Welcome to Glasgow!

On behalf of the NCRI and the Conference Scientific Committee, we’re delighted to welcome you to the 14th NCRI Cancer Conference, hosted for first time in Glasgow. A lot of progress has been made in the last year and the 2018 Conference aims to showcase these scientific developments that are already resulting in measurable benefits for patients.

A hallmark of the NCRI Cancer Conference, our programme spans the breadth of cancer research from basic science to policy research. Some of the highlights of the multi-disciplinary programme we’ve created this year include world-leading experts speaking on cancer treatment consequences, data driven technologies, immunotherapy, the microbiome, precision oncology, radiotherapy combinations, environmental exposure and cancer prevention, cell function and tumour formation, cancer screening and digital pathology.

We hope that attendees at the 14th NCRI Cancer Conference will be able to catalyse ideas and broker new interdisciplinary collaborations. Over the next few days, you’ll have the opportunity to choose from over 50 sessions and meet more than 150 UK and international speakers, read more than 500 abstracts and visit many exhibition stands. Our exciting programme will be presented over the course of three days spanning across five streams: Cancer discovery / underpinning research; Prevention; Early detection, diagnosis and prognosis; Treatment; Cancer control, living with and beyond and cancer outcomes. Delegates will be able to use the Conference App to schedule which sessions they’d like to attend, note which posters to see, and which stands to visit.

Following the success of previous years, we’re welcoming back the ever-popular Clinical Trials Showcase which provides updates on practice-changing trials, and introducing a Best of Translational science session which will showcase a success story of translation of research into the clinic. The popular Dragons’ Den workshop, led by the NCRI Consumer Forum, is another not-to-be-missed session which provides a great opportunity for researchers to pitch their study proposals to a panel of patient experts, and receive feedback based on their unique perspectives and experiences. We have added several proffered paper sessions to encourage early career researchers to orally present their studies to a broad audience as well as additional sessions specifically targeted at trainees and junior investigators. On Tuesday 6 November, for the ninth year in a row, we’ll be welcoming 40 A-level students from local schools to further their understanding of cancer research and inspire them to follow a career in science.

We would like to thank all members of the Scientific Committee for their insight, advice and support and the speakers who have agreed to come along and will no doubt contribute to make the 14th NCRI Cancer Conference a thought-provoking and informative meeting.

Thanks to all exhibitors and sponsors whose contribution allows the NCRI to continue to run this excellent event and to offer an affordable Conference to all.

None of this would be possible without the support of the NCRI Conference and Events Team whose dedication and hard work facilitates what happens behind the scenes and ensures that the highest standards of multi-disciplinary cancer research is showcased at our annual Conference.

Have a great Conference!

Margaret Frame
Joint Chair, 2018 NCRI Scientific Committee
Science Director, CRUK Edinburgh Centre and Director, MRC Institute of Genetics and Molecular Medicine (IGMM) – University of Edinburgh, UK

Owen Sansom
Joint Chair, 2018 NCRI Scientific Committee
Director – Cancer Research UK Beatson Institute, UK

P.S. Make sure you share your experience with colleagues back in your institutions and with the wider scientific community. For the latest news and updates at the Conference, join us on Twitter and get involved by using #NCRI2018 – but please be mindful not to post pictures of unpublished data!
Uncovering cancer when there are comorbidities

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What does multi-morbidity mean for cancer treatment and outcomes?

Sunday afternoon Specialist session will look at the implications of treating an ageing population that increasingly experiences cancer alongside other conditions, with Katriina Whitaker, a Psychologist and Reader in Cancer Care at the University of Surrey, UK, taking to the podium to share her expertise.

She will be exploring how diagnosing cancer is influenced by comorbidities, but from a behavioural science point of view. As a specialist in early diagnosis and cancer, Dr Whitaker is particularly interested in what encourages or prevents people to seek out help, as well what influences decisions further along the cancer care pathway. “I will be covering how multi-morbidity may influence cancer diagnosis by considering evidence on the impact it has on symptom interpretation, help-seeking and symptom presentation in primary care,” she told NCRI Daily News.

