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NCRI Daily News

Official newspaper of the NCRI Cancer Conference

Welcome to NCRI 2019

On behalf of the NCRI and the Conference Scientific Committee, we're delighted to welcome you to the 15th NCRI Cancer Conference. The Conference aims to showcase the latest scientific developments that often are already resulting in measurable benefits for patients. We hope that by attending the Conference you will be able to catalyse ideas and start new interdisciplinary collaborations.

Over the next few days, you'll have the opportunity to choose from over 50 sessions and meet more than 150 speakers from the UK and overseas. In the exhibition hall you will get the chance to read over 400 abstracts and visit several exhibition stands. We invite you to make use of the Conference App to schedule sessions you'd like to attend, note which posters to see, which stands to visit and contact other users. You can also win prizes by taking part in the Passport Competition and the step challenge every day. The App has been significantly developed following last year's feedback and is a really useful tool to make the most of the Conference. You will be able to access speakers' slides and e-posters directly from your device. Going forward you'll be able to use it for other NCRI events too.

Our multi-disciplinary programme is a hallmark of the Conference and spans across four streams: Cancer discovery / underpinning research; Prevention, early detection, diagnosis and prognosis; Treatment; and Living



Clare Isacke
The Institute of Cancer Research

with and beyond cancer. Some of the 2019 highlights include world-leading experts speaking on topics such as: consequences of cancer treatment, data driven technologies, nutrition and cancer, immunology, radiotherapy combinations, cancer prevention, cell function and tumour formation, cancer screening and digital pathology.

Given the popularity of cancer immunotherapy sessions at last year's Conference, this year we have included a number of sessions that will address new developments in immunotherapy and our understanding of basic immunology to improve targeted treatments. To encourage younger researchers to present their studies to a broad audience, we have added several proffered papers sessions to the programme. Furthermore, we targeted many sessions to trainees and junior investigators throughout



Ruth Plummer
Newcastle University

the three days of the Conference. These can be identified on the App by filtering the programme by relevant profession e.g. 'trainees'.

To celebrate the 15-year anniversary of the Conference, on Monday 4 November we are holding the 1st edition of the NCRI Excellence Awards. All winners will give a short talk about their projects so don't miss the opportunity to hear it first-hand. On Tuesday 5 November, for the 10th year, we'll be welcoming sixth formers from local schools at the NCRI Schools Event. We hope their understanding of cancer research will be furthered and that this important engagement event will inspire them to pursue a career in science.

Finally, we would like to thank all members of the Scientific Committee for their insight, advice and support. We are grateful to all the speak-

ers who have agreed to come along and participate in the Conference. Without a doubt, their contribution will make the 15th NCRI Cancer Conference a thought-provoking and informative meeting.

Many thanks to all exhibitors and supporters, whose support allows the NCRI to continue to run this excellent event and to offer subsidised rates to junior attendees and patient experts.

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

With our renewed thanks, we hope you will have a great Conference!

P.S. Make sure to share your experience with colleagues and with the wider scientific community on social media. For the latest news and updates, join us on Twitter and get involved by using #NCRI2019. Please be mindful not to post pictures of unpublished data and respect colleagues' request not to share online as appropriate!

Professor Clare Isacke and Professor Ruth Plummer
2019 NCRI Cancer Conference Joint Chairs

Follow event highlights on #NCRI2019  

PLENARY SESSION

Breaking the obesity-cancer link: New targets and strategies **Lomond Auditorium Sunday 3:05-3:45 pm**

Breaking the obesity-cancer link: New targets and strategies

The role that obesity plays in the risk, treatment and survival of cancer will be laid bare this afternoon during a plenary lecture that outlines past, present and (potential) future approaches to break the obesity-cancer link.

The prevalence of obesity has increased dramatically over the past 50 years, and when compared to individuals of normal weight, obese cancer patients typically suffer poorer prognoses, are more resistant to chemotherapy and are at higher risk of developing distant metastases.¹

As such, modern cancer research has rallied to try and understand more about the obesity-cancer link, hoping to make headway in better prevention of cancer in the future. "There's been a lot of good work evaluating obesity as a risk factor for cancer,"

Continued on page 2

Breaking the obesity-cancer link: New targets and strategies

Continued from page 1

Stephen D Hursting (Department of Nutrition and Nutrition Research Institute, University of North Carolina, NC, USA), told *NCRI Daily News* ahead of his lecture.

For instance, the Third Expert Report from the Continuous Update Project (World Cancer Research Fund, WCRF) has reviewed decades of evidence on diet, nutrition, physical activity, and cancer prevention and survival, correlating cancer incidence with variables including the type of food and drink we consume, how much exercise we get, our weight, and other metrics such as breast-feeding.²

“These are rigorous systematic reviews and meta analyses of the world’s literature,” said Professor Hursting. “They point to obesity being involved in up to 15 cancers when you put the data together. It shows that research in this field has gotten stronger, and has led to people paying more attention to what appears to be broader problem than perhaps first thought.”

In addition, reports from the World Health Organization’s (WHO) IARC (International Agency for Research on Cancer) analyses looking at cancer and obesity found that cancer was attributable to overweight or obese individuals at a rate more than twice that previously believed.³

Interdisciplinary evaluations of prevalent cancer causes are also outlined in extensive documents such as the IARC Handbooks of Cancer Prevention⁴. In Handbook 16, ‘excess body fatness’ was the focus, covering the risk of cancer in obese individuals, and what benefits an ‘absence’ of excess body fat brings.

“There were three main teams involved in the publication,” said Professor Hursting. Two of the teams focused on animal models and the mechanisms of cancer, respectively, while a third, epidemiologic team looked at the scope of problem, i.e. the number and type of cancers clearly associated with obesity.

“Interestingly, that team was also tasked with ascertaining the evidence of reversibility for obesity associated cancer, and it was a clear picture that wow, we really don’t have the data on that yet. It identified a major gap in the field,” he added.

Indeed, he went on to stress that while the focus in recent years has been on capturing just how big obesity’s impact on cancer might be, the attention paid to possible solutions is still relatively new. “That’s the crux of the issue: what are we going to do about this?” continued Professor Hursting. “Now that we’ve identified the scope of the problem, what might be the best way to try to reverse it? Frankly, predictions are dire regarding this ‘tsunami’

of obesity-related cancers facing many people and many countries worldwide unless preventive approaches can be identified and implemented.

