EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

Exploratory Workshop Scheme

Standing Committee for the European Medical Research Councils (EMRC)

ESF Exploratory Workshop on

Bacterial Infection as a Cause of Cancer

London (UK), 2-4 October 2011

Convened by:

Alistair Lax, Teresa Frisan, Carla Fiorentini and Eric Oswald

Local Organisers: Alistair Lax and Agamemnon Grigoriadis

SCIENTIFIC REPORT

Co-sponsored by

KING'S College LONDON
University of London

1. Executive summary

The link between viral infections and cancer has long been established, but *Helicobacter pylori*, the primary cause of gastric cancer, is the only bacterial infection widely acknowledged as a carcinogen. Nevertheless, the great diversity of bacteria makes it highly likely that there are numerous other bacterial carcinogens. Many bacteria are known to have evolved mechanisms for perturbing eukaryotic cellular signalling linked to cell cycle regulation and growth control – features that are potentially pro-carcinogenic. The most exciting development in this field concerns a group of around ten bacterial toxins that display a "carcinogenic signature". In addition many bacteria cause chronic infections, another key factor in carcinogenesis.

Scientific Objectives The main aim of the workshop was to dissect in detail the major candidate bacteria that have potentially oncogenic characteristics and assess how they could contribute to carcinogenesis. A related goal was to raise the profile of this topic, to foster collaboration amongst the applicants and others and to suggest ways that this topic could be taken forward in terms of research, future funding and translational application. A longer term aim from this work is to provide a more detailed understanding of the role of bacteria in carcinogenesis in order to identify target pathways and facilitate improved preventative therapy.

Meeting Agenda The meeting was arranged into 4 sessions, each chaired by one of the participants. Most talks were 20 minutes, with 5 minutes scheduled for discussion, although enthusiastic discussion often extended beyond that. The workshop opened with a short session on cancer to provide a basis for discussing how bacteria could impinge on the carcinogenic process. This was followed by a session entitled "Lessons from *Helicobacter* and viruses". The other two sessions of the workshop examined the candidate bacteria and their potential carcinogenic signature, with the discussion broadening out to consider other interacting factors such as diet. There were also general discussion sessions led by a couple of participants, and the meeting ended with a detailed debate about the next steps to take.

The opening session established the different stages where bacterial actions could impinge on the carcinogenic process. Importantly this included both inflammatory and non-inflammatory mechanisms and this topic in particular produced a passionate debate. The second session emphasised the many different ways that *Helicobacter* can influence carcinogenesis and it was particularly noteworthy that new mechanisms are still being described. The discussion of oncogenic viruses showed that they, like potentially oncogenic bacteria, can also be commensal needing other factors to trigger carcinogenesis, and showed that the stimulation of particular signalling pathways was sufficient to promote carcinogenic properties.

The first session on candidate bacteria opened with a talk on *Bacteroides fragilis*, for which there is good evidence to suggest it has direct carcinogenic properties in animal models. This was followed by 6 talks on individual bacterial toxins that either stimulate signalling pathways or have DNA-damaging activities. The last session considered bacteria where there was less hard molecular evidence for a carcinogenic mechanism, but nevertheless data to substantiate a bacterial role in carcinogenesis. The meeting also discussed the evidence for fungal involvement in cancer and the role that diet could play. This latter topic emphasised the important of considering the whole human microbiota and the role it must play in promoting and preventing carcinogenesis.

Meeting Organisation and Atmosphere The workshop was held on the Guy's Campus at King's College London from 2-4 October 2011. The scientific sessions were held in a small lecture room with a nearby room being used for registration and coffee and lunch breaks.

Wireless access was arranged for all delegates both at the meeting and at the hotel, and a computer was also available. All delegates apart from those based in London stayed in a hotel located a short underground trip from the university. We ate together at the hotel on the first evening and had a private room in a small restaurant the second evening after a short historical walk. These arrangements provided an informal atmosphere for delegates to interact. The format of the enabled every one of the participants to have a direct role in the meeting, and all took part in the lively debates both during the scientific sessions and more informally at breaks and meals.

