Minutes WG2 meeting (3) (Action BM1204)

24 November 2014
Start: 17.30 – 19.30

Participants: refer to official participation list

Agenda points

17:30-18:00	Welcome and general update on achievements since last meeting, with discussion - Progress report WG2 (Kristel) - Ongoing activities (all)
18.00-18.30	Focus on "survey" and consequences for future activities of WG2 (moderator: Nuria Lopez-Bigas)
18.30-19.30	Identification of milestones and goals to be achieved in the 3rd year of the COST Action (all)

Minutes

Meeting slides (appendix 1) served as a basis to lead the discussions. Below is a summary of some points of attention that came up during the meeting.

- ***Update and achievements***

  Should we be worried about a decreasing participation rate at TCs and WG meetings?

  WG2 is very heterogeneous. The WG2 leaders chose right from the beginning to invite investigators from different backgrounds, both wet-lab and dry-lab scientists, medical trained scientists and scientists more involved in analytic methods development and application. This is clearly a strength to our WG2 and people with the "right" background *will* be able to play a significant role at different time points of the Action's lifetime. For instance, when data analysis results become available, an interaction is anticipated between methods developer

and data analysts at one side and clinicians and medical trained scientists in the group at another side. Also, in the future, we will try to formulate some action points towards common objectives. This will also allow the involvement of all WG2 members. These common objectives may or may not lead to a white paper (dissemination). Topics or specific research questions can be communicated to Kristel, Nuria or Jörg.

How to actively participate?

There are several ways to participate in the COST Action. One of which is via the proposal of STSMs. This may help in bridging the gap between wet and dry lab expertise and may offer a foundation for future transdisciplinary work. Let us motivate the young(er) researchers in the Action!

At the basis of research lies research data; how to assess that what we have is sufficient for …?

To this end a survey was sent around. The results have been presented during the WG2 meeting. See next point. The next issue is which questions can we answer with these data and how to access the data? In terms of creating a data base, we do not need to reinvent the wheel. During the Heidelberg meeting Claude Chelala was open to extend the PED data bases to different data types and/or to provide a secured private data access system for "approved" COST Action members. It is good to also involve Andrew Biankin however. This will be followed up further by Nuria Lopez-Bigas.

Specific objectives: how are we doing on optimization and standardization?

We are doing well on all specific objectives previously formulated. The objective on optimization and standardization has always been a bit cumbersome though. What exactly should be done or can we do, given the broader scientific landscape and global (world-wide) activities on the topic. For that reason we had already modified the specific objective a bit, adding the word "methods" (methods optimization and standardization). The November meeting led to a discussion about how to further concretize the objective and the following was agreed upon:

- We list and discuss methods for particular situations of relevance to the COST Action and write it down in a review paper.
    - Methods for:
        - Low purity
        - Patient-derived xenografts
        - Circulating DNA/cells
        - Single cell sequencing
    - Attention points include:
        - Subsequent analysis technique is technology dependent; a few leads / suggestions can be given
        - The role of the stroma and how to characterize it (cfr. Jörg Hoheisel)
    - Lead: Stephan Ossowski

How to increase our visibility?

We should acknowledge the Action via a standard phrase (see EUPancreas website). In addition, please connect to LinkedIn. When giving presentations and a reference is made to the COST Action, please communicate this to the EUPancreas webmaster.

- ***Survey***

THANK YOU for having completed the survey. If you still wish to do so, please send a mail to Jörg Hoheisel and Nuria Lopez-Bigas. Details about the survey can be obtained via Nuria Lopez-Bigas; she is responsible for pooling the contributions.

We will ask Taesung Park (via Nuria Malats), Manuel Hidalgo (via Nuria Malats) and Andrew Biankin (via Nuria Lopez) to fill out the survey as well. This will complete the picture and/or bring more clarity about whether or not we have the availability of "adequate" control data.