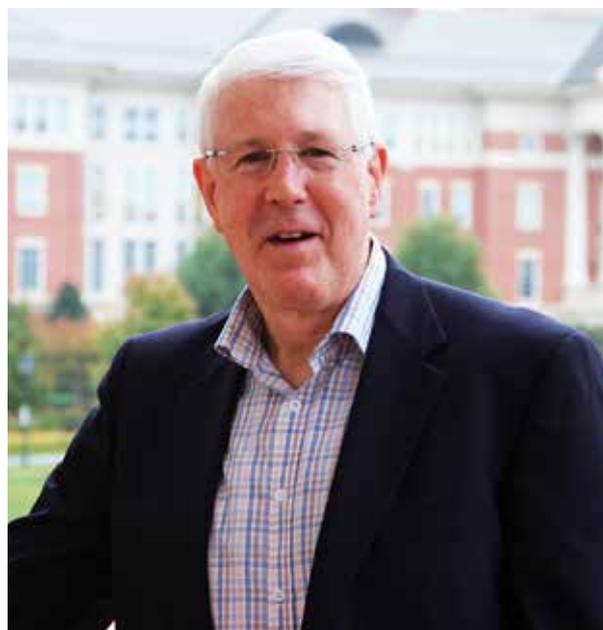
“So how can we empower future research to reduce the burden of obesity associated cancers? We’re really behind on that key question, but it has become a major focus in my lab and many others too.”

When looking at the links between cancer and obesity, there are several key areas of study that are being pursued. Much of the study follows on from observations that obese individuals can be expected to have increased secretion a number of factors that promote growth factor signalling and inflammation, including leptin, insulin, insulin-like growth factors (IGFs), free fatty acids, tumour necrosis factor (TNF)- α and interleukin (IL)-6.¹ What’s more, hormonal changes such as elevated oestrogen – the production of which is elevated by excess adipose tissue in both women and men – is also implicated in some cancers and is therefore of great interest.¹

However, the role of adipose tissue itself may not be so clear cut. Professor Hursting’s work in mouse models of basal-like breast cancer compared: tumour growth; levels of circulating hormones, growth factors, and cytokines; mammary epithelial cell signalling; and global methylation in control-fed mice, obese mice, or formerly obese mice whose weight normalised after switching from a long-term obesity-inducing diet to a control diet for 12 weeks.⁵

They found that elevated IGF-1 and inflammatory cytokines remained for some time after weight loss in mice, and that inhibiting insulin and IGF-1 in mice reduced the formation and progression of number of cancers.⁵ As such, it appears that the impact of obesity is not localised to adipose tissue, and rather there are metabolic perturbations that accompany obesity.⁵

Describing more about his work, Professor Hursting continued: “What we’re seeing is that obesity imparts immunosuppressive pressure on the tumour microenvironment. It affects cellularity, changing how immune cells are able to attack the tumour. There’s a concept of T-cell exhaustion that is at the root of several current, very promising immunotherapy approaches, but what we see is that obesity seems to enhance T-cell



“How can we empower future research to reduce the burden of obesity associated cancers?”

Stephen D Hursting

exhaustion and actually excludes T-cells from the tumour microenvironment in many cases.”

Emerging evidence also indicates that the microbiome – the powerhouse community of microorganisms found within the gut – is depleted of its optimal composition and diversity in obese individuals, leading to systemic inflammation and increased cancer risk.¹

Another knock-on effect that is somewhat underrated is the impact that obesity has on chemotherapy, continued Professor Hursting. Specifically, the transport, metabolic processing and pharmacokinetics of chemotherapy drugs can all be affected by obesity-driven factors including inflammation as well as the thickening and scarring of connective tissue (which acts as a barrier to drug delivery) and dysregulated metabolism.⁵

“This issue is of rising importance in our lab,” he commented. “I have several students that are focused on this and I think it is a bit of an underappreciated part of the obesity-cancer connection. If cancer arises in an obese individual, very often the response to therapy in that individual is going to be impaired relative to a normoweight patient with a similar cancer type. There are a number of very important drug classes that seem to fit into this profile where obesity seems to impair effectiveness. That’s a major concern.”

To combat this, there is some research by Professor Hursting and others which indicates that nanoparticle formulations of certain drugs are able to avoid several of these generalised and specific resistance mechanisms and thereby improve therapeutic

“What we’re seeing is that obesity imparts immunosuppressive pressure on the tumour microenvironment.”

Stephen D Hursting

tic response.³

But what about the core issue here: helping patients to return to a healthy, normal weight and thereby reduce cancer risk? One of the most interesting observations is the reduction of cancer risk in bariatric surgery patients. In fact, bariatric surgery is the only weight loss intervention consistently associated with reduced cancer risk.¹ “But it’s not going to be a viable solution to the obesity-cancer problem. It’s just too expensive and comes with risk of adverse effects,” said Professor Hursting.

“That being said, I think we can learn some lessons, and part of what we’ve been doing in our lab is comparing bariatric surgery with various dietary interventions in our mouse models of obesity and cancer.”

Crucially, Professor Hursting and colleagues are interested in the metabolic reprogramming that might occur with dietary interventions. For instance, there has been some elegant work in particular mutations of the phosphoinositide 3-kinase pathway that tends to make certain cancers “addicted” to glucose, he said. “As such, researchers have seen much improved responses when they place these kinds of patients on ketogenic diets,” he said.

In fact, the ketogenic, “5-2” intermittent fasting and calorie-restricted diets are all

important options being researched, said Professor Hursting: “This is a very intriguing and fast-moving area right now. To explore further, we need to emphasise the kinds of dietary regimens that are easy to follow, yet still effective in terms of addressing metabolic problems associated with obesity and cancer.”

Precision medicine

Looking to the future, Professor Hursting stressed that a precision-medicine approach will be one of the core goals in the fight against the obesity-cancer connection. He added that while great steps are being made in identifying cancer risks associated with diet and other obesity related factors – particularly the work of WCRF and IARC as mentioned earlier – in truth some of the findings thus far paint with broad strokes.