The twenty-five delegates came from ten European countries, with one delegate from the USA. All invitees to the meeting displayed great enthusiasm for the topic and this interest continued both during the meeting and afterwards. Delegates seemed genuinely pleased to have been invited and very keen to promote this important topic further.

Meeting Conclusions The delegates noted that the topic had gained increased scientific credence over the past 20-30 years. This was because first *Helicobacter* research had shown that bacteria could cause cancer and secondly hard molecular evidence identified ways that bacterial products could disturb eukaryotic functions with the potential to influence the carcinogenic process. The meeting attendees were excited by the convincing evidence that several bacteria and their toxins showed the molecular potential to cause cancer. Nevertheless it was agreed that the topic was being held back by a lack of awareness amongst the wider scientific community of the evidence available. This in turn hindered the ability of those in the field to attract the funding necessary to move the field forward. The meeting agreed that two major priority actions were required:

1. All should use every opportunity to promote the topic. This should include *inter alia*
    a) information about the workshop
    b) suggesting and/or organising sessions on this topic at national and international microbiology, cell biology and cancer meetings
2. Strenuous efforts to obtain both individual and joint funding for projects in this area
    a) lobbying at the European level for transnational funds for this topic
    b) individual or joint applications for relevant funds

It was also agreed that the convenor would set up a web page to spread information about the meeting and the topic, and the convenors agreed to write a review about the current state of the field.

2. Scientific content of the event

The meeting opened on Sunday 2nd October with a welcome from Chris Mottershead, Vice-Principal for Research and Innovation at King's College London. The Convenor, **Alistair Lax**, presented a brief overview of the history of the subject and the origins of the meeting. He pointed out that field had been held back by erroneous information on the internet about the role of bacteria in cancer. However, there was already good evidence for a cancer link not only for *Helcobacter pylori*, but also for several other bacteria. The meeting was particularly timely because a number of other bacteria are now known to have carcinogenic potential. The ESF Rapporteur, **Martin Röllinghoff**, explained the aims of the ESF Workshops.

The first sesson, chaired by **Agi Grigoriadis**, began with an overview of the basic principles and current themes and technologies underlying cancer research, with the aim that these concepts would permeate throughout the meeting and form a basis of discussion and interaction amongst the delegates. We were extremely fortunate to have **Tim Hunt** open the scientific part of the Workshop. He gave a wonderful historical overview of a disease where 50 years ago nothing was known about how normal cells become malignant, to the present day where advances in genome sequencing, genetics, imaging technologies and cell biology, and the genes that control the cell cycle, have revolutionised the way cancer is studied today. His presentation was decorated with personal anecdotes and was an ideal opening talk that set the stage for the rest of the meeting.

A key question in basic cancer cell biology is what molecular mechanisms underlie cell migration in both normal pathological settings. **Staffan Strömblad** presented recent work developing a novel imaging technology termed 'systems microscopy', which combines fluorescence microscopy, quantitative image analysis, data mining and microarray platforms to analyse cell movement in real time in living cells, and to follow them in time and space. This promises to shed light on tumour cell adhesion and how tumour cells disseminate to distant metastatic sites.

MicroRNAs (miRNAs) have emerged as an important class of regulatory molecules that can act either as oncogenes (oncomiRs) or tumour suppressor genes. **Antonio Strillacci** highlighted the benefits of obtaining a miRNA signature that represents individual tumours and their microenvironments, with specific examples presented from his work on colorectal cancer (CRC) and the discovery of several miRNA clusters that are deregulated in CRC cells. One such important miRNA, miR-101, targets the inflammatory molecule, Cox-2. Upregulation of Cox-2 is well-established in CRC and the downregulation of miR-101 demonstrated it tumour-suppressor potential. This raised the intriguing possibility that bacterial infection/toxins that cause inflammation could impart carcinogenic properties on cells by modifying specific miRNAs. The role of Cox-2 was further discussed by **Enzo Spisni**, who showed that activation of Cox-2/PGE2 signaling in CRC cells could promote tumourigenesis. In addition Cox-2 stimulated a metastatic signature, including epithelial-mesenchymal transition and expression of metalloproteinases and angiogenic molecules leading to increased experimental metastasis. The potential for targeting the Cox-2 pathway therapeutically, including through miRNA manipulation was very intriguing.