The majority of those seeking help are doing so because they see what so-called cancer alarm symptoms picked up through the media or by other means. “Alarm symptoms are those that may give an early warning sign of cancer,” said Dr Whitaker. “I study how people make sense of these alarm symptoms and act on them.” The cancer alarm symptoms, based on warning signs published by Cancer Research UK, include, for example, an unexplained cough or hoarseness, persistent unexplained pain, and an unexplained lump for example. The problem is, when patients have other conditions, establishing exactly what they may or may not have can be a difficult process for both the patient and the GP.

Dr Whitaker will be highlighting research at the Conference, including previous papers which have looked at how people seek help for cancer, but the reality is that not much exists in the way of literature focusing on help-seeking in people with comorbidities. “The research so far is quite mixed,” she said.

Some studies suggest comorbidities may lead to prompt help-seeking in patients with upper and lower gastrointestinal cancers. “Sometimes multi-morbidities appear to be helpful. For instance, it gets people to the doctor,” said Dr Whitaker. However, other studies suggest comorbidities can be unhelpful. For instance, they may mask a new condition, just as chronic obstructive pulmonary disease (COPD) often does with lung cancer.

Indeed, Dr Whitaker has been studying how patients with COPD react to the possible onset of lung cancer symptoms. The fact is lung cancer rates are four times higher in people with COPD compared to the general population. But distinguishing between respiratory system symptoms can be very difficult. Many participants in the study she will present had automatically attributed their chest symptoms to COPD, and no other cause was considered. Others who might have spotted alarm symptoms were not always able to seek help because of fatigue or other symptoms of COPD. “Greater awareness of increased lung cancer risk and support to act on symptom changes is essential for people with COPD,” said Dr Whitaker.

What complicates matters is how little research there has been to date. “The area of multi-morbidity and cancer diagnosis has received little attention until now and this lack of literature applies both here within the UK and more widely,” said Dr Whitaker.

Things are changing however. There is a bigger emphasis on multi-morbidity research and a move towards what’s known as whole person care, said Dr Whitaker. “It means looking at the person in an integrated way, and not just as a cancer patient or patient with heart problems, but as someone with a number of potential challenges that need support,” she explained, adding that it presents its own challenges. “We tend to do research in disease silos – some of us are focused on cancer or diabetes for example,” she said.

Other challenges include funding, which doesn’t really reflect the amount of research interest yet. Also, the way that research is organised does not necessarily lend itself to multi-morbidity issues.

Again, there are signs of change more recently. “There is already some shift. Cancer Research UK funded us to do the work looking at how people with COPD appraise lung symptoms,” said Dr Whitaker. Certain charities have been jointly funding projects too – the British Heart Foundation and Cancer Research UK are two examples.

But for more cancers to be diagnosed, a great deal more needs to be done to shorten the time between the appearance of symptoms and presentation. “Diagnosing cancer in the context of multi-morbidity is challenging,” said Dr Whitaker. “More research is needed, using underpinning theory, to help understand what is going on. The patient voice in all of this is also incredibly important in order to understand what outcomes are most important to people.”
Repairing the pathway to better cancer treatments

A historical view of some of the most exciting discoveries in basic research will be the focus of Monday’s plenary session featuring Stephen West of the DNA Recombination and Repair Laboratory at the Francis Crick Institute, London, UK.

In an interview with NCRI Daily News, Professor West relayed how he was inspired by the three scientists, Tomas Lindahl, Paul Modrich and Aziz Sancar, who won the Nobel Prize for their work demonstrating that DNA was inherently unstable. “The fact that DNA is unstable means there is a need for repair, otherwise it would simply decay over time,” he explained.

“The DNA in our body is always suffering damage, and consequently is continually in need of repair.”