“I feel that in order to really make progress we have got to become more precise,” said Professor Hursting, noting that more general guidelines to avoid certain foods, activities etc. do not take into account a person’s individual risk profile.

“It’s a bit of a one-size-fits-all right now, so how do we get to where it’s a little more prescriptive and a little more precise? For instance, how do you account for the genetic heterogeneity or different microbi-

“I feel that in order to really make progress we have got to become more precise.”

Stephen D Hursting

omes seen in each person? The complexity of a sudden goes way up.”

One solution might lie in technology that can map metabolic, chemical and molecular insights from patients, including specific innovations such as single-cell sequencing which have revolutionised understanding of cellular compositions in cancer. The challenge, however, will be to integrate information from multiple types of technologies and transpose it to break obesity-cancer links. “It’s a brave new world,” said Professor Hursting. “The tools are getting better and better. I’m very optimistic, and I’m sure we will see rapid progress, but there is still much work to do.”

References

1. Smith LA, O’Flanagan CH, Bowers LW, et al. Translating Mechanism-Based Strategies to Break the Obesity-Cancer Link: A Narrative Review. *J Acad Nutr Diet*. 2018;118(4):652–667.
2. WCRF. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. The Third Expert Report. Available at: <https://www.wcrf.org/dietandcancer>.
3. IARC. Media Centre. Genetic analyses indicate that the effect of overweight and obesity on cancer risk is at least double what was previously thought. Available at: <https://www.iarc.fr/news-events/genetic-analyses-indicate-that-the-effect-of-overweight-and-obesity-on-cancer-risk-is-at-least-double-what-was-previously-thought/>.
4. IARC Handbooks of Cancer Prevention. Available at: <http://handbooks.iarc.fr/>.
5. Bowers LW, Hursting SD, O’Flanagan CH. Breaking the Cancer-Obesity Link. *The Scientist*. Nov, 2015. Available at: <https://www.the-scientist.com/features/breaking-the-cancer-obesity-link-34583>.

DON'T MISS!



Tomorrow's relaxation session

We’d like to invite all delegates to start the second day of the Conference with a pre-conference relaxation and mindfulness session, taking place on **Monday 4 November between 8:15 and 8:45 am in the Igloo (Hall 4)**.

The session will be run by Yogability, Glasgow and it is aimed at everyone: no prior experience is required, and no gym wear is required – simply head over in your business attire.

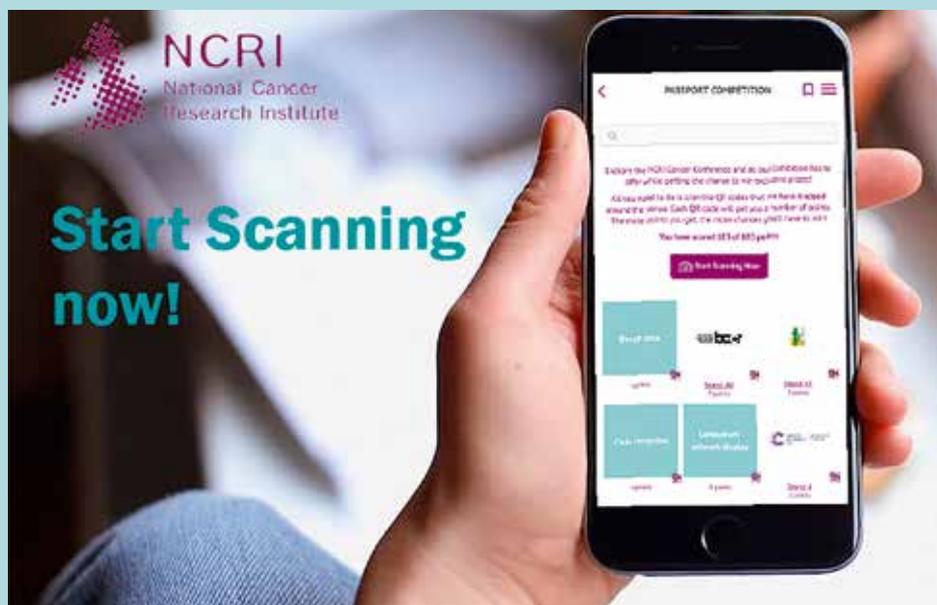
Come along to start the day feeling refreshed and ready to learn!

Passport Competition

There are many prizes to be won by enjoying your time at the Conference!

Go around the venue, network with exhibitors and scan the QR codes that have been distributed around the venue. Each QR code will get you points. The more points you collect, the more chances you have to win.

Download the App and start scanning now!



PARALLEL SESSION

Influence of nutrition on oncogenesis, prevention and clinical outcomes during and after treatment **Hall 1** Sunday **5:05–6:35 pm**

Population-based food, nutrition and obesity interventions to reduce cancer risk



Annie Anderson

During this afternoon's session dedicated to the influence of nutrition on oncogenesis, prevention and clinical outcomes during and after treatment, Annie Anderson (University of Dundee, UK) will present her perspectives in population-based food, nutrition and obesity interventions to reduce cancer risk.

Professor Anderson leads the population health work stream for the National Institute for Health Research's (NIHR) Cancer and Nutrition Collaboration¹, and is Co-Director of the Scottish Cancer Prevention Network (SCPN).²

Professor Anderson will begin her presentation by talking about population-based tobacco interventions, offering it up as a lesson in how to put potential into practice: "The reduction of cancer risk if we all stop smoking tobacco is estimated to be about 15% of total cancer risk, but the question is how can you put that into practice? How can you help people to stop smoking?"

One avenue is to raise awareness of the risks of cancer from tobacco smoking via campaigns and education programmes. However, awareness is unlikely to change behaviour on its own, noted Professor Anderson. Yet it does influence cultural norms and beliefs, which in turn can cause a shift in understanding and practices surrounding a particular disease.

"A core aspect of raising awareness is to get the public onside to generate support for healthy public policy – it's not just about education."

Annie Anderson

"In terms of smoking, for example, there came a turning point after which people would stop giving gifts of cigarettes to people," she said. "The public began to understand the risks of smoking and wanted to walk away from it."

