona, is taking over the role from Magali and was introduced to everyone. We are all sure that she will do a fantastic job!

Leo was followed by Magali, who gave an update on the project as a whole. The exploratory phase of the study was designed to ensure that all biological samples from each cohort were delivered successfully to the laboratories involved. These samples have been received and processed over the course of the last year, and this phase should be completed by the end of January 2015. The LIFE cohort, based in the USA, is no longer taking part

in the initiative and was replaced by the AMI cohort, which includes samples taken from participants randomly selected from the farmers in the rural Gironde area in south-western France. These participants were aged at least 65 years and had to have been involved in agriculture for at least 20 years.

The distribution of participants in the exploratory phase was as below:

Cohort	Frail	Non-frail
INCHIANTI	210	317
3C	383	525
AMI	240	320
ETES	362	425

The numbers and types of variables (e.g., demographic data, frailty measures, rating scales etc) selected for analysis are described in more detail in the minutes of the meeting. Variables were selected carefully to ensure that they could also be useful in the cardiovascular disease-related sub-studies. Scales used to measure

Day 1 continued...

the variables have been harmonised so that all laboratories are measuring the same parameters. YouHealth are currently constructing models to facilitate the analysis of the data.

The second phase of FRAILOMIC, the validation phase, will include cohorts from ENRICA, SARDINIA, MAPT, SAGE and COURAGE (WHO cohorts), and ETES. A meeting will be arranged in January 2015 to consider key information regarding each cohort (for example, types of clinical and biological information available, types and amounts of samples available, and any legal or ethical issues that are specific to any cohort). During the meeting Somnath Chatterji raised the issue that samples from the WHO cohorts (SAGE and COURAGE) can't be analysed outside the respective country in which they were obtained (China, Ghana, India, Mexico, Russian Federation and South Africa). The team discussed possible work arounds to address this issue. The SAGE cohort currently stands at approximately 50,000 respondents.

Following Magali's presentation, each

FRAILOMIC partner presented slides describing their progress. Short summaries are provided below.

- Evercyte: Matthias Hackl began with an update stating that his team are currently examining circulating microRNA in the samples received from the TOLEDO and INCHIANTI cohorts. This analysis is ongoing and should be finished in January 2015.
- SistemasGenómicos: Rebeca Miñambres was up next and shared with everyone the news that genotyping has begun in samples received from the TOLEDO and AMI cohorts. Expression analysis is on target to be completed in February 2015.
- Mosaiques Diagnostics: Urinary proteomics was discussed next, by Thomas Köck. Two hundred and 68 urine samples were received and 281 of these have been successfully analysed.
- Azienda Ospedaliero-Universitaria di Parma: An update on biomarkers was the next presentation. Between March and September 2014 samples from ETES,

3C and AMI were received: plasma and serum from ETES and AMI and serum from 3C. However, some aliquots were not large enough to allow processing. Different processing techniques, using different instruments, are being used to identify the most feasible and valuable assays with which to analyse the relevant biomarkers.

- University of Innsbruck: Pidder Jansen-Duerr gave a presentation describing the most important biomarkers of senescence-associated secretory phenotype components. Currently, three biomarker candidates have been tested in over 800 samples. Two antigens were not measured for technical reasons, and these may be replaced by other markers (this is being discussed). The next step is to select markers for the validation phase.
- Cardiff Metropolitan University: Lee Butcher discussed technical aspects of analysing Eotaxin-1, AGEs and sRAGE biomarkers and compared the results so far with those seen previously by other researchers.
- German Institution of Nutrition: Tilman Grune described the biomarkers analysed in the 1568 samples received. The plasma protein analysis data were unreliable, and it was postulated that fluctuating temperatures may have affected the samples. Two possibilities are being discussed: (i) to run the analysis again or (ii) to check whether the rest of the biomarkers are affected in these samples.
- University of Valencia: José Viña presented data on the metabolomics and oxidative stress parameter analysis. Thus far, 419 blood plasma samples have been measured using NMR spectroscopy and 94 spectral regions have been integrated for analysis. Before the end of 2014 pending tasks include analysing isoprostanes in 288 urine samples from the INCHIANTI cohort, and analysing MDA in 313 plasma samples from the AMI cohort and 156 plasma samples from the TOLEDO cohort.
- SERMAS: This presentation concerned hypoxia inducible factor. Their first