“As such, for the last 40 years, I’ve been working on DNA repair pathways that have an important role in protection against cancer.”

Professor West’s interest has focused primarily on the specific DNA repair pathway by which chromosome breaks are repaired. The BRCA2 protein plays an important role in these reactions. The importance of this repair pathway is demonstrated by the fact that individuals with a faulty version of the BRCA2 gene are at a greatly increased risk of breast and ovarian cancer.

As a basic scientist, his job has been to discover exactly how this repair pathway works, as well as the roles of the different proteins. “As biochemists we try to isolate these proteins and find out the mechanisms by which they act upon the DNA, how they manipulate it, and how they promote these repair reactions,” he explained.

Monday’s plenary session will provide an overview of many of the discoveries his group has made over the years, including new understanding of how the pathway works. “These are not simple reactions. They are reactions driven by about 20 different proteins, so they are very complex,” he explained. “But they are remarkably interesting and we have made substantial progress in the last few years.”

Professor West’s group was the first to isolate and understand the BRCA2 protein. “We were the first to purify BRCA2, we were the first to visualise it, and established exactly how it acts in DNA repair,” he said.

“Understanding how BRCA2 functions inside the cell gives us important knowledge about the defects that arise in patients who don’t have the BRCA2 protein.”

Furthermore, Professor West’s group has looked at how cells promote chromosome repair. “When the DNA helix is broken, BRCA2 together with a series of other proteins cooperate to promote the repair of the broken DNA. We are beginning to understand the precise mechanism by which these reactions take place.”

The knowledge gleaned from understanding these mechanisms has already been used by drug discovery groups. Some have devised drugs aimed at attacking other DNA repair mechanisms, in essence causing a ‘synthetic lethality’ with the defect in BRCA2. For instance, drugs have been developed that inhibit the PARP protein. “In patients who don’t have an effective BRCA2 gene, when you inhibit PARP, those cells die. It is now clear that these inhibitors are remarkably effective for patients with BRCA2-related breast and ovarian cancers, and the prognosis for these patients is now very good,” he explained. This phenomenon is being used by many other drug discovery groups working on the BRCA2 gene.

Despite the fact that these drugs are now in general use, there is still much more to understand about DNA repair mechanisms, explained Professor West: “We know that in the same pathway of repair there are many other proteins, and have been able to purify and characterise them in the laboratory. I will be talking about these proteins in Glasgow.”

In his present work, Professor West is focusing on a particularly complex research problem: BRCA2 does not work on its own, but in conjunction with another tumour suppressor protein called PALB2. “At the present time, no one has been able to purify the BRCA2-PALB2 complex, so this remains an important challenge,” he explained. But their isolation is not trivial according to Professor West.

“Working out the mechanism of action of each individual protein isn’t the only aim, continued Professor West. The ultimate goal is much bigger. “The Holy Grail for a biochemist is to reconstitute the entire DNA repair reaction in a test tube,” said Professor West. “Once you can do that then you really do understand the mechanism by which these proteins manipulate DNA. If you can do it in the test tube, that gives you a really good indication of what the cell does.”

As of yet, this particular pathway reaction has not been reconstituted in a test tube. “This is more complex than others, so it’s taken many years – I started work on this in 1977 and the progress over the past few years has been amazing. For sure, it’s a very vibrant area of research.”

There is a great deal of excitement in the field as a result, said Professor West. “The fact is that we’ve made great progress. That’s what’s important. And I think the more knowledge we get about these reactions, the more chance we will have of finding cures,” he concluded.

“As biochemists we try to isolate these proteins and find out the mechanisms by which they act upon the DNA, how they manipulate it, and how they promote these repair reactions.”

Stephen West

DON’T miss!

Today in Hall 4 – Igloo presentations

Head to the Igloo to hear from NCRI Partners, sponsors and exhibitors:

- 19.45–19.55 – MSI as a Biomarker for Colorectal Cancer, Lynch syndrome and Immunotherapeutic Research – run by Promega UK
Today’s session on tumour immunology and metabolic immunotherapy explores the cellular and molecular mechanisms that control immune responses.