Crucially, once the public was engaged, government and policy could follow suit. "Governments by and large don't vote in a lot of policies that people don't like because they don't like being voted out of office," said Professor Anderson. "So you have to get your population onboard to exert pressure and achieve change in policy. I think tobacco is a really good example of how we did that."

UK legislation surrounding tobacco advertising and public exposure has been gradually tightened in recent decades. While advertisements featuring people actively smoking tobacco products was banned from television in the UK as far back as 1965 (and the early 1990s for a blanket tobacco/cigarette advertisement ban on television), it would be 2003 when the first bans for tobacco advertising on billboards and in the press would surface.²

Bans on cigarette vending machines came in 2011, and in 2012 further regulations came into force requiring all large shops and supermarkets in England to hide cigarettes, tobacco products and displays from public view.²

These changes, largely focused on the exposure and availability of tobacco, came alongside the provision of higher tax rates on tobacco products, as well as the comprehensive smoke-free laws for enclosed public spaces that many countries inside and outside the EU have now established for more than a decade.

"Today we are able to demonstrate that

smoking has decreased, and so have cases of lung cancer, at least in men," stressed Professor Anderson. "This is a very good example of a theoretical model of behaviour change, the different stages that are required, and how it has an impact on cancer. And when it comes to alcohol, we're now beginning to see something similar."

Indeed, a number of measures to reduce alcohol consumption have been initiated, including taxes, restrictions on purchasing, treatment measures for alcohol dependence and other short-term GP-led interventions, noted Professor Anderson.

In fact, as outlined in a recent paper published in the *BMJ*, the implementation of minimum price laws for alcohol in Scotland has led to successful reduction in the amount of alcohol purchased in households across the country.³

So what about food and the risk it causes for cancer? "Well, the first campaigns that we really had about the link between food, diet, nutrition and cancer were focused on fruits and vegetables," continued Professor Anderson. "That's a bit of an interesting history because in 2005 Cancer Research UK [CRUK] partnered with the supermarket chain Tesco. CRUK were in partnership with the Department of Health on their 'five-a-day' fruits and vegetables campaign at that time, and very much making a point about cancer.

"So, what followed was a slogan used in the vegetable/fruit departments in Tesco which encouraged customers to eat at least five portions of different fruits and vegetables a day to help prevent cancer. However, Trading Standards took issue with the initiative [and others elsewhere] ... now, retailers are not allowed to use such messages indicating that consumption of a specific food decreases

cancer risk. So that has made life harder. We don't have the support of public policy regulation there, in fact you could say they have been quite unhelpful."

Perhaps unsurprisingly, therefore, while awareness of the importance of fruits and vegetables appears to have risen, Professor Anderson has data from 2001–2016 that indicates that consumption really has not changed in Scotland.

"Many of us in the nutrition field have, for a long time, recognised the association of sugar with a number of disorders. But in terms of obesity, it's actually very difficult to pin down a single nutrient or food to blame."

Annie Anderson

The story is a little different for salt and sugar. As Professor Anderson relayed, consumption for the former went down following pressure that was put on the food industry by the UK Government to lower salt levels in their products or else face stricter regulation. While this was initiated with salt's negative role in hypertension to mind, not cancer, the result was still fruitful. "However, it was really fear that the industry responded to in that case," she noted.

Tackling the issue of sugar, Professor Anderson continued: "Many of us in the nutrition field have, for a long time, recognised the association of sugar with a number of disorders. But in terms of obesity, it's actually very difficult to pin down a single nutrient or food to blame.

"At best we can say that sugary drinks contribute to obesity in childhood, and may do so in adulthood too. And indeed, a government report six or seven years ago reported just that, which was then a cue for the government's Public Health England body to leap into action."

Since then there has been a campaign for the reduction of sugar, including a sugar "tax" levied on soft drinks. "Ever since, the reduction in sugar [consumed from these drinks] has been 21.6%. That's really a lot, that's fantastic," said Professor Anderson. "But in other products that contain sugar,

"You have to get your population onboard to exert pressure and achieve change in policy. I think tobacco is a really good example of how we did that."

Annie Anderson

the reduction is only 2.9%. And, if you look at sugary biscuits, consumption has increased!"

As such, she again underlined how implementing tangible regulatory changes – such as that for soft drinks – clearly can have an effect on consumption, much more so that simply by promoting awareness.

"In my presentation I'm also going to say something about obesity campaigns with respect to cancer," continued Professor Anderson. "I'm not going to focus on government work in obesity because it's very wide-ranging, but I do want to say something about CRUK's awareness-raising campaign in obesity and cancer. A core aspect of raising awareness is to get the public onside to generate support for healthy public policy – it's not just about education. Therefore, we

must be very careful during campaigns not to lose public support: I think that needs to be discussed.

"I also want to talk about advocacy because I think as a cancer community we need to put weight on government to try and get effective policy into action, and to also flag up the complexity that comes with changing food intake. Change can be at an individual level – i.e. providing support and guidance etc. – but it's also about the bigger picture: how can we change the marketing, pricing and availability surrounding products?"

She added: "Nobody's yet tackled this issue of availability. It's something that's far too sensitive. But I think it's interesting to speculate how many shops one might've been in recently, including cancer charity shops, where there are sweets near the cash register. There just seems to be a real juxtaposition between the effort that we put into trying to reduce cancer risk on one hand, yet on the other hand we lay out sweets and cakes for any occasion."

References

1. NIHR Cancer and Nutrition Collaboration. Available at: www.cancerandnutrition.nihr.ac.uk.
2. <https://www.politics.co.uk/reference/tobacco-advertising>
3. O'Donnell A, Anderson P, Jané-Llopis E, et al. Immediate impact of minimum unit pricing on alcohol purchases in Scotland: controlled interrupted time series analysis for 2015-18. *BMJ*. 2019;366:15274.

DON'T MISS!

'Our Cancer Journey' – Artistic expressions of living with cancer

All days, Hall 4, Poster Boards

'Our Cancer Journey' is a consumer artwork display aimed to bring together people living with cancer to reflect and share on their diagnosis through the creation of two reflective mono-prints.

This project is a collaboration between cancer researchers Anthony Matthews, Yuki Alencar and Camille Maringe from the London School of Hygiene and Tropical Medicine, and Jayne Dent, a Newcastle-based artist.