Yinon Ben-Neriah addressed the role of inflammation in cancer by focusing on mouse models of CRC. Using gene knockouts of the Casein Kinase 1alpha (CKIα) gene in gut epithelium, he showed that deletion of CKIα stimulated canonical Wnt signaling, but only resulted in highly invasive carcinomas following the additional deletion of the p53 tumour suppressor gene. This suggested important cross-talk between CKIα and p53 in the growth control of normal and pathologic intestinal epithelial stem cells and implied the existence of a "p53-suppressed invasiveness signature" (PSIS), whose targets included the cyclin-dependent kinase inhibitor, p21, as well as genes associated with cell polarity and tissue remodelling which

are potential novel biomarkers for CRC. As the inflammatory components of inflammatory bowel disease stimulate PSIS genes as well, the CKIα/p53 double mutants provide an excellent model for understanding the mechanisms underlying inflammatory bowel disease and CRC.

The ensuing discussion supported the concept that the issues raised by these talks were highly relevant to the research topic. As a quarter of all cancers are believed to occur on a background of chronic inflammation, this session set the tone for the meeting and provided food for thought for our fledgling field.

The second session chaired by **Carla Fiorentini** dealt with infectious agents that are widely recognised as carcinogenic, with two talks on *Helicobacter* pathogenesis and a couple of talks on virally-induced cancers. **Thomas Meyer** discussed the role of *Helicobacter pylori* and other bacterial pathogens in stimulating pro-survival pathways combined with mechanisms leading to somatically heritable changes in the host cell's epi-genome. Survival and growth promoting signals, via the pro-inflammatory NF-κB and MAP kinase pathways as well as the β-catenin/Wnt pathways may facilitate the emergence of transformed cells by inhibiting safeguards against transformation such as apoptosis, senescence and the physiological shedding of cells. **Silja Wessler** discussed the novel finding that *H. pylori* HtrA, a chaperone with serine protease activity, cleaves the ectodomain of E-cadherin to disrupt barrier function thus enabling *H. pylori* to access the intracellular space. The discovery of an inhibitor for HtrA suggests a novel approach to block HtrA function and potentially *H. pylori*-induced oncogenesis. **Päivi Ojala** talked about the potential oncogenes in Kaposi sarcoma herpesvirus (KHSV) using a 3-dimensional organotypical model for KSHV-infected lymphatic endothelial cells that mimics gene expression in Kaposi sarcoma biopsies. This showed that KSHV induced an endothelial to mesenchymal transition to upregulate invasion-related genes. **Maria Masucci** showed that 3 proteins from Epstein-Barr virus (EBV), which leads to Burkitt's lymphoma, use different mechanisms to promote genome instability by inducing DNA damage, inhibiting DNA repair and inactivating cell cycle checkpoints. There followed a lively general debate led by **Carla Fiorentini** and **David Smith** that highlighted the crucial role of microbial persistence, the subtle interplay between pathogens and the host, and the importance of the immune response. It was agreed that these important factors had to be considered for a full understanding of oncogenic pathogenicity.

Taken altogether, the data presented in Session 2 demonstrated how these well-studied infectious agents interact with the molecular and cellular circuits involved in the development of cancer. This detailed understanding helps to identify a characteristic infectious oncogenic signature, that is of use when considering the potential carcinogenicity of other pathogens.