A major theme of the session is the tumour immune microenvironment, the heterogeneity of which within the metastatic setting will be explored by Martin Miller (Cancer Research UK Cambridge Institute University of Cambridge, UK).

Dr Miller and colleagues recently reported on the heterogeneity among tumour-immune microenvironments of metastases in a single patient with stage IV high-grade serous ovarian adenocarcinoma following multiple types of chemotherapy. Using immunogenomic approaches, including whole-exome sequencing, RNA expression data, immunohistochemistry, neoepitope prediction, in situ T-cell receptor sequencing of tumor-infiltrating immune cells, and T cell-neoepitope challenge assays with intracellular cytokine staining (ICS), the group identified distinguishing characteristics of regressed metastatic lesions that were absent in those that had progressed. In particular, the presence of active CD8+ T-cells was associated with tumour regression, whereas a divergent pattern of molecular features – immune cell exclusion (Wnt signalling) and immune activation (including HLA expression, IFN-γ, CXCL9, TAP1, etc.) – was observed in progressing tumours.¹

This work highlights the importance of investigating the tumour-immune interface and how this is affected by chemotherapy, with implications for the development of therapeutic targets (particular with respect to therapeutic resistance). Subsequent study, which Dr Miller will present today, applies the same methodology in an expanded number of subjects.

¹There is much less known about the immune microenvironment in the metastatic setting.”

Martin Miller

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**DON’T MISS!**

**Today in Hall 4 – Silent theatre presentations**

Oral presentations will take place in the Silent theatres during the coffee and lunch breaks, and are a chance for abstract submitters to present their research. A full schedule can be found below:

**Silent theatre 1**

15.20 Georgina Appleyard Information Giving in Breast Cancer: A Service Review of the Mid-Yorks NHS Trust

15.26 Yu Sun Multiple myeloma increases autophagy in the bone marrow stromal cells which is regulated by NRF2 signalling

15.32 Chih-Yuan Cheng A systematic review update on cost-effectiveness of colorectal cancer screening: identification of an optimal strategy in Europe

19.40 Tamir Chandra Notch signalling is essential for secondary senescence and confers a facultative senescence end point in primary cells


19.52 Paul McNulty European Cancer Incidence is Significantly Reduced in Huntington’s Disease Patients – Unravelling its Protective Mechanisms.

19.58 Michela Raponi Tackling the Tgf-beta paradox via engineered organoids

20.04 Patrizia Cammareri Defining novel mechanisms critical for colorectal tumourigenesis

20.10 Vignir Helgason Identification and targeting of metabolic vulnerabilities in leukaemic stem cells using integrated omic approach

20.16 Adam Hall Investigating the role of dysregulated RNA splicing in colorectal cancer initiation and progression

20.22 Lenoj Kanageswaran Exploring the barriers and facilitators to uptake of colorectal screening within ethnic minority groups

20.28 Silvia Halim Analysis of cell proliferation and tissue remodelling in colorectal cancer uncovers a KLF4 transcriptional activity signature associated with poor prognosis
Chemotherapy has a dramatic effect on the composition of the immune cells of the microenvironment."

Martin Miller

"We took an unbiased bioinformatics approach where we try to characterise these samples, having no prior conceptions of what we think would be going on," explained Dr Miller. "We looked at the immune microenvironment again with informatic methods. Immunogenomics is the workhorse that we use."

"We corroborated that we have different immune microenvironments within the same patients. Our findings even point to some mechanisms that we found in the case study, such as that immune-suppressing Wnt signalling is high in the tumours that have very little CD8+ cytotoxic T-cell infiltration."