Throughout all three days of the Conference you will have the opportunity to see this display in one of the poster areas in Hall 4.



DON'T MISS!

Today in Hall 4 – Igloo presentations

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

- **19:00–19:10** How Cancer Research UK can help you with PPI
- **19:15–19:25** UK Top 10 Living with and Beyond Cancer (LWBC) Research Priorities – a year on
- **19:30–19:40** Funding opportunities at the MRC
- **19:45–19:55** Secondary Care Hub Recruitment with Primary Care PICs in UK clinical trials – Chase Clinical
- **20:00–20:10** Development of a NanoBIT biochemical assay as a new drug screening tool for challenging protein targets RAS/PI3K

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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 taken to a splash screen with a button that says **'Connect'**.

No password is required

PLENARY SESSION

Tumour cell plasticity as a challenge for targeted therapies **Lomond Auditorium Monday 9:45-10:25 am**

Dismantling tumour cell plasticity

Tomorrow morning plays host to a plenary lecture on tumour cell plasticity by Frederic J de Sauvage, Vice President of Molecular Oncology at Genentech, South San Francisco, California, USA. Dr de Sauvage runs a large group at Genentech dedicated to the discovery of new drugs that target tumour cells – mostly focused on oncogenic pathways – his work led to the development of the first Hedgehog Pathway Inhibitor for the treatment of advanced basal cell carcinoma (BCC).

Currently, Dr de Sauvage's own research interests have moved to the Wnt pathway, intestinal stem cells and their role in colorectal cancer. "I still have my own lab and postdocs and I will talk about our work tomorrow," he told *NCRI Daily News*.

"We know the Wnt pathway is mutated and activated in most colon tumours. The problem is that in most tumours – with a few exceptions – the pathway is mutated at the level of the tumour-suppressor APC [adenomatous polyposis coli]. It is a real challenge; nobody has yet uncovered a way to effectively block the pathway downstream of APC."

Furthermore, as the Wnt pathway plays critical roles



"We have known for some time that the biology is quite complex, but it seems there are even more challenges to treating advanced tumours than we first thought."

Frederic J de Sauvage

in a number of adult tissues such as bones and intestine, developing safe inhibitors of the Wnt pathway remains a very big challenge that is still being faced right now in the development of a targeted agent for colon cancer, stressed Dr de Sauvage.

His team have spent some time studying a subset of colon cancer where pathways mutated higher up in the cascade, at the level of R-spondins – secreted proteins which potentiate the Wnt pathway: "These works showed us that targeting the Wnt pathway had a strong effect on the cancer stem cell compartment, leading to differentiation of these tumours."

To that end, they decided to look at whether killing cancer stem cells directly might be a viable strategy, even if it is a purely academic exercise at the present time. "We don't have drugs to do this specifically," noted Dr de Sauvage, "so we used an engineering trick to kill colon cancer stem cells in an orthotopic mouse model of colon cancer. What we uncovered was that tumours could compensate for the loss of the stem cell compartment. We call this ability of cells to adapt to environmental changes 'plasticity'. It is also at play in the normal intestine where the

stem cell compartment can be damaged by challenges such as infections or inflammation.

"The tumour microenvironment is also key in driving plasticity. It was therefore important to study the tumours in their natural environment, so we developed a model where the tumours are implanted in the colon directly instead of under the skin, as is commonly done. What we found is that, with the right combination of driver mutations, tumour cells could readily metastasise to secondary sites such as the liver and the lungs – the same sites where colon tumours preferentially metastasise in humans. This model also allowed us to study the role of cancer stem cells on the metastatic process as well as the difference between various tissue microenvironments."

This mechanism of plasticity presents a novel layer of challenges for the treatment of cancers, he went on, allowing tumour cells to escape drug activity by adopting alternative cell identities that do not depend as much on the drug target. "We discovered that escape mechanism in BCCs treated with Hedgehog Pathway Inhibitors but that issue is likely to be much broader."

All-told, this highlights a

key problem in the treatment of these advanced forms of cancer, where heterogeneity at the cellular level provides a mechanism whereby cells can escape therapy directed at them. "We have known for some time that the biology is quite complex, but it seems there are even more challenges to treating advanced tu-

"The tumour microenvironment [is] key in driving plasticity."

Frederic J de Sauvage

mours than we first thought," noted Dr de Sauvage.

For now, the priority is to understand the mechanisms underlying this plasticity, he concluded: "We want to discover and understand what pathway is driving these phenotypic changes, i.e. how the tumour senses that the stem cell compartment is missing, and whether we can block these mechanisms to prevent plasticity in combination with other targeted agents."

References

1. Soufiane Boumahdi, de Sauvage FJ. The great escape: tumour cell plasticity in resistance to targeted therapy. *Nat Rev Drug Discov*. 2019. [Epub ahead of print].

DON'T MISS!

Join us for an early morning jog

We'd like to invite all delegates to kick their morning off with a short run before the Conference begins. The run will start at **7:00 am on Monday 4th November** at the **Front Entrance of the Crown Plaza Hotel**, following a route alongside the River Clyde. All fitness levels are encouraged to attend – you are 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.



DON'T MISS!

Well-being Programme: Sunday, Hall 4

Incredible you colouring session

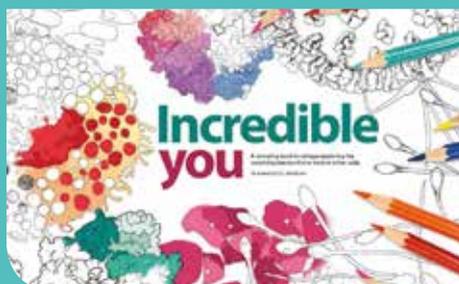
15:45-16:15

Come and relax at this colouring session that reveals the intricate structures and patterns of life.

The colouring-in resources developed by science-based artist Dr Lizzie Burns explore the beauty of your body on a tiny scale.

The illustrations offer the chance to explore all 17 pathology specialities and can prompt in-depth discussion amongst participants about their work while they are colouring.

At the end of the session we invite you to take home your design and share them on social media.



Let's get creative with Lego

19:00-19:30



During this well-being session, you will have the opportunity to use your imagination and create various structures using Lego.