During the remainder of year 2, it is the idea to formulate clear research questions on the basis of the identified data in the consortium (or data that can be made available to the consortium). Year 3 will then be devoted to analyzing the data and drawing clinically relevant conclusions. These results may serve as a step-up to future research grant applications.

- ***Identification of milestones and goals for year 3***

For more general goals and milestones, please refer to Appendix 1. Action points for year 3 are highlighted in orange and (usually) presented in the form of questions. No objections were raised during the WG2 meeting to actually put these action points on the work plan for year 3.

During the WG2 meeting we discussed a potential strategy to "analyze data" (taking into account interesting niches …). The priorities agreed upon are:

- Re-analyze all pancreas exomes from scratch (germline / somatic)
    - Motivation:
        - the field has gained novel insights in how to deal with technological issues;
        - the field has contributed to novel developments in terms of analytic techniques (Spain – Nuria L, Nuria M, Manuel, Stephan, Belgium - Kristel, Germany - Jörg, …);
        - there is an increased number of exomes
    - Please identify yourself if you wish to contribute (samples, man power for analysis, etc)
    - Funding?
        - For now within existing grants should be used.
        - However, please share with WG2 members other funding opportunities. Funding opportunities such as http://www.kbs-frb.be/call.aspx?id=312829&langtype=1033 may be a possibility as well.

The Fund Maaike Lars Trees was created to support research in the genetic causes and clinical aspects of hereditary cancer. The Fund is launching a first call for projects unraveling the genomic mechanisms and hereditary aspects of pancreatic cancer. The research must be jointly led by at least two research teams of different universities.

The call is open to researchers from universities in Belgium and abroad. The project must be a collaboration between at least 2 research centers. The team who introduces the application must be based in Belgium.

- Give a (renewed) role to proteomics data
    - Motivation:
        - the survey revealed that those data are available (f.i. Jörg will be recontacted)
        - the data can be analyzed as such or can serve as a vehicle to steer subsequent (exome) analyses. For instance, proteomics networks can serve as a template for subsequent network analysis using other omics data types (Kristel)

- ***Miscellaneous***

    - Multi stakeholder meeting in Brussels (Nov 2014): there is an opportunity to participate into specific work groups at the European level. In particular “awareness”, “registries”, “diagnostics”. Please contact Kristel or Nuria Malats for more information.

    - <u>Next meetings</u>:

        - During the week of Jan 20 a doodle will be sent out with dates for a WG2 TC in February.
        - Note that the fourth WG2 meeting will be held in Barcelona (spring 2015 – details to be communicated by Nuria Lopez-Bigas)

APPENDIX 1

WG2 MEETING (3)

COST Action BM1204

24 November 2014 – GIGA, Liege (Belgium)

WG2 leader: **Kristel Van Steen** (Liège, Belgium).

Co-leaders: **Joerg Hoheisel** (Heidelberg, Germany) and **Nuria Lopez-Bigas** (Barcelona, Spain)

Presentation of WG2

Co-leaders: Jörg Hoheisel and Nuria Lopez-Bigas

Part of a whole

- WG1 Research tool harmonization
- WG2 Integration of omics data
- WG3 Translational research
- WG4 PDAC patient management

PROGRESS REPORT

WG2-specific objectives

1. **Optimization and standardization of methods for omics analysis** of pancreas tumoral and normal tissue samples
2. Establishment of **standardized approaches for omics data deposit**
3. **Identifying and documenting** available **algorithms for omics data integration**

   Issues to be considered include: the data high dimensionality - small sample size problem, the inherently noisy nature of the data, the stability and reproducibility of the models, the incorporation of domain knowledge.

How to best achieve progress on ALL objectives?