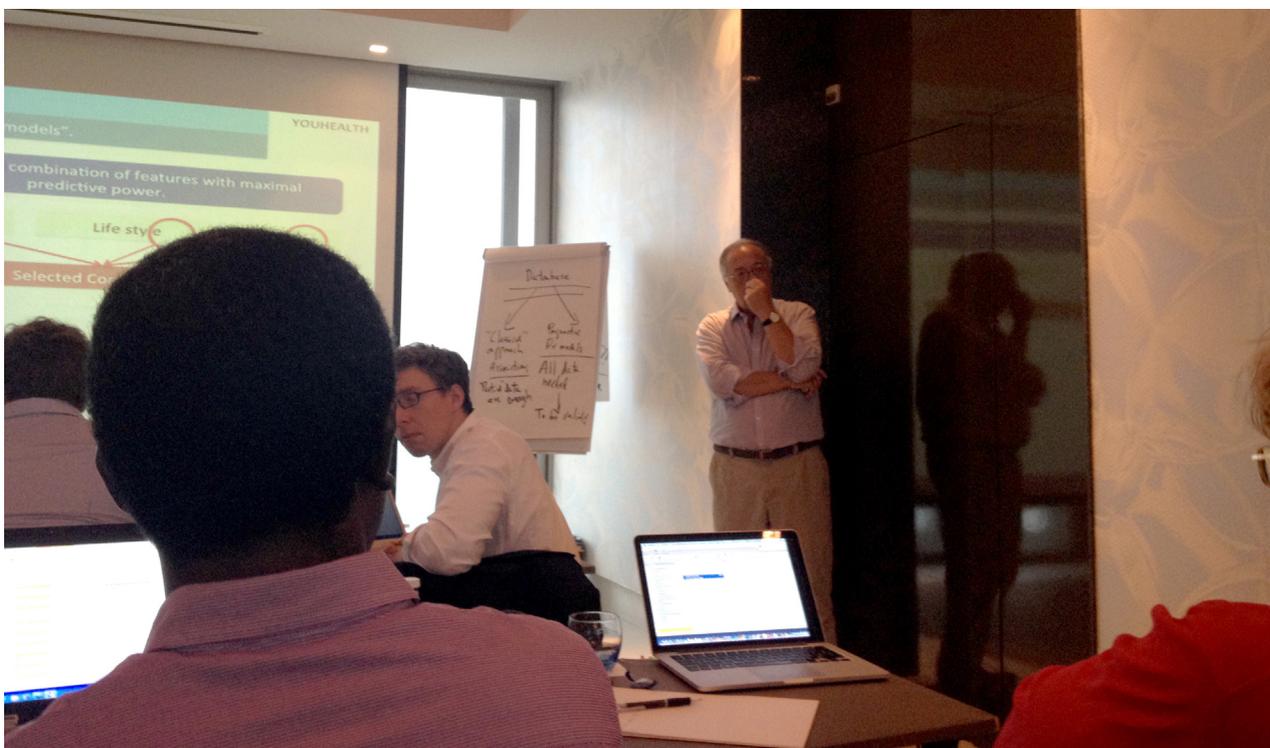
Day 1 continued...

task was to determine the expression of several genes modulated by HIF that regulate cell functions closely related to frailty and its mechanisms. The second task was to measure serum levels of HIF. The expression of 22 genes has been tested in 364 samples, and 381 serum samples have been analysed for HIF levels.

- Niche Science & Technology Ltd: Anna

Durrance-Bagale gave the penultimate presentation before dinner, discussing the progress made thus far with manuscripts, the FRAILOMIC website and newsletters.

The first day of the meeting closed with a delicious buffet dinner and a chance for the partners to relax, gossip and discuss non-FRAILOMIC related issues!



Day 2

On the second and final day emphasis was placed on discussion of the various study cohorts and the statistical analysis.