The session on bacterial toxins was chaired by **Eric Oswald** and **Teresa Frisan**. **Elizabeth Wicks** discussed the possible role of *Bacteroides fragilis*, a member of the normal gut microflora, in CRC. Some strains produce a toxin that is a zinc-dependent metalloprotease. In immunocompetent mice, infection with enterotoxigenic *B. fragilis* (ETBF) induces acute, symptomatic colitis, which can further develop into a persistent subclinical colonic inflammation and hyperplasia. In the Min mouse model of CRC, ETBF infection strongly promotes tumour development. This outcome is associated with the induction of a proinflammatory response and infiltration of the specific Th17 subset of CD4 positive T helper lymphocytes. This effect is characterised by secretion of IL17, which was shown to be a key factor for tumour development. These data show for the first time how adaptive immunity, and not just innate immunity and inflammation, can contribute directly to tumour development in a chronic infection.

Carla Fiorentini dealt with the cytotoxic necrotizing factor (CNF1), that is produced by pathogenic *E. coli* strains, mainly associated with urinary tract infection. CNF1 activates small GTPases of the Rho subfamily (RhoA, Rac and CDC42), leading to actin cytoskeleton re-arrangements. However, the Rho proteins, in promoting NFκB activation, are crucially involved in the development of inflammation. CNF1 promotes cell survival by increased expression of

anti-apoptotic members of the Bcl-2 family, Bcl-2 and Bcl-XL. This in turn activates the pro-inflammatory Rac1/PI3K/Akt/IKK/NF-kB pathway. Furthermore, CNF1 can promote the expression and activity of proteins related to cell adhesion, thus stimulating cell spreading that can prevent anoikis and potentially promote migration of cells undergoing transformation.

Cycle inhibiting factors (Cifs) are produced by diverse pathogenic bacteria. Cifs inhibit the eukaryotic cell cycle and disrupt the control of the actin network, inflammation and apoptosis. **Frédéric Taieb** described how Cif acts to deaminate and inactivate the ubiquitin-like molecule Nedd8. Neddylation is a key post-translational modification essential for the Cullin Ring E3 ligase (CRL) family activity, so the net effect of Cif intoxication is a general downregulation of this CRL and consequent stabilisation of their substrates, such as the cyclin-dependent kinase inhibitors p21 and p27, and the transcription factor NFκB. Cif might represent a fitness factor that facilitates bacterial evasion from the host immune response, via inhibition of inflammatory in dendritic cells of the gut-associated lymphoid tissue. In addition the cell cycle inhibition might delay epithelial cell renewal, thus favouring gut colonisation.

Alistair Lax discussed the pro-carcinogenic properties of the *Pasteurella multocida* toxin (PMT), which is a very potent mitogen both *in vivo* and for cultured cells. PMT is known to act on the α subunits of 3 of the 4 families of heterotrimeric G-proteins, leading to their chronic activation. This in turn leads to the activation of numerous proteins known to be associated with transformation. Although it appears unlikely that PMT represents a serious threat to human health as most human infections are caused by non-toxigenic strains, PMT presents an important paradigm for understanding bacterial involvement in cancer, in particular in helping to unravel how G-proteins are regulated.

Andrés Ferreri presented very interesting data linking the presence of DNA from *Chlamydophila psittaci* to ocular adnexal marginal zone B-cell lymphoma (OAMZL). The bacterium has been identified within monocytes and macrophages from peripheral blood (PB) and from within tumour biposies of OAMZL patients. The presence of bacterial DNA in the PB could be further used as a diagnostic tool in larger epidemiological studies, since blood samples are easier to collect than biopsies. Bacterial eradication with antibiotic treatment resulted in spontaneous tumour regression in the majority of the cases. **Neils Ødum** focused on the role of *Staphylococcus aureus* superantigens in disease progression in cutaneous T cell lymphoma (CTCL). *S. aureus* is often present on the skin surface, where the CTCL starts as erythematous skin patches which can further progress to a serious disseminated disease, with metastasis of the malignant T cells to lymph nodes and internal organs. Most patients die from bacterial infection. The disease blocks efficient clearance of pathogens allowing invasion of the host via the tumour-damaged skin. Both studies illustrate the merit of combining clinical research, epidemiology and cellular microbiology to study the causal relation between persistent bacteria infection and cancer.