While Wnt signalling were associated with immune cell exclusion in treatment-naive patient high-grade serous ovarian cancer samples, comparisons of treatment-naive and post-chemotherapy samples revealed the constraining or fostering role that the tissue microenvironment can play. "Chemotherapy has a dramatic effect on the composition of the immune cells of the microenvironment," explained Dr Miller. "Based on gene expression signatures of immune cells from bulk tumour mRNA, we find an increased presence of natural killer cells and cytotoxic T-cells after chemotherapy. But the results have to be verified by more traditional approaches such as antibody-based staining of proteins specific to individual immune cell types."

Interestingly, this increase was only found in site-matched samples. In comparisons of samples that were not site-matched, heterogeneity could not be accounted for, indicating the importance of site-matched analysis.

Site-matched comparisons of immunogenic activity found an increase in cytotoxic activity driven by chemotherapy and, similarly, T-cell receptor (TCR) sequencing found a significant increase in T-cells and TCR clonality. "Some T-cell subsets with a specific TCR are proliferating within the tumour," confirmed Dr Miller. "This hasn't been shown before to that extent – that there is such a dramatic effect of chemo-

Continued on page 6
Co-existing tumour-immune microenvironments in advanced ovarian cancer

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therapy on the immune system in the local tumours. “We don’t know how chemotherapy mediates its immunogenic effects – whether more antigens are released, new antigens potentially – but that is something we will address in future studies.”

In his concluding remarks Dr Miller stressed the challenges of unbiased and systematic analysis given the heterogeneity of tumour microenvironments – complex cellular compositions and interactions between cancer, immune, and stromal components, each of which must be understood uniquely. Computational methods that provide robust and accurate estimates of non-cancerous cell populations in the tumour microenvironment from tumour bulk expression data are therefore very important.

Dr Miller and colleagues have recently conducted comprehensive benchmarking of six widely used tumour microenvironment cell estimation methods, as well as developing a consensus tool that integrates the gene sets for immune cell types that these six tools use in common. This work is expected to see publication soon. “We are trying to do systematic analysis using bioinformatics methods to analyse the tumour immune microenvironment in a manner as robust and accurate as possible. “Then, we will be able to do it across cancer types, from The Cancer Genome Atlas and the International Cancer Genome Consortium data. We are keen on developing our computational approaches to do this.”

The session, ‘Tumour immunology and metabolic immunotherapy’ takes place today between 16:35 and 18:35 in the Lomond Auditorium.

References

recent advances session

Environmental exposure and cancer prevention M2-4 Monday 11:00–12:30

The role of alternative nicotine delivery devices in harm reduction

The most up-to-date research into alternative nicotine delivery devices will be the focus tomorrow in a presentation by Lion Shahab, an associate professor in health psychology at University College London, UK. He specialises in tobacco control, in particular epidemiology and biomarker research, recently giving evidence at a Parliamentary Select Committee hearing on the effectiveness and safety of e-cigarettes, and has contributed to a report on e-cigarettes for Public Health England.

Dr Shahab will be talking broadly about the prevalence of these products in the UK and their safety. His analysis has concluded that e-cigarettes contain a relatively innocuous mixture of simple ingredients that do not include tobacco. “These are the contents of smoke machines in discos with added nicotine,” he said. “Exposure among users of electronic cigarettes is not really that bad, in cancer terms, because there is no burning or combustion going on.”

In terms of the safety, says Dr Shahab, the evidence hasn’t changed an awful lot. E-cigarettes appear to be safer than cigarettes, he said, but that doesn’t necessarily mean they are safe. “The picture in cancer is quite clear – people aren’t really exposed to the kind of chemicals you see in smoking. But for cardiovascular disease, this is not as clear-cut,” he added. “And the inhalation of particles into the respiratory tract might have an impact.”

Burning changes the properties of the components within combustible cigarettes and in turn produces carcinogens. That’s why Dr Shahab will also briefly discuss the so-called “heat-not-burn” devices, marketed by tobacco companies, that contain tobacco. They aim to reduce the impact of combustion on the formation of carcinogens by heating rather than burning the ingredients.

