Exploratory Workshop Scheme

Standing Committee for the European Medical Research Councils (EMRC)

Standing Committee for Life, Earth and Environmental Sciences (LESC)

Standing Committee for Physical and Engineering Sciences (PESC)

Standing Committee for the Humanities (SCH)

Standing Committee for Social Sciences (SCSS)

ESF Exploratory Workshop on

Physics of Cancer

Varenna (Italy), 13-16 September 2012

Convened by:
Caterina La Porta
Stefano Zapperi

SCIENTIFIC REPORT

1. Executive summary

The workshop has taken place in the beautiful and historical setting of Villa Monastero in Varenna (Italy) directly on the shore of the Como lake (http://www.villamonastero.eu/), 70Km away from Milano. The workshop was held form 13 to 16 September 2012 (see the workshop website at http://www.cancerphysics.unimi.it/ for a list of all the abstracts). The final participants were 17 (13 invited speakers and 2 convernors and 2 ESF representatives). The speakers came from Sweden (1), UK (2), France (2), Denmark (1), Germany (2), Israel (2), USA (1), Italy (1), Portugal (1) and the convenors from Italy (2). The Villa offers twelve rooms and other rooms were reserved in a nearby Hotel (at walking distance). The nice surroundings permitted additional interaction, in particular during dinner time. The general atmosphere was informal, open to discussions and friendly.

The main aim of the workshop was to put together scientists from different background to explore the possibility to study cancer from a computational physics and mechanic perspective. Thus we invited computational physicists, experimental biophysicists, and cancer biologists. The topics to be covered included statistical models of cancer growth, models for angiogenesis, the role of mechanical forces on cancer growth and invasion, genetic aspects of cancer progression. All these topics could have important implications for cancer biology but the contribution coming from physics is often neglected mostly due to a lack of communication between the different fields. The present ESF exploratory workshop was trying to help bridge this gap.

The program was based on a set of lectures given by the invited speakers with room for ample discussion. The workshop also included specific discussion session at the end of each day. The first day the discussion session served the purpose of introducing all participants to each other, with each participant introducing him/herself and declaring his/her expectations with respect to the workshop. The second day discussion was a scientific one and turned out to be extremely stimulating with an open discussion on what the field of cancer physics ought to be. Finally, the last day discussion was focused on organisational and strategic issues. The main point was to find concrete strategies to allow the emerging field of cancer physics to mature and expand.

The scientific program of the workshop revolved around a number of themes and followed an interesting path switching back and forth from cell biology to theoretical physics and experimental biophysics. The first talk by Y. Cao provided a broad introduction to angiogenesis in cancer and was followed by the talk of G. Scoles who gave a review of nanotechnological devices for life science. In the second day, the program was divided in three session. The first session was on tumor modeling and included a talk by M. Ben Amar on the morphology of melanoma studied by mathematical models, a review by T. Antal on evolutionary models for cancer progression and finally E. Domany reported on his experimental and theoretical results on cellular transcription. The second session focused on aging, senescence and cancer. It started with a general introduction to the field by J. P. Magalhaes and by a joint talk by

C. La Porta and S. Zapperi on an interdisciplinary approach to cancer stem cells and senescence. The third session focused on cancer genomics and again the topic was address from two complementary angles: V. Rotter discussed the role of p53, a crucial gene involved in cancer, and H. Flyvbjerg discussed his physics based approach to compare genomic data without actually sequencing the DNA but just by looking at it. The final day was divided in two session. The first session on biomechanics started with an experimental talk by J. Käs who discussed the role of cell elasticity in promoting metastasis, followed by a theoretical talk by H. Hannezo who discussed mathematical models for tissue growth. The session was closed by R. Austin who gave a general introduction to cancer physics in the USA and discussed his experimental results on cancer cell invasion. The final session had a talk on the basic mechanisms of cell division by H. Maiato and a final talk on cell membranes by A. Smith.

Judging from the response of the participants the workshop was an all-round success: discussion session were lively and interesting, talks were ridden with questions and discussions that continued through the coffee breaks and to the dinner. We had the impression of witnessing the shaping of a new interdisciplinary field and this created quite some excitement in all the participants. We therefore think that it would be interesting to have follow-up activities in the future both in terms of other conferences and research networks. The main problem so far has been the involvement of biologists which are not always interested in interacting with physicists on a topic that they probably feel belongs to their field. There is clearly a problem in inviting leaders of large groups that really drive cancer research because they tend to be extremely busy. It is our hope however that as this interdisciplinary field progresses it will be able to attract more interest in biology. The other problem that was discussed during the workshop is that, contrary to the USA, the EU is currently lacking specific funding programs focused on interdisciplinary research between biological and physical sciences.