Some bacteria are able to directly cause DNA damage. **Jean-Philippe Nougayrède** presented elegant work on the possible role of colibactin, a putative hybrid peptide-polyketide genotoxin encoded in the *pks* island in both commensal and pathogenic *E. coli*, in promoting genomic instability in *in vitro* models and DNA damage in *in vivo* models. Short-term exposure of the CHO cell line to psk^+ *E. coli* at low multiplicity of infection induced DNA damage that was only partially repaired. The induced chromosomal instability was further associated with an enhanced rate of mutation frequency and an increased ability for anchorage independent growth. Expression of the *pks* island and its genotoxic activity have been shown to be important factors in an *in vivo* model of *E. coli* infection. **Teresa Frisan's** talk concentrated on the cytolethal distending toxin (CDT), another bacteria toxin that induces DNA damage in target cells. Exposure to sub-lethal levels for 7 months led to increased mutation frequency that was associated with an altered response to DNA damaging agents and progression toward a more malignant phenotype. In addition activation of survival signals was observed. A genome wide

yeast screen in *Saccharomyces cerevisiae* identified 78 genes that promoted cell survival in response to CDT intoxication. Bioinformatics analysis revealed the importance of DNA repair and endocytosis. These two talks illustrated the progress being made to elucidate the molecular mechanisms by which bacteria infection could contribute to tumour initiation. This also demonstrates the need for good *in vivo* models to test the effect of bacterial genotoxins in a context of a persistent/chronic infection.

Oleg Alexeyev gave a very interesting talk on the presence of *Propionibacterium acnes*, usually found on skin, in the prostate. Using fluorescence analysis he identified *P. acnes* in the majority of prostate cancer biopsies. Moreover, *P. acnes* could be detected for up to 6 years in the prostate tissue, suggesting the establishment of a persistent infection. Interestingly large biofilm structures formed in some instances which is likely to inhibit antibiotic-based therapy. The talk highlighted the pathogenic potential when a bacterium colonises a new niche that can support persistent infection and possibly inflammation. It also demonstrated the need to match data from several sources such as cancer register, microbiology data, and biobank of the patient's samples.

Celia Murciano's talk on *Candida albicans* showed that eukaryotic microbes are also linked to carcinogenesis, via inflammation and alteration of key signalling pathways, such as MAPK. In the oral cavity, *Candida* infection was linked to the progression of leukoplakic lesions, a pre-cancerous state of oral cancer. The hyphal invasive form of *C. albicans*, but not the budding commensal form, was associated with a strong activation of the MAPK kinase pathways, resulting in the secretion of a a broad array of pro-inflammatory cytokines. The fungal protein responsible for this activation has been identified. The discussion after this talk focused on themes common to all potentially carcinogenic pathogens, namely the need to develop new tools and models to study the complex interplay between pathogen induced signalling (activation of pro-survival signals and inflammation), and the host immune response in a persistent infection.

Marco Candela presented a very detailed analysis on how the intestinal microflora is dynamic and can be shaped by diet and life style and how in turn gut microbiota is associated with several chronic metabolic diseases, such as obesity and diabetes. This is extremely relevant when considering how the gut microbial community could create an ecosystem where "normal" symbionts such as *E. coli* or *B. fragilis* may express their pro-carcinogenic properties. This lecture highlighted the key issue of the potential role of the human gut microbiota in carcinogenesis and the need to explore this world in detail.

There followed a detailed and animated discussion on the key issues touched on at the meeting, and the need to progress the science. This is discussed in the next section. There was uniform agreement that the meeting had provided a valuable opportunity to focus on this under-researched topic. We also agreed that this area had the potential to make a huge contribution to understanding cancer, and also to provide suggestions for preventative intervention.