Whether heat-not-burn devices are as safe is unclear, said Dr Shahab. “Virtually all evidence on heat-not-burn devices comes from studies that are published by or funded by the tobacco industry,” he said. “We can assume that given there is less combustion they should be safer than cigarettes, but we can only take that at face value at the moment because...”

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InterTradeIreland

All-Island Cancer Trials Network

Collaboration between Cancer Trials Ireland and the Northern Ireland Cancer Trials Network

Synergy
Harnessing the power of cross-border collaborations

VISIT US AT STAND 10
The role of alternative nicotine delivery devices in harm reduction

Continued from page 6

of the lack of independent research.”

His group is currently conducting a study focusing on heat-not-burn devices, although the results will not be ready before the conference. “I think it would be sensible to be cautious when it comes to the risk reduction compared with e-cigarettes,” he explained.

Despite lower concerns with regards to e-cigarettes and cancer, Dr Shahab, who conducts biomarker research, reckons better evidence is still required. The fact is most research uses biomarkers, rather than health outcomes. “In terms of the safety, the studies that are required now should look at actual health outcomes. There are other correlates of health we can look at,” he explained.

For example, today, a common biomarker measure is arterial stiffness. It’s associated with hypertension and the subsequent development of other cardiovascular diseases. But it’s not ideal. “The problem is if you look at arterial stiffness alone as an indicator, it also increases when you exercise. But you wouldn’t say that exercise is correlated with cardiovascular disease along the line. This marker is not particularly specific therefore,” he said.

As a result, his team is looking at outcomes and the association between e-cigarettes and incidence of myocardial infarction on a population level instead. “That’s an actual outcome. With that association you can be sure that there is a risk,” he added. “It’s more relevant to policymakers because people don’t die of arterial stiffness, they die from myocardial infarction.”

Luckily some biomarkers are better than others. Take tobacco-specific nitrosamines (TSNA) for example, that were tracked during Dr Shahab’s study on the safety of e-cigarettes. There are longitudinal studies that show a strong association between TSNAs and lung cancer. “The reason why we are very confident that the impact of e-cigarettes on cancer is actually a meaningful one, is because this marker has a very clear association with lung cancer in animals and humans. And the reduction is about 95%,” he explained.

Dr Shahab plans to talk about recently published data on e-cigarettes to prove they have an impact on smoke cessation. The study looked at population-level data over the last decade of cigarette smoking prevalence and compared the use of e-cigarettes with combustible cigarettes. “What you see is for every 1% increase in the use of e-cigarette there has been a commensurate decline in combustible cigarette use,” he said. “So there’s a correlation; it drives down cigarette use in the UK.”

Similarly, a recent Cochrane review has conducted systematic evaluations of randomised controlled trials, confirming e-cigarettes are as effective as traditional nicotine-replacement therapy. Dr Shahab added a caveat that there are still relatively few studies currently available. He’d like more evidence, for example, on the effectiveness amongst specific population segments.

E-cigarettes are cheaper too, and therefore may have an impact on cessation more broadly than existing therapies said Dr Shahab. There is effective treatment already available: “Behavioural therapy for several weeks, and concurrent varenicline pharmacotherapy is the most effective,” said Dr Shahab. “I would say that these findings shouldn’t really discourage people from using these methods to stop.” The problem is, although effective, the uptake of these services is relatively low in the population compared with the seemingly larger appetite for e-cigarettes.

Dr Shahab believes that e-cigarettes are also seen as more of a consumer rather than a medical product. “Different smokers have different attitudes towards their own behaviour and what they want to do,” he reasoned. “E-cigarettes offer an additional benefit over cessation medication in that they don’t medicalise the whole process.”

In the end, it’s down to personal choice. “Some people prefer to quit using traditional cessation methods and then use nothing at all. For other people it’s very difficult to stop smoking completely or some people don’t want to stop smoking. Then it’s more of a long-term lifestyle switch,” he said.