Human resources

- WG2 members
  - active participation to TCs decreased: communication tool?
  - mailing lists were reduced and "members" were asked to explicitly state whether they would like to be kept informed or not
  - coordinating office advised us to also include invited speakers to WG workshops → 50 + 2 from 24 November Workshop
  - includes a new member: María Evangelina LÓPEZ DE MATURANA
    WELCOME!
  - need for cross-talk/interaction with other WG leaders will increase as our tasks become more explicit and linked to WG1/3 activities
  - **need to increase the involvement of young investigators**

Human resources follow-up

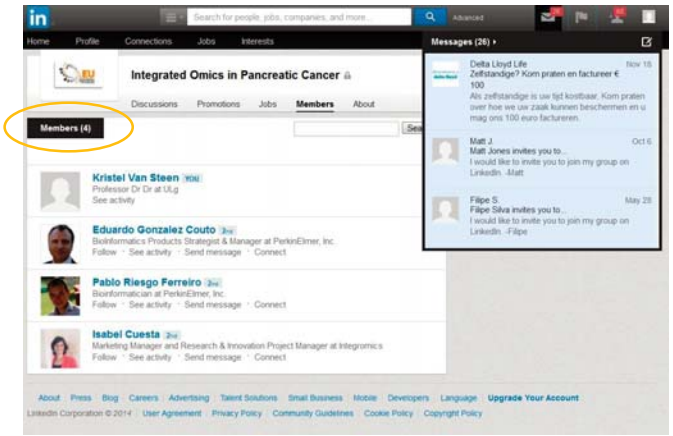
Involve young investigators

- Included in work plan for year 1, year 2 (STSMs)
- Transparency regarding what COST means and what it can offer
  - It is essential to update the Action's website and to provide information about COST in general →

Who volunteers to channel this information?

Human resources follow-up

Human resources follow-up



Human resources follow-up

- Obtain funding:
  - HORIZON2020 project was submitted by the coordinator in which data integration plays a prominent role
  - New opportunities: multi stakeholder platform - EU Parliament
- Obtain data:
  - Data cataloguing
    - Combine surveys of different WGs (joint meeting will shed more light)
    - Exchange info on good quality publicly available data to address some questions of interest (which topics? See later)
    - Data repository (green light from Claude Chelala – with restrictions; "patient registries" as one priority of EU Parliament

WG2-specific objectives

1. **Optimization and standardization of methods for omics analysis** of pancreas tumoral and normal tissue samples

   Best work breakdown structure? Work plan year 3?

2. Establishment of **standardized approaches for omics data deposit**

   √ Via platform Claude Chelala (but may need to be put in the larger context of the activities of the multi stakeholder platform on pancreatic cancer.

3. **Identifying and documenting** available **algorithms for omics data integration** **√ Book chapter accepted**

WG2 Specific deliverables

1. WG2 Meetings
2. Work plan for June 2014-2015 **(June 2015 – May 2016)**
3. Identify / prioritize opportunities of research and for funding
4. Establish contact with other consortia (i.e., ICGC, ---) and SMEs and explore opportunities for collaboration
5. Short-Term Scientific Missions (STSM)
6. **Biannual internal progress report and annual report**
7. **Common guidelines to apply technologies and to integrate omics data in PDAC research**
8. (e)Publication / CD / WEB

[all but 7 are relevant for year 2 "reporting";
suggestion to put 7 as a priority for year 3]

WG2 Activity Report Year 2

Deliverable 1: WG2 Meetings

- 3rd WG2 meeting
  - Satellite of Annual Meeting 2014
- TCs in year 2: April, June, September
- 2nd Workshop: 24 November 2014
- 1st Mini-conference: Session II of CSCDA 2014
- 4th WG2 meeting to be scheduled in April/May 2015 (where?)

THANKS to Isabel Cuesta (GO2Meeting)

WG2 Activity Report Year 2

Deliverable 2: Work plan 1 June 2014 – 31 May 2015 (see mail June 7)

- Maintain interest of WG2 members and its organization **(see before)**
- Specific Objective 1: Optimization and standardization of *methods for* omics analysis
  - **Who takes the lead?**
  - **Include a work breakdown structure in work plan for year 3**
    - Standardized data collection?
    - Standardized data analysis?
    - What is it that we want to achieve with this objective? (cfr. discussion about focusing on "methods for" omics analysis, which links to Specific Objective 3 but is not the same ….)