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

One of the key issues that emerged from the meeting was that the candidate bacteria expressed similar types of pro-carcinogenic mechanisms. Related to this was the commonality of these mechanisms to those expressed by known viral and bacterial carcinogenic pathogens, namely the ability of some chronic infections to promote growth, block apoptosis and stimulate inflammation. However, non-inflammatory mechanisms were also described and believed to be important. Another major theme was the increasing realisation of the relevance of the interplay of human microbiota, immune function and particular bacteria in cancer.

Therefore key directions for future research were

a) to facilitate better cooperation amongst clinicians, epidemiologists, microbiologists, immunologists and cell biologists.
b) to understand the role of the microbiota in the carcinogenic process
c) the development of improved animal and organotypic experimental models, to study how chronic infection with particular candidate bacteria can interact with the rest of the microbiota and the host response to produce a carcinogenic outcome

Whilst it was obvious that the subject of bacteria and cancer had gained considerable momentum over the past two decades, and very pleasing to note that the non-microbiologist delegates were impressed and enthused by the evidence available, it was also clear that the field was being held back by a lack of awareness amongst the wider biological community. This had a knock on effect of making it difficult to secure the necessary funding to take the subject forward. The meeting therefore agreed two major priority actions to resolve this problem:

1. All delegates to promote awareness of the topic, to include *inter alia*
    a) disseminating information about the workshop
    b) suggesting and/or organising sessions on this topic at national and international microbiology, cell biology and cancer meetings
2. Strenuous efforts to obtain both individual and joint funding for projects in this area
    a) lobbying at the European level for transnational funds for this topic
    b) individual or joint applications for relevant funds

It was also agreed that the convenor would set up a web page to spread information about the meeting and the topic, and the convenors agreed to write a review about the current state of the field.

4. Final programme

Sunday 2 October 2011

12.00-13.30	*Arrive at Tower Wing, Guy's Campus and Lunch*
13.30-13.40	**Welcome and Opening of Workshop** **Chris Mottershead** (Vice-Principal, Research, King's College London, UK)
13.40-14.00	**Welcome by Convenor** **Alistair Lax** (King's College London, UK)
14.00-14.15	**Presentation of the European Science Foundation (ESF)** **Martin Röllinghoff** (ESF Standing Committee for the European Medical Research Councils (EMRC)
14.15-17.15	**SESSION 1: Cancer** **Chair: Agi Grigoriadis** (King's College London, UK)
14.20-14.50	**The cell biology of cancer** **Tim Hunt** (Cancer Research UK. London, UK)
14.55-15.15	**A systems microscopy approach to understand cell adhesion and migration** **Staffan Strömblad** (Karolinska Institute,Stockholm, Sweden)
15.20-15.40	**Onco-miRNA and cancer** **Antonio Strillacci** (University of Bologna, Italy)
15.45-16.05	*Coffee / Tea Break*
16.05-16.25	**Inflammatory links to tumor progression in animal models of human cancer** **Yinon Ben-Neriah** (Hebrew University, Jerusalem, Israel)
16.30-16.50	**Cox-2 and cancer** **Enzo Spisni** (University of Bologna, Italy)
16.55-17.15	**Discussion** led by **Agi Grigoriadis** (King's College London, UK)
17.15-18.00	*Transfer to Burns Hotel and hotel registration*
19.30	Dinner at the Burns Hotel, Earl's Court

Monday 3 October 2011

Breakfast served at hotel from 7.00 & leave hotel by 8.10 to arrive at Guy's by 8.50