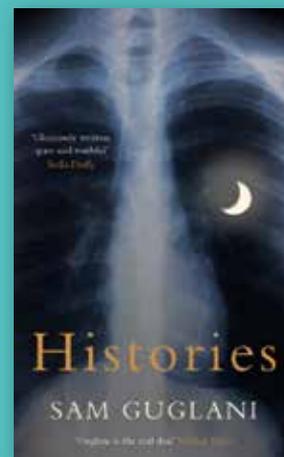
We will be occupying space for your mind to explore alongside the main conference sessions. Come and say hello!

Oncology book club

19:45-20:15

The Oncology book club will include a live discussion on the book 'Histories' by Sam Guglani.

The book club will be facilitated by a group of oncologists. You can follow the conversation on Twitter @BookOncology, @NCRI_Partners.



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Where top cancer genetics expertise meets product excellence

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PLENARY SESSION

Treatment strategies to tackle breast cancer heterogeneity **Lomond Auditorium** Monday **9:05-9:45 am**

Circumventing heterogeneous advanced breast cancer

Treatment strategies to tackle breast cancer heterogeneity will be laid bare on Monday morning when Nicholas Turner, a medical oncologist at The Institute of Cancer Research, London, UK steps up to the podium to deliver his plenary lecture. Professor Turner, who is also Genotyping, Phenotyping and Cancer Evolution Theme Lead for The Royal Marsden and ICR NIHR Biomedical Research Centre (UK), leads a laboratory looking at non-invasive ways to monitor and treat breast cancer.

He will be talking about the development of a new circulating tumour DNA biopsy to describe and monitor heterogenic changes in advanced breast cancer, as well as some of the work he and his group have been doing in overcoming heterogeneity. "I'll also talk about some of the studies we are doing and some of the other ways we are trying to dissect heterogeneity," he told *NCRI Daily News*.

The goal, said Professor Turner, is to



be able to more accurately ascertain which post-operative breast cancer patients are cured, who are at risk of relapse, and decide on further treatment.

Professor Turner's lab has developed a liquid biopsy – a blood test that can detect cancer DNA in the bloodstream to describe the genetic profile of advanced breast cancer. "I've led studies which have demonstrated its clinical utility: you can use this to guide treatment and improve outcomes," he explained.

One of the largest studies to date, which Professor Turner will preview during his lecture, is the plasmaMATCH trial¹, a multiple parallel-cohort, open-label, multi-centre

"One of the ways to get over heterogeneity is to start treatment much earlier than we do now for advanced breast cancer."

Nicholas Turner

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

15:50 Body composition and chemotherapy toxicity in women with early breast cancer: The Cando-3 study

Ramsey Cutress

15:56 International Trends in Oesophageal Cancer Survival by Histological Subtype: A population-based study from seven high-income countries 1995-2014

Eileen Morgan

16:02 Activation of HER2-ELF3-KRAS axis specifically deteriorates KRASG13D mutant colorectal cancer

Soo-Yeon Hwang

18:50 Assessment of the effect of oncolytic virotherapy in combination with cavitation ultrasound in the treatment of colorectal liver metastases using a precision cut tumour slice model

Marcos Kostalas

18:56 Patients experience of nutritional care during cancer treatment

Lesley Turner

19:02 Bioelectrical impedance changes during chemotherapy for early breast cancer: The Cando-2 study

Stephen Wootton

19:08 Molecular and functional studies on a sub-population of T cells resistant to Galectin-9

Thi Bao Tram Tran

19:14 Hormone-related diseases and prostate cancer: an English national record linkage study

Eleanor Watts

19:20 Smoking cessation for cancer prevention: Can incentives play a role? Evidence from a Cochrane review

Caitlin Notley

19:26 Reduction of full-length transglutaminase 2 (TG2-L) expression decreases cisplatin chemoresistance in an MCF-7 model of hormone-positive breast cancer

Peter Coussons

19:32 Assessment of CCR5/Maraviroc immunotherapy in combination with PD1 and MR-Guided radiotherapy for treatment of pancreatic cancer

Simone Lanfredini

19:38 The antitumoral activity of the tomatine against human hepatocellular carcinoma

César Echeverría

19:44 Flavonoids potentiated anticancer activity of cisplatin in lung cancer by inhibiting histone deacetylases

Vivi, Wei Yan

19:50 SWATH mass spectrometry: Quantitative mapping of soft tissue sarcomas by digital proteome profiling

Lukas Krasny

19:56 Can we cure oligometastatic rectal adenocarcinoma with synchronous liver metastasis: a pre-operative short-course radiotherapy and induction chemotherapy regimen

Shagufta Mirza

20:02 Investigate a potential link between sensitivity of basal subtype of Breast Cancer BCa to RNAP1 inhibitors and the levels of activated rRNA synthesis

Sameerh Alshafi

20:08 Resveratrol's effects on a BRAF mutant mouse model of colorectal carcinogenesis

Grandezza Aburido

20:14 Atezolizumab for locally advanced or metastatic urothelial carcinoma of the urinary tract: Analysis of UK patients treated in the international SAUL study

Robert Huddart

phase IIa clinical trial of circulating tumour DNA screening to direct targeted therapies in patients with advanced breast cancer. "It's a study of a thousand women recruited in 20 sites in the UK," said Professor Turner.

Blood samples came to the central laboratory at the Royal Marsden Hospital for analysis by digital PCR using ctDNA assays for hotspot mutations in oestrogen receptor 1 (ESR1), human epidermal growth factor receptor 2 (HER2), AKT serine/threonine kinase 1 (AKT1) and phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) with HER2 copy number assessment.

If specific mutations were found that matched a targeted therapy, patients could be treated accordingly, noted Professor Turner (e.g. those with ESR1 mutation received extended-dose fulvestrant).

As Professor Turner underlined, liquid biopsies might also be used to anticipate which breast cancer patients are likely to relapse². "If you can identify patients who are

"We hope treatments will be a lot more effective at preventing people from relapsing."

Nicholas Turner

going to relapse earlier, and start treatment early enough, the cancer may be a lot more homogeneous," he reasoned.