2. Scientific content of the event

The first day started with the greeting of the organisers and the ESF representatives who presented the scope and perspectives of the ESF. The scientific program consisted of 30 minutes presentations and discussion sessions. At the end of each presentation during all the three days of the workshop there were 10-15 minutes of time dedicated to discussion. This time was always very useful and very productive and many question were raised from the listeners. The opening scientific lecture was held by Prof. Cao from Karolinska Institute (Sweden) who introduced the role of tumor angiogenesis for tumor growth and new ideas on the use of an anti-angiogenic therapy for the treatment of cancer. Questions were raised during the discussion about the applicability of physics based model to angiogenesis. Then, there was the lecture of Giacinto Scoles (University of Udine) who described his new project called MONALISA with a very interesting science application using molecular nanotechnology. The organisers anticipated Scoles's talk since he had a serious health problem and was forced to leave the conference after the first day. After his lecture each participant was invited to introduce him/herself briefly describing his/her affiliation, background and expertise and to describe what are the main topics that he/she is studying. In addition, the participants were asked their personal opinion about the relevance of physics of cancer research. The aim was to try to create a friendly atmosphere and to help the participants to interact with each other. In general, all participants were interested in the general idea of mixing physics and cancer, with some participants already active in the field and others that looked to the workshop as a way to understand the potential of this cross-disciplinary topic.

The second day there were five lectures in the morning. The first part of morning secssion was devoted to modelling of tumor growth. The first speaker of this session was Prof. Martin Ben Amar from ENS, Paris (France). She is a theoretical physicists which is now studying the morphological pattern of tumors, in particular melanoma, in a more quantitative ways using phase field models. The discussion mostly focused on how her model might be relevant for diagnostic purpose since up to now diagnosis is principally dependent on the morphological observation of bioptic samples relying on direct observation by pathologists without the aid of more quantitative tools. The second speaker was Tibor Antal (University of Edinburgh, Edinburgh, UK) who described a mathematical approach for tumor progression, showing how different models for mutations yield different prediction that can then be compared with clinical data. The last speaker before the coffee break was Eithan Domany from Weitzman Institute (Israel) who described an integrated approach to study the complex dynamics of cellular transcriptional response. He used biological experiments and computational physics approach to show that the transcriptional response displays a peculiar dynamics with a fast acceleration in the beginning of the process. There was a debate in the discussion about the mechanism that the cell employs to enforce this dynamics.

After the coffee break the second part of morning section was devoted to ageing and senescence. The first speaker (Pedro Magalhaes, University of Liverpool, Liverpool, UK) is a biologist and introduced the problem of ageing and senescence from a biological point of view. The discussion mostly focused on the role of ageing and senescence in cancer. The second speakers described recent studies showing the presence of cancer stem cells in melanoma and the role of senescence in their growth using a multidisciplinary approach (Stefano Zapperi and Caterina AM La Porta, MIlan). The questions concerned the possible role of phenotypic switching of cancer stem cells and the way to model it. During the lunch break there was enough time for free discussion between the speakers.

The main topic of the afternoon session was cancer genomics. The first speaker was Varda Rotter (Weitzman Institute, Rehovot, Israel) who described a key gene involved in tumor progression, p53. In particular she focused on the role of p53 in the life of stem cells and in cancer. Then, H. Flyvbjerg (Technical University of Denmark, Lyngby, Denmark) introduced a new method to map single molecule denaturation of DNA using a nanofluidic chips. The method is very appealing because allows to compare two different sequences just by looking at them, without actual sequencing. The following discussion revolved around possible applications to cancer screening.

After the afternoon section, all the speakers moved on a round table discussion section in the beautiful Polvani Room room of Villa Monastero. The organisers summarised the main topics of the day and all the participants were invited to give their opinion. This was mainly a scientific discussion where the main topic were: (i) the relevance and predictive powers of mathematical models for cancer; (ii) the relation between aging, senescence and cancer stem cells (iii) the importance of genomics for cancer through specific genes and the role of new physics based sequencing methods. The result was very stimulating and everyone participated enthusiastically.