- YouHealth: Imad Abugessaisa and David Gomez-Cabrero explained the different phases of the statistical analysis: these include the validation of the biomarkers, identification of relevant variables and construction of the final models. All variables collected in the cohorts will be analysed, even if the variable has only been collected in a single cohort and not over all cohorts. YouHealth stated that it would take approximately 2 months to construct models once all data have been received (approximately at the end of February 2015). Issues to be resolved include agreeing how data should be presented in the spreadsheets sent to YouHealth; this will help with harmonising the data before they are analysed especially as some variables have not been examined in as much detail in all cohorts. Definitions of clinically relevant variables to be included in the analysis need to be finalised. This may be done in a workshop attended by clinicians and laboratory representatives. Once the data have been entered into the database and cleaned each partner can have a copy of the database to enable them to analyse the data and use them to answer their own specific research questions.
- TOLEDO cohort: Francisco José Garcia Garcia presented an update of this cohort. This study began in 2006 and has recruited patients in three waves: the first recruited 2488 patients, the second included 2323 patients and the third, running from 2014 to 2016, has 1205 robust patients, 265 frail patients and 699 prefrail patients. It is planned to run sub-studies examining patients with diabetes, cardiovascular disease and cardiovascular risk factors, and also examine the effects of nutrition and exercise.
- ENRICA cohort: Fernando Rodriguez Artalejo discussed this cohort, which is part of a cross-sectional study. In 2008 3200 participants aged at least 60 years were enrolled. Telephone

Day 2 continued...

surveys, physical examinations, diet history and DNA were examined. In 2012 the cohort had 2200 participants aged at least 63 years – biological samples were not obtained from this group. The last group will be evaluated in 2014 and early 2015.

respondents in countries including China, Ghana, India, Mexico, the Russian Federation and South Africa. The biological samples (dried blood spots, urine and saliva) taken from these participants can't be analysed outside the country where they were

- SARDINIA cohort: Angelo Scuteri updated the participants on this cohort, which enrolled 6138 volunteers (95% had four grandparents born in Sardinia). Of the participants 898 are aged at least 65 years. One issue with this cohort is that no tissue or DNA can be removed from Sardinia for analysis.
- World Health Organisation: Somnath Chatterji gave a presentation on the Study on Global Ageing and Adult Health (SAGE) cohort, which has enrolled approximately 50,000



obtained. This issue requires further discussion to see if a solution can be found.

- University of Toulouse: Bertrand Fougère discussed the Multidomain Alzheimer Disease Preventive Trial (MAPT), a 3-year prospective study

Day 2 continued...

of frail older people randomised to treatment (omega-3 and/or multi-domain intervention) or placebo. The study is being run at four centres in France and has enrolled 1680 participants aged at least 70 years. Biological samples were collected

Following this last cohort presentation there was a general discussion and it was decided to add two more members to the Intellectual Property Committee, Catherine Féart from the University of Bordeaux and Tilman Grune from the German Institute of Human Nutrition. It

was also agreed that the expected date for unblinding would be around the end of March 2015, even if not all the data are available at this time.

After this discussion the meeting participants enjoyed a lunch of tapas (with wine for some!) before going to the airport for flights

initially and at each annual visit. The data from this study should be available at the beginning of 2015. A 2-year extension follow-up study is also being run.

home. I'm sure we are all looking forward to the next meeting – and not just for the sun!



Publications Update

The third FRAILOMIC newsletter was disseminated before Christmas 2014, and this Mallorca meeting special is the fourth newsletter. The website has been updated over the course of the year, with the most recent update in December 2014.

Manuscript 1 has been submitted to the journal *Gerontology*, and it was decided at the meeting that manuscripts 2 and 3 will be integrated into one document.

This second manuscript is currently being reviewed in-house at Niche and will be released to the authors for their comments shortly. It was also decided that all manuscripts will include the statement 'on behalf of the FRAILOMIC consortium' so that all partners are included.

The first two review manuscripts are regarded as 'publicity' for FRAILOMIC, to promote the project and make it more widely known. Once the data have been analysed, the consensus was that one or two papers should be submitted to high impact journals.