The session will address worries about the uptake of e-cigarette use in people who don’t smoke. Those worries have been heightened by the release of products marketed towards the youth segment. “There is concern that a new generation of nicotine-addicted kids is being reared,” said Dr Shahab. He and his colleagues will present data during the session looking at the levels of e-cigarette use among children who don’t smoke. “The data I can tell you now in the UK are not too concerning,” he said.

Of course, there are slightly difficult issues around disentangling causal mechanisms, he concedes. Just because a child tries an e-cigarette and then goes on to smoke cigarettes it doesn’t automatically mean use of e-cigarettes caused the leap to cigarettes. It may also be because some children like to try one thing and then are just as likely to try another, explained Dr Shahab. “It’s a tricky area,” he cautioned. “To get a handle on this, the best thing is to look at population-level data on smoking among kids, and the use of e-cigarettes among them.”

And the data available on that score is rather a relief. “Between 5 and 10% of children – who never smoke – will try an e-cigarette once or twice and that’s it. Just 1% will go on to use cigarettes for any length of time,” he said. “So this is not really an issue of concern in the UK at the moment.”

“The data on smoking prevalence in the UK suggest that smoking rates have been declining, if anything, more rapidly since e-cigarettes were introduced.”

DON’T MISS!

Join us for an early morning jog
Kick your Monday morning off with a short run before the Conference begins. Head to the Front entrance of the Crown Plaza Hotel for 7:00 am where our team will lead you through a nice route alongside the River Clyde. All fitness levels are encouraged to attend – you are very welcome to jog or walk the route instead.

Keep active throughout the Conference and greet speakers with a standing ovation!
As part of our Wellbeing Programme we want to get you moving throughout the day, which is why our session chairs will be encouraging you to give a standing ovation at the end of each session.

www.ncri.org.uk
Could your idea accelerate cancer research?

Beyond the Horizon is a new meeting series that brings the right people together to have the right conversations at the right time.

We want you to suggest topics in areas of potentially transformative science and technology, or in fields that are not currently applied to cancer research, and could be harnessed to make a real difference to cancer research in the future.

Submit your topic suggestion by 12 November: www.ncri.org.uk/beyond
Attacking the right cells

A preview to an exciting and important discovery will be given tomorrow by Burkhard Becher, professor and Chair of the University of Zurich's Institute of Experimental Immunology, Switzerland. His presentation, on a crucial discovery in inflammation, will be revealed at the conference ahead of publication. "We are proud of the work and think it might be quite visible," he said.

Professor Becher will outline a rather serendipitous discovery related to the way haematological malignancies such as leukaemia can be treated. His research interest is in inflammation, but specifically the desired effect that can often be seen in cancer. "On the one hand inflammation can drive cancer but now we know that inflammation is what you want to in order to eliminate cancer," he explained. "Understanding the mechanisms by which inflammation comes about is vital to understanding how to combat cancer."

He'll outline the procedures surrounding bone marrow donation and the problems that often arise when a donor is not genetically very closely matched with the recipient. "The patient is conditioned to wipe out stem cells that live in the bone marrow because haematological malignancies almost all come from the bone marrow," he said. "Autologous positive stem cell transplantation is very difficult to do successfully."

Explaining graft-versus-host disease, Professor Becher added: "The transplanted immune system does not know the difference between cancer and normal host tissue. It also attacks the host."

But he has been studying the rather interesting but similar effect, graft-versus-leukaemia, when the donor is poorly matched. "One of the things that happens is cancer cells living in the bone marrow that have not been killed by the conditioning procedure will now be attacked by these fresh immune cells from the wrong donor so to speak," he said. "It turns out that this also kills this cancer cells. It's called the graft-versus-leukaemia effect and it's wonderful. That's what you want.

"You don't need immunotherapy. You understand there is a mismatch and this is the mismatch that forms the basis of the attack of the leukaemia cells."