In the last day, we had two seminar sessions, one focused on biomechanics and the other one on cellular process. In the first session there was the lecture of Josef Käs (University of Leipzig, Leipzig, Germany) who showed how changing mechanical properties of tumor cells it is possible to change tumor progression. Next, Edourd Hannezo (Institut Curie, Paris, France) who described growth and instabilities properties of epithelial cells showing the role of mechanics in changing key function of cells. Finally, Robert Austin (Princeton University,

Princeton, USA) discussed the status of cancer physics in the USA and then described his recent data on the role of metabolism in changing dynamics properties of tumor cells. His talk stirred a great debate on how much has been achieved by cancer research in the past decades and on the role of physics for future research. During the second part of morning section, Helder Maiato (University of Porto, Porto, Portugal) described the role of chromosomal forces during mitotic spindle multipolarity independent of centrosome amplification. Questions were asked on the way to model these forces and on their strength. Finally, Ana Smith (University of Erlangen-Nuremberg, Erlangen, Germany) described a model of interactions of membranes, showing how nucleation and growth of adhesion domains of ligand-receptor bonds seems to play a major role.

In the afternoon of the last day, there was a general discussion on cancer physics in Europe, highlighting future actions to be taken.

3. Assessment of the results, contribution to the future direction of the field, outcome

The workshop had lively discussion during and after each talk. This was allowed by the relatively small number of participant and by the informal setting that proved to be very convenient. In addition to those discussions, we had other discussion session at the end of each day that tried to summarise what has been reported during the days. The main issue that has emerged has been the way to shape a fruitful interaction between physicists and biologists: all participants agree that this interaction has to be strengthened in order for this field to make crucial contributions to the fight against cancer. Biologists tend to use quantitative methods as a service (bionformatics), in which some experts are handed the data and return the answer without a real integration. We would need a change of mentality in which biologists work side by side with physicists and other hard scientists. This is needed in order to avoid that the physics of cancer would be reduced to the study of physical aspects of cancer cells or tumor tissues without any relation with therapeutic perspectives that should ultimately be the goal of cancer research.

A special session of the workshop was devoted to more organisational aspects of this emerging field, especially in terms of funding. Robert Austin who directs a Physical-Oncology center funded by the National Cancer Institute (NCI) gave a brief presentation on the current initiatives present in the USA to fund physics of cancer. Now the NCI program on cancer physics is undergoing an evaluation to see how to continue it. This evaluation process involved a panel study (http://wtec.org/aphelion/) that analysed the status of cancer physics research in the EU. The recently released report highlighted our ESF workshop on cancer physics and concluded that research in this emerging field in thriving in Europe. Yet, there are no specific initiatives in the EU and this is generally felt as a problem by the (mostly European) audience. The ESF representatives pointed out that there is a certain degree of uncertainty on the future of ESF programs. ESF Research Networking Programmes, that appeared to represent the natural instrument to coordinate research in this field, are at present unavailable.

It was argued that future networking activities should involve physicists, cancer biologists but also social scientists and epidemiologists. There are no specific activities that seem available in the EU-FP7 programme and in Horizon 2020, except for the European Research Council (ERC). While the ERC funds interdisciplinary research through synergic grants, this instrument are not appropriate for research networks but fund a very limited number of research groups. Hence, the discussion session concluded that the participant would write a short position paper based on the outcome of the meeting arguing about the importance of fostering specific networking actions on cancer physics within the EU. This paper should be publicized

and submitted for attention to EU research officers, in order to stimulate the debate on this issue. On the other hand all the participants were ready to look for opportunities within existing funding instruments. Finally, Prof. Käs is editing a special issue of the open access journal New Journal of Physics on the “Physics of Cancer”. Participants to the workshop were invited to submit their contribution.

4. Final programme

Thursday 13 September 2012

15.30-15.15 Opening

15.30-15.45 Welcome by Convenors
Caterina La Porta (University of Milano, Milan, Italy)
Stefano Zapperi (CNR-IENI, Milan, Italy)

15.45-16.15 Presentation of the European Science Foundation (ESF)
Marcela Morvova (ESF for Physical and Engineering Sciences (PESC)) Giovanni Pacini (ESF Standing Committee for the European Medical Research Councils (EMRC))

16.15-17.00 Aftrenoon Session: Angiogenesis

16.15-17.00 Tumor angiogenesis and antiangiogenic cancer therapy
Y. Cao (Karolinska Institutet, Stockholm, Sweden)

17.00-18:15 MONALISA: Molecular Nanotechnology for life science applications
G. Scoles (Università di Udine, Udine, Italy)

18:15-19:15 Speed Dialogues

20.00*Dinner*

Friday 14 September 2012

09.00-11.15 Morning Session: Modeling tumor growth

09.00-09.45 Emergence of microstructural patterns and morphological changes in skin cancers
M. Ben Amar (ENS, Paris, France)

09.45-10.30Stochastic Models of Tumor Progression
T. Antal (University of Edinburgh, Edinburgh, UK)

10.30-11.15 Complex dynamics of cellular transcriptional response: how do cells get on the fast lane?
E. Domany (Weitzman Institute, Rehovot, Israel)