A recent independent, prospective, multicentre study² looked at the clinical validity of this approach to relapse detection in 101 early-stage breast-cancer patients. In a sub-analysis of 80 patients who had blood samples taken prior to treatment, 41 with circulating cancer DNA were found to have an almost six-fold higher risk of relapse during the first three years after treatment when compared with those without detectable levels of cancer DNA at that time.

Importantly, these findings suggest that molecular relapse detection has high levels of clinical validity, Professor Turner affirmed, underscoring that clinical trials focusing on treatment initiated at molecular relapse (without waiting for incurable metastatic disease to develop) are warranted. "One of the ways to get over heterogeneity is to start treatment much

earlier than we do now for advanced breast cancer," he said.

As such, the next step will be to test how well early treatment works, Professor Turner outlined: "It's a very rich field and there is substantial amount of research going on in it. We hope treatments will be a lot more effective at preventing people from relapsing, although that's only going to be potentially proven in the studies we are now starting."

.....
Professor Turner will delve deeper into treatment strategies to tackle breast cancer heterogeneity during his plenary lecture, held tomorrow from 9:05 to 9:45 am in the Lomond Auditorium.

References

1. PlasmaMATCH. Available at: <https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/clinical-trials/plasmamatch>
2. Garcia-Murillas, I, Chopra N, Comino-Méndez I, Beaney M; Tovey H, Cutts RJ et al., Assessment of Molecular Relapse Detection in Early-Stage Breast Cancer JAMA Oncol. 2019;5(10):1473-1478.

20:20 Delivery of radiotherapy clinical trials: Recommendations for best practice across Clinical Trial Units (CTU) and the National Radiotherapy Trials Quality Assurance Group (RTTQA)
Lisette Nixon

Silent Theatre 2

15:50 Cachexia-related biomarkers predict shortened survival and treatment-related adverse outcomes in a population receiving palliative chemotherapy for lung cancer
Joanna Bowden

15:56 Modulation of tumour microenvironment by targeting cancer associated fibroblasts in dendritic cell-based immunotherapy
Sheefa Mirza

16:02 Serum hormones and prostate cancer incidence and mortality in UK Biobank
Ruth Travis

18:50 Non-Attendance in Two-week wait and Urgent Colorectal Cancer Referrals
Harpreet Sekhon Inderjit Singh

18:56 TOPARP-B: A Phase II Randomised Trial of the Poly(ADP)-Ribose Polymerase (PARP) Inhibitor Olaparib for Metastatic Castration Resistant Prostate Cancers (mCRPC) with DNA Damage Repair (DDR) Alterations
Nuria Porta

19:02 Age differences in patient concerns after Breast Cancer. An analysis of UK Electronic Holistic Needs Assessment data
Richard Simcock

19:08 Role of cholesterol in colon cancer and its impact on AOM/DSS induced mouse intestinal tumorigenesis
Shyamananda Singh Mayengbam

19:14 18F-FDG-PET in Guided Dose-Painting with Intensity Modulated Radiotherapy in Oropharyngeal Tumours Final Toxicity and Disease Outcomes of FiGaRO Phase I
Delali Adjogatse

19:20 Clinical Utility of Autoantibodies in Early Detection of Breast Cancer
Daniyah Alfattani

19:26 Genetic inhibition of HMG-CoA reductase and epithelial ovarian cancer risk: a Mendelian randomization analysis
James Yarmolinsky

19:32 Assessment of the Outcome of Treating Spinal Oligometastases with Stereotactic Ablative Body Radiotherapy
Helen Saxby

19:38 An investigation of eating problems in people with stage I-III colorectal cancer receiving Systemic Anti-Cancer Therapy (SACT): the potential for nutritional care to potentiate cancer treatment
Jane Hopkinson

19:44 Repurposing of niclosamide (a putative STAT3 inhibitor) to potentiate chemotherapeutic drugs in treating colorectal cancer
Mia Mingxia Wu

19:50 Repurposing loperamide to overcome gefitinib resistance by triggering apoptosis independent of autophagy induction in KRAS mutant NSCLC cells
Christy Wing Sum Tong

19:56 Nr4a1-loss causes an acceleration of Myc-driven lymphomagenesis and an induction of gene of the B7-CD28
Alexander Deutsch

20:02 The association between palliative healthcare service provision and place of death: a population study of cancer patients
Maria Kelly

20:08 Top Ten Research Priorities in Cancer Early Detection: a priority setting partnership between patients and healthcare professionals
Elena Badrick

20:14 Antiproliferation and anti-invasion of 1-Acetoxychavicol acetate on hormonal-resistant breast cancer cells
Nalinee Pradubiyat

20:20 Tumour Deposits as an independent prognostic factor for Colorectal Cancer
Jinpo Xiang

PARALLEL SESSION

Precision medicine platforms to guide patient management in gastrointestinal cancers **M2-4** Sunday **5:05-6:35 pm**

A new era in gastro-oesophageal cancer research

New and exciting avenues for research into gastro-oesophageal cancer targets will be presented today by Russell Petty, a medical oncologist and a clinician scientist, who splits his time between research and clinical practice at the University of Dundee, UK.

It's an exciting time in the field that follows several years of disappointing results, Professor Petty told *NCRI Daily News*: "It's been really quite challenging to develop medical approaches in gastro-oesophageal cancer," he said. "What's changed is that now that we have a far greater biological knowledge and we can try to move forward and minimise problems using that understanding."

Progress in delivering effective biomarker-directed targeted therapies in gastro-oesophageal cancer has traditionally lagged behind other cancer types, noted Professor Petty. In other cancers there have been several different targets that can be used in the precision approach. "In lung cancer, for example, you will have several biomarkers and each of those can point you to several different targeted drugs. With gastro-oesophageal cancer we only have one," he explained.

Today, patients with overexpression of the human epidermal growth factor receptor 2 (HER2) – in up to 20% of stomach and gastro-oesophageal tumours – show a benefit from the use of the monoclonal antibody trastuzumab. This step forward was reported in 2010 during the ground-breaking Trastuzumab for GAstic cancer (ToGA) study¹. ToGA showed survival benefits when trastuzumab was given with chemotherapy in such patients. It was the first randomised, prospective, multicentre, phase-III trial to study the efficacy and safety of this treatment in HER2-positive [HER2+] patients.