9.15-11.50	**SESSION 2: Lessons from *Helicobacter* and viruses** **Chair: Carla Fiorentini** (ISS, Rome, Italy)
9.20-9.50	**Role of *Helicobacter pylori* and other bacterial pathogens in human cancer** **Thomas Meyer** (Max-Planck Institute, Berlin, Germany)
9.55-10.15	***Helicobacter pylori* HtrA: a new secreted virulence factor** **Silja Wessler** (University of Salzburg, Austria)
10.20-10.40	*Coffee / tea break*
10.40-11.00	**Virus-host interactions in tumorigenesis by Kaposi Sarcoma herpesvirus** **Päivi Ojala** (Genome Scale Biology, Helsinki, Finland)
11.05-11.25	**Mechanisms of virus-induced genomic instability of EBV oncogenesis** **Maria Masucci** (Karolinska Institute, Stockholm, Sweden)
11.30-11.50	**Discussion** led by **Carla Fiorentini** and **David Smith** (Edinburgh, UK)
12.00-13.00	*Lunch*
13.00-16.55	**SESSION 3: Bacterial toxins and cancer** **Chairs: Eric Oswald** (Université Toulouse, France) **Teresa Frisan** (Karolinska Institute, Stockholm, Sweden)
1305-13.35	***Bacteroides fragilis* as a potential cause of cancer** **Elizabeth Wick** (Johns Hopkins University, Baltimore, USA)
13.40-14.00	**The Cytotoxic necrotizing factor 1 from *E. coli*: a janus toxin playing with cancer regulators** **Carla Fiorentini** (ISS, Rome, Italy)
14.05-14.25	**The bacterial type III effector Cif blocks the host cell cycle by hijacking the ubiquitin-dependent degradation pathway** **Frédéric Taieb** (Université Toulouse, France)
14.30-14.50	**The pro-carcinogenic properties of the *Pasteurella multocida* toxin** **Alistair Lax** (King's College London, UK)
14.55-15.15	*Coffee / tea break*
15.15-15.35	**Chlamydophila psittaci and lymphomas** **Andrés Ferreri** (San Raffaele Science Institute, Milan, Italy)
15.40-16.00	**Bacterial toxins in cutaneous T cell malignancies** **Niels Ødum** (University of Copenhagen, Denmark)
16.05-16.25	**Genotoxic *Escherichia coli* in the intestinal tract: a role in colorectal cancer?** **Jean-Philippe Nougayrède** (Université Toulouse, France)
16.30-16.50	**Carcinogenic properties of the bacterial cytolethal distending toxin** **Teresa Frisan** (Karolinska Institute, Stockholm, Sweden)
17.15-19.00	Guided historical walk around Southwark and the Thames, London
19.30	Dinner at RSJ Restaurant

Tuesday 4 October 2011

Check out of hotel after breakfast

09.15-10.35	**SESSION 4: Infection and cancer** **Chair: Peter Parker** (Cancer Research UK, UK)
09.20-09.40	***Propionibacterium acnes* and prostate cancer: applying Koch postulates to common bacterium in common cancer** **Oleg Alexeyev** (Umeå University, Sweden)
09.45-10.05	**Candida and cancer** **Celia Murciano** (King's College London, UK)
10.10-10.30	**Diet, intestinal microbiome and colorectal cancer onset** **Marco Candela** (University of Bologna, Italy)
10.35-10.50	*Coffee / Tea Break*
10.50-12.20	**SESSION 5: The way ahead - follow-up activities and collaboration**
10.50-11.05	**The lessons learned so far** **Eric Oswald** (Université Toulouse, France)
11.05-11.20	**Presentation on options for future activities** led by **Convenors**
11.20-12.05	**Open Discussion**
1205-12.20	**Summary of agreed actions** **The Convenors**
12.20	*Lunch*
12.20 onwards	*End of Workshop and departure*

5. Final list of participants

Convenor:

1. **Alistair Lax** Department of Microbiology, Dental Institute, King's College London, SE1 9RT UK

Co-Convenors:

2. **Carla Fiorentini** Department of Therapeutic Research and Medicines Evaluation, Istituto Superiore di Sanità, viale Regina Elena 299, 00161, Rome, Italy

3. **Teresa Frisan** Department of Cell and Molecular Biology, Karolinska Institutet, SE-171 77, Stockholm, Sweden

4. **Eric Oswald** USC INRA, U1043 INSERM, Ecole Nationale Veterinaire de Toulouse, 23 chemin des Capelles BP 87614, 31076 Toulouse Cedex 3, France