- Main Objective 3: Available algorithms and methods of analysis
  - Contribution to book chapter for "Big Data Analytics in Bioinformatics and Healthcare" or related publication (postponed due date) in year 1
  - Continues in year 2 → accepted / in print
  - **Communicate presentations given about particular omics analytics** [Make reference to COST Action when possible + disseminate this info to the web master ?]
- In order to PERFORM ANALYSIS or ACTIVELY USE ALGORITHMs, data are needed → Specific Objective 2

- Specific Objective 2: Standardization of omics deposit
  - Claude Chelala is willing to accommodate data sources that are currently not yet accessible through the Pancreas platform
  - Survey was distributed to know minimal information about available omics in WG2 and the consortium at large
  - Survey results available (see later)
  - **Remaining months of year 2**: Re-establish contacts with Claude Chelala to have a first version available of a consortium specific (secure) PED data base → who will take the lead?
- In order to PERFORM ANALYSIS or ACTIVELY USE ALGORITHMs, particular research questions are needed (driven by the Action's global objectives)

- Research topics – results of 2nd WG2 meeting:
  - General comment: Combining data for analysis will involve implementing meta-analytic approaches and is complicated, even for one data type such as sequencing data (cfr. discussion led by Ivo Gut at WG2 workshop in Heidelberg, February 2014). Sanger testing and PCR need to be included in the final analysis plans but require sufficient funding …
  - Characterization of the 2% cancer patient survivors – is this possible with the available data in the Action?
  - Understanding the switch to metastasis?
  - Quality of life reconsidered? (in view of the potential active participation of the EORTC GI and QoL group + EU Multi stakeholder platform)

- In order to PERFORM ANALYSIS or ACTIVELY USE ALGORITHMs, particular research questions are needed (driven by the Action's global objectives)
  - **Based on results of survey (+ discussions with WG1 and WG3?), decide about priorities (for integration)**
    - When no data are available within the Action, initiate larger data collections (long-term; role of coordinator - ongoing)
    - Team up with other pancreatic cancer research activities to investigate the application of new analytic tools on "their" data (invitation of Taesung Park to CSCDA2014, 25 November)
  - **Remaining months in year 2**: priority list

Deliverable 3: **Identify / prioritize opportunities of research and for funding**

- Identifying interesting calls and taking actions accordingly is included as part of the work plans for year 1, 2 and 3
  - HORIZON2020
  - **Other actions to be mentioned for WG2?**

Deliverable 4: Opportunities for collaboration (nourish contacts in year 2)

- EU initiatives → ELIXIR. Belgium proposal will include a module on medical genetics. No specific focus on pancreatic cancer. Situation for other countries unknown. HORIZON2020 initiatives (**year 3?)**
- Pharma → GSK and J&J were approached informally. No focus on pancreatic cancer
- ICGC –> Andrew Biankin as invited speaker to CSCDA 2014 (session II)
- EORTC → participation to Annual Meeting 2014 (JL Van Laethem)
- **Local Cancer Registries (year 3)**:
  - Connect to local cancer registries – in collab with WG1?
  - Ongoing: Belgian cancer registry

Deliverable 5: Short Term Scientific Missions

- Stay tuned for new calls …
- There were 2 calls in year 1:
  - in Febr Francesco Gadaleta from WG2 moved from Belgium (ULg) to Spain (Integromics). Contacts still exist. Follow-up slowed down due to different operating environment of Integromics. Representative gives talk at CSCDA2014.
  - **1 STSM in year 2? Bridging the gap between wet and dry lab research?**