But this positive step forward was followed by a rather disappointing few years where subsequent trials, building on ToGA, produced negative results, said Professor Petty. "It was very demoralising for both the patients and for us," he said.

Recently, however, a better understanding of the biology underlying such cancers has emerged, because several international consortia – including the Cancer Genome Atlas (TCGA) and International Cancer Genome Consortium (ICGC) – have sequenced large numbers of gastro-oesophageal cancer patients.

By mapping the genomic landscape, their work has pushed the field forward, said Professor Petty, who has collaborated with the OCCAMS (Oesophageal Cancer Clinical and Molecular Stratification) study, a UK member of the ICGC. OCCAMS



comprises a network of clinical centres recruiting patients for tissue collection. The tissue samples are analysed to characterise the molecular genetic landscape, determine disease sub-types and find new therapeutic targets for clinical trials.

"We are really lucky to have OCCAMS in the UK network," said Professor Petty. "By mapping the genomic landscape we've uncovered new insights."

One discovery is just how treatment resistance relates to HER2+ patients, said Professor Petty. "We have reached an understanding of why those previous trials were negative and why they were so challenging."

When some patients become resistant to trastuzumab, their biopsies reveal that the target for the drug had disappeared. "What many of these trials were doing, when patients became resistant

developing resistance to the drug were undergoing a phenomenon called HER2 conversion. "When a patient becomes resistant, they convert from being HER2+ to negative [HER2-]," said Professor Petty. "And all the trials after 2014 were doing the same thing – going after the same target that had disappeared without actually understanding this detail in the biology."

The discovery of HER2 conversion has meant an evolution in the way new precision-medicine trials are being developed "When we see trastuzumab resistance, we will biopsy the patient's tumour again and if HER2 expression is lost we will adopt a different approach to treat them," said Professor Petty. "If HER2 positivity is retained, however, we will continue to try and target it, but try new combination partner drugs."

There have been considerable lessons learned from the last few years, said Professor Petty, particularly in terms of the importance of basic science. "You have to make sure that your biological understanding of cancer is precise enough, ideally at the individual patient level (if you can), before you try and find a precision strategy medicine for patients," he said.

"What I'm going to talk about today is how the biological understanding that we had previously was insufficient. If we had known the biology at the time, we could have predicted that these trials would be negative."

But most importantly, the genomic mapping exercise has enabled a new level of precision in the biological understanding of gastro-oesophageal cancer and how it might interact with targeted therapies, noted Professor Petty, who will be walking delegates through some of the most promising new targets in his talk.

"Many of those are targets for which we have medicines already, and have been investigated in other tumour types," he said. "We will now have the opportunity to evaluate those in gastro-oesophageal cancers."

Indeed, the next stage of the OCCAMS network will be to conduct trials with such drugs, dubbed the Oelixir trials. They are seen as the next level in precision medicine in gastro-oesophageal cancers and are in the advanced planning stages. With funding, they are scheduled to begin next year. "It's a very exciting time," concluded Professor Petty.

"It's been really quite challenging to develop medical approaches in gastro-oesophageal cancer."

Russell Petty

"You have to make sure that your biological understanding of cancer is precise enough...before you try and find a precision strategy medicine for patients."

Russell Petty

to trastuzumab, was still trying to aim at the same target," he said. "But they didn't work because in many patients the target had gone."

It is now known that many patients

References

1. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet* 2010;376(9742):687-97.

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COUNT YOUR STEPS!

Get fit at the 2019 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 be in with the chance to win a prize. 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 **TODAY** and tweet it to **@NCRI_partners** by 20:30
- Tag **@SECglasgow** including the hashtags **#NCRIsteps**, **#NCRI2019** & **#healthyvenue**



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Welcome to NCRI 2019

On behalf of the NCRI and the Conference Scientific Committee, we delighted to welcome you to the 9th NCRI Cancer Conference. The Conference aims to showcase the latest scientific developments that offer already existing or measurable benefits for patients. We hope that by attending the Conference you will be able to catalyse ideas and start new interdisciplinary collaborations.

Over the next few days, you'll have the opportunity to share your own research and meet more than 500 speakers from the UK and overseas. In the exhibition hall you will get the chance to read over 400 abstracts and meet your peers. We have also set up the Conference App to enable you to find like to attend, see which papers to see, which stands to visit and connect with other experts. You can also enter by taking part in the Passport Competition and the step challenge every day. The App has been significantly developed following last year's feedback and is a really useful tool to make the most of the Conference. You will be able to access speakers' slides and e-posters directly from your device. Check forward if you're able to use it for other NCRI events too.

Our multi-disciplinary programme is a hallmark of the Conference and spans across four streams: Cancer Discovery, understanding mechanisms, Prevention, early detection, diagnosis and prognosis, Treatment, and Care.

Without a doubt, their contributions will make the 9th NCRI Cancer Conference a thought-provoking and informative meeting. We hope you will have a great Conference!

With our renewed thanks, we hope you will have a great Conference!

PS. Make sure to share your experience with colleagues and with the wider scientific community on social media. For the latest news and updates, join us on Twitter and get involved by using #NCRI2019. Please be reminded to post pictures of unpublished data and respect colleagues' requests not to share online as appropriate!

Professor **Chris Hanks** **Ruth Purmer** **Professor** **Ruth Purmer**
 Head of Cancer Research, University of Glasgow
 Head of Cancer Research, University of Glasgow

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PLANNED PRESENTATION
 Breaking the obesity-cancer link: New targets and strategies. **Lemond Auditorium** Sunday 3:05 pm

Breaking the obesity-cancer link: New targets and strategies

The role that obesity plays in the risk, treatment and survival of cancer will be laid bare this afternoon during a plenary lecture that outlines past, present and potential future approaches to break the obesity-cancer link.

The prevalence of obesity has increased dramatically over the past 50 years, and when compared to individuals of normal weight, obese cancer patients typically suffer worse prognosis, are more resistant to chemotherapy and are at higher risk of developing distant metastases.

As such, modern cancer research has called to identify and understand more about the obesity-cancer link, hoping to make headway in better prevention of cancer in the future. There's a lot of good work going on exploring obesity as a risk factor for cancer.

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