11.15-11.45*Coffee / Tea Break*

11.45-13.15 Morning Session: Aging and senescence

11.45-12.30 Cancer and aging: dangerous ties and overlapping mechanisms
J. P. Magalhaes (University of Liverpool, Liverpool, UK)

12.30-13.15 Senescent cells in growing tumors: population dynamics and cancer stem cells
C. La Porta (University of Milano, Milan, Italy) and S. Zapperi (CNR, Milan, Italy)

13.30-14.30*Lunch*

14.30-17:30 Afternoon Session: Cancer Genomics

14.30-15.15 The role of p53 in the life of stem cells
V. Rotter (Weitzman Institute, Rehovot, Israel)

15.15-16.00 Single-Molecule Denaturation-Mapping of DNA on a nanofluidic chip
H. Flyvbjerg (Technical University of Denmark, Lyngby, Denmark)

16.30-18.15 Discussion: a critical summary of the day

20.00*Dinner*

Saturday 15 September 2012

09.00-11.15 Morning Session: Biomechanics

09.00-09.45 Are biomechanical changes necessary for tumor progression?
J. Käs (University of Leipzig, Leipzig, Germany)

09.45-10.30 Growth and instabilities of epithelial tissues
E. Hannezo (Institut Curie, Paris, France)

10.30-11.15 Experimental Studies of Fundamental Cancer Dynamics
R. Austin (Princeton University, Princeton, USA)

11.15-11.45*Coffee / Tea Break*

11.45-13.15 Morning Session: Cellular processes

11.45-12.30 Mechanism of mitotic spindle multipolarity independent of centrosome amplification – the role of chromosomal forces
H. Maiato (University of Porto, Porto, Portugal)

12.30-13.15 Modeling interactions of membranes: The nucleation and growth of adhesion domains of ligand-receptor bonds
A. Smith (University of Erlangen-Nuremberg, Erlangen, Germany)

13.30-14.30*Lunch*

14.30-16:30 Afternoon Session: Closing

14.30-16.00 Discussion: Cancer physics in Europe, follow-up activities/networking/collaboration

16:00-16:30*Closing remarks*

End of Workshop and departure

5. Final list of participants

Organizers:
Caterina La Porta (University of Milano)
Stefano Zapperi (CNR-IENI, Milano)

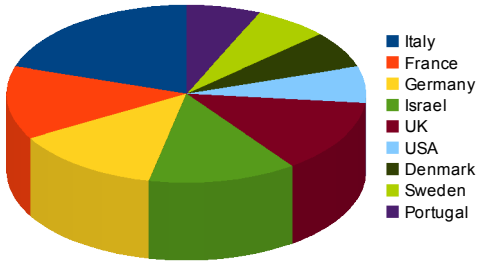
Invited Speakers:
Tibor Antal (University of Edinburgh)
Robert Austin (Princeton University)
Martine Ben Amar (ENS, Paris)
Yihai Cao (Karolinska Institute)
Pedro De Magalhaes (University of Liverpool)
Eytan Domany (Weizman Institute)
Henrik Flyvbjerg (Technical University of Denmark)
Eduouard Hannezo (Institut Curie)
Josef Käs (University of Leipzig)
Helder Maiato (University of Porto)
Varda Rotter (Weizman Institute)
Giacinto Scoles (University of Udine)
Ana Suncana Smith (University of Erlangen)

***ESF official representatives*:**
Marcela Morvova (Comenius University, Bratislava – Standing Committee for Physical and Engineering Sciences)

Giovanni Pacini (CNR, Padova – Standing Committee of the European Medical Research Councils)

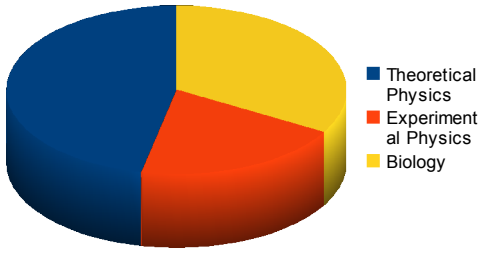
6. Statistical information on participants

Country of origin:	
Italy	3
France	2
Germany	2
Israel	2
UK	2
USA	1
Denmark	1
Sweden	1
Portugal	1



Gender		
Male	11	73.33%
Female	4	26.67%

Scientific fields	
Theoretical Physics	7
Experimental Physics	3
Biology	5



Age brackets:		
less than 35	1	5.88%
35-44	5	29.41%
45-54	3	17.65%
55-64	2	11.76%
65 or more	4	23.53%