Deliverable 8: Dissemination plan

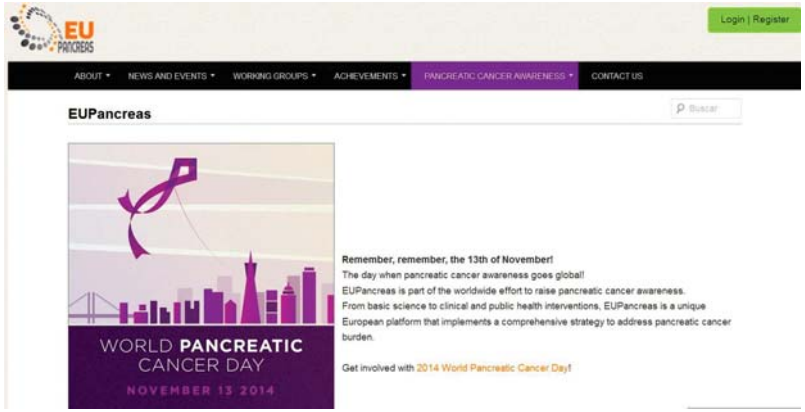
- Special issues related to objectives of WG2:
  - Via editor of genetic epidemiology
    - Editor agreed
    - Guest editors agreed:
    - Delay in kick-start due to overload of KVS
    - **Due date for submissions is expected to fall within the year 2 period for the Action**

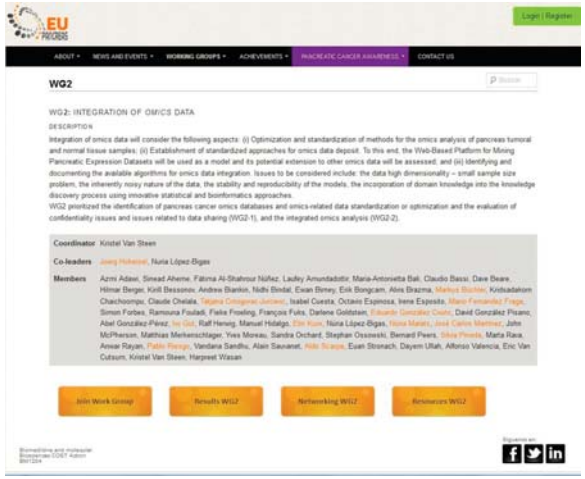
- White paper/ position paper on focal points (~ identification of "topics") → **year 3?**
  - Via earlier discussions we agreed to pay special attention to questions that can only be addressed by COST members via specific unique data
  - Global topics were discussed (revision needed based on survey and joint WG meeting / Annual Meeting):
    - **Integromics for prevention (high on EU priority list)**
      - Requires looking at healthy individuals; large-scale omics not feasible…
      - For targeted groups (obese, smokers, etc – see EU symptom drafts) make an omics profile → prospective follow-up is needed

- **Integromics for detection and prognosis**
  - Brooks 2012: "Application of genomic approaches to many malignancies has produced thousands of candidate biomarkers for detection and prognostication, yet very few have become established in clinical practice. Fundamental issues related to tumor heterogeneity, cancer progression, natural history, and biomarker performance have provided challenges to biomarker development."
  - Assess biomarker robustness using integromics (in collab with WG3)
  - Use integromics to find subgroups of patients via omics data → patient heterogeneity

- "Integrated" **gene-gene and gene-environment interaction** analysis (**in year 3?**)
  - Re-analysis of Duell, Bracci and Moore 2008 paper on pancreatic cancer
    - Kristel will inquire with Eric Duell (WG3), during 24-26 November
  - Appended with novel insights from WGs
  - Definition of "integrated" here depends on the available data:
    - Different omics
    - Genetic and non-genetic
    - Using prior biological knowledge and integrate in the analysis pipeline for interaction studies (Gusareva et al. 2014: practical aspects paper on large-scale interaction studies)

- Provide info on the eupancreas.com **(years 2 + 3)**





SURVEY

(report by Nuria Lopez-Bigas and Joerg Hoheisel)