And here's where his study comes in. "Until recently, most haematologists and oncologists would assume that graft-versus-leukaemia and graft-versus-host disease have the same mechanistic underpinning," he said. "Both are mechanistically very closely related so it makes sense to assume that."

No so, say his group: "We found, by accident, that the inflammation within these processes are largely independent of one another," explained Professor Becher. "This may end being a rather important discovery, therefore. "We are thinking about the therapeutic options that would allow graft-versus-leukaemia to play out but graft-versus-host disease to be blocked."

Professor Becher will describe the different mechanisms during his presentation, including cytotoxic T cell-mediated killing, a process which mediates graft-versus-leukaemia. "T lymphocytes are killing the cancer cells," he said. "We find that the mechanism of graft-versus-host disease, which is not host specific but much more inflammatory, is mediated by innate leukocytes, specifically phagocytes."

"We think T-cells are central to this process because of the cytokines that allow the immune cells to communicate with each other. When a T cell is activated, it starts communicating with the other cells. When it's very activated, it tries to get every aspect of the immune system going," he added. "The killing T-cells do not require much additional help, but T-cell activated phagocytes lead to phagocyte-mediated immunopathology."

"We think this is what graft-versus-host disease is. To a large extent it's T cell-driven phagocyte-mediated immunopathology. And we think we can block the latter to a large extent without interfering with graft-versus-leukaemia killing."

So, blocking that mechanism is key, continued Professor Becher: "The killing should still happen but the immunopathology that is secondary to that becomes merely a side effect that we can probably stop. We have been able to do it in mice and we would like to try this in people."

Discovering and being able to stop one of these mechanisms might have profound consequences, said Professor Becher. For a start, it would mean graft-versus-host disease, which is a potentially fatal condition, might be ameliorated.

And importantly, the range of donors available to a cancer patient might become larger. "Right now, one of the big difficulties if you are a cancer patient is finding an appropriate donor who will just give you enough kick without overwhelming the system," he explained. "We think that now, if we can control graft-versus-host disease, we can be potentially aggressive in looking for donors more genetically further away, who are less compatible.

He added: "We hope that we get a stronger graft-versus-leukaemia effect because now we can control graft-versus-host disease. That's our hope. That's our pipedream."

In terms of the clinical applications, Professor Becher stressed that this is something immediately translatable to the clinic, and interest from industry to do more research – while time-consuming – is also picking up momentum.

Professor Becher hopes delegates at the 2018 NCRI Conference will be inspired to participate and reproduce the research. Importantly, he'd quite like some other groups to begin trials on this mechanism. "I do hope that at the meeting there will be a good number of eager haematologists with a bit of political clout who'll say, 'Let's push the issue and do small studies and see what happens,'" he said.

"The patients are in desperate need and maybe we could bypass some of the pharmaceutical company-related problems and have an academic outlook on this. That would be nice."
**COUNT YOUR STEPS!**

Get fit at the 2018 NCRI Cancer Conference and take part in our Daily Step Challenge. The person with the highest number of steps accumulated by the end of the day will win the chance to win a restaurant or sports voucher. The winner will be contacted via Twitter tomorrow morning. Here’s how to take part:

- Download a pedometer or health app on your smartphone, or use your own pedometer such as a fitbit or iPhone Health
- Follow the official NCRI Twitter account: @NCRI_partners
- Take a screen shot or photo of the total number of steps you’ve accumulated on Sunday 4 November and tweet it to @NCRI_partners by 21:00
- Tag @SECglasgow including the hashtags #NCRIsteps #NCRI2018 & #healthyvenue

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**CONNECT TO THE WI-FI**

To connect to the Wi-Fi please go to the Wi-Fi settings on your mobile device and choose the following network: **SEC WIFI**

You will be asked to enter your email address. **No password** is required.

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**DON’T MISS!**

**Welcome to Glasgow!**

**AVAILABLE TOMORROW!**