ESF Representative:

5. **Martin Röllinghoff** Erlangen-Nuremberg Universität, Erlangen, Germany

Participants:

6. **Oleg Alexeyev** Department of Pathology, Umeå University Hospital, S-90185 Umeå, Sweden

7. **Yinon Ben-Neriah** Hebrew University –Hadassah Medical School, Ein Karen, Jerusalem 91120, Israel

8. **Marco Candela** Department of Pharmaceutical Sciences, Via Belmeloro 6, University of Bologna, Italy

9. **Andrés Ferreri** Department of Onco-Hematology, San Raffaele Scientific Institute, Milano, Italy

10. **Agi Grigoriadis** Department of Craniofacial Development and Orthodontics, Dental Institute, King's College London, London SE1 9RT, UK

11. **Tim Hunt** Cancer Research UK, Clare Hall Laboratories, South Mimms, Herts, EN6 3LD, UK

12. **Maria Masucci** Department of Cell and Molecular Biology, Karolinska Institutet, SE-171 77, Stockholm, Sweden

13. **Thomas Meyer** Department of Molecular Biology, Max Planck Institute for Infection Biology, Charitéplatz 1, D- 10117 Berlin, Germany

14. **Celia Murciano** Department of Microbiology & Ecology, University of Valencia, C/ Dr. Moliner, s/n E-46100 Burjassot, Valencia, Spain

15. **Jean-Philippe Nougayrède** USC INRA, U1043 INSERM, Ecole Nationale Veterinaire de Toulouse 23 Chemin des capelles BP 87614, 31076 Toulouse Cedex 3, France

16. **Niels Ødum**
    Institute of Molecular Biology, Blegdamsvej 3B, 2200 Copenhagen, Denmark

17. **Päivi Ojala** Finnish Cancer Institute of Biotechnology, Biocenter 1, University of Helsinki, PO Box 56 (Viikinkaari 9), FIN – 00014, Finland

18. **Peter Parker** Cancer Research UK, London Research Institute, Lincoln's Inn Fields Laboratories Room 22, 44 Lincoln's Inn Fields, London, UK

19. **Jeremy Sanderson** Department of Gastroenterology, 1st Floor, College House, St. Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH, UK

20. **David Smith** The Moredun Research Institute, Pentlands Science Park, Bush Loan,Penicuik Midlothian EH26 OPZ, UK

21. **Enzo Spisni** Department of Experimental Biology, University of Bologna, Via Selmi 3, 40126 Bologna, Italy

22. **Antonio Strillacci** Department of Experimental Biology, University of Bologna, Via Selmi 3 40126 Bologna, Italy

23. **Staffan Strömblad** Department of Biosciences and Nutrition, Karolinska Institutet, Novum, G-building floor 6, SE-141 83 Huddinge, Sweden

24. **Frédéric Taieb** USC INRA, U1043 INSERM, Ecole Nationale Veterinaire de Toulouse 23 Chemin des capelles BP 87614, 21076 Toulouse Cedex 3, France

25. **Silja Wessler** Department of Molecular Biology, University of Salzburg, Hellbrunnerstrasse 34 5020 Salzburg, Austria

26. **Elizabeth Wick** Cynthia Sears Laboratory, Johns Hopkins Centre for Global Health, 1550 Orleans Street, Baltimore, MD21231, USA

6. Statistical information on participants

There were 25 delegates, who came from 10 European countries, with one delegate from the United States. The list of suggested delegates in the original application contained 18 males and 9 females, but several of those invited were unable to attend and suggested replacements who were male. Every effort was made to invite more female delegates, but with limited success. The eventual break down of delegates was 18 male and 7 female.

The age range of the delegates was very broad - from early post-doctoral fellow to “emeritus retired”. Exact ages are not known, but the delegates comprised:

1 retired emeritus Nobel Laureate
4 senior group leaders/directors of institutes
15 group leaders
5 postdoctoral/senior postdoctoral fellows