Autumn 2018

WCB newsletter

Wales Cancer Bank
Banc Canser Cymru

Clinical Director: Prof Richard Adams Manager: Dr Alison Parry-Jones
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Getting Personal about Lung Cancer

Abby MacArthur

Human nature, and 'being British' often leads us to undersell ourselves, whether it be the job we do or the shirt we wear – "Oh this old thing? It's really nothing". I'm the same when someone asks what I do for a living – my stock answer tends to be, "Oh I work in Cancer Research for the Wales Cancer Bank." I'm guilty of trivialising the work I do just because we don't like to toot our own horns. Cancer, however, isn't a trivial matter – new research suggests that cancer directly affects 1 in 2 of us, and the effects of the disease and its treatments can spread even wider to family and friends. The people who ask me that simple question want to talk more about it, they've had first or second-hand experience and there is genuine curiosity about the advances in science and medicine in cancer research. Even more so when I get animated about my role in Cancer Research UK's (CRUK) Stratified Medicine Programme. The project focuses on 'personalised', 'targeted' or 'precision' medicine which looks not just at the diagnosis, but at the genetic make-up of the tumour in combination with the patient's clinical needs.

Wales Cancer Bank (WCB) is one of the top performing clinical hubs involved in the programme – contributing high patient recruitment numbers and consistently reaching monthly targets set by CRUK. Nearly 5 years into Phase 2 of this UK-wide programme, WCB is the only clinical hub in Wales approaching eligible late-stage lung cancer patients for consent. Since January 2016, almost 500 Welsh patients have given permission for us to send their surplus tissue for genetic testing, with a number successfully recruited on to the National Lung Matrix Trial (NLMT) as a result. This innovative trial is designed to be able to adapt to the research going on around it; as new drugs are identified, then new arms can be added and the number of patients that may benefit from this trial can increase.

There are difficulties though – personalised medicine is not quite ready to realise its full potential and become integrated into the primary care pathway. Many of the reasons need ongoing research – cancer cells are caused by mutations which continue to mutate throughout their lifetime. Many factors affect their genetic make-up – the environment, cancer treatments, and age to name just a few. Cancer is evolving and research needs to keep up with it to remain effective. Some factors,however can be more readily addressed – the Wales Cancer Bank are currently only able to reach a small proportion of the Welsh population. Limited engagement and funding in some local health boards only allows us to see patients in South Central and South East Wales – almost creating a 'postcode lottery' for eligible patients across the rest of our small country. We need more funding to allow increased staffing in hospitals in West, Mid and North Wales; local health boards are often already under increased pressure. A patient's medical treatment must always remain top priority. However, without research there would be no treatment so a balance must be found to ensure that we are, at least, on a level playing field in the battle against cancer.

For further information on SMP or Matrix visit www.cancerresearchuk.org

Advances from WCB: How new breakthroughs in cancer research have been facilitated by patients' donated samples...

Precision virotherapies: a new weapon for treating ovarian cancer?

Ovarian cancer samples donated by patients at Velindre Cancer Centre have been used to help develop "precision virotherapies" as a new therapy for patients with ovarian cancer that has become resistant to chemotherapy, in research just published in Clinical Cancer Research (http://clincancerres.aacrjournals.org/content/24/17/4215.long)

Ovarian cancer is the most common gynaecological cancer, and the 6th leading cause of cancer related mortality in women in the UK, with over 7,000 new cases each year (www.cancerresearchuk.org/about-cancer/ovarian-cancer). Commonly dubbed "the silent killer" because there are often very few or no symptoms, ovarian cancer often presents at an advanced stage when it is harder to treat. Advanced disease is characterised by the formation of secondary tumours and the accumulation of fluid (ascites) in the abdominal area. Patients often respond well to first line platinum-based chemotherapies, but rapid development of drug resistance can result in disease recurrence either locally or in other parts of the body in late stages. These limitations have resulted in a stagnation in the 5-year survival statistics for ovarian cancer, which have remained stubbornly unchanged at around 45-50% for the last 25 years. Consequently, new and more effective forms of therapy for platinum-resistant ovarian cancer are under investigation.

One such therapeutic approach being examined is known as virotherapy - a treatment which uses viruses to treat cancer. This may seem unusual but using viruses as cancer treatments has several compelling "USPs" that can be exploited. Firstly, as a biological agent, the therapy can reproduce itself at the point of need. They replicate, producing millions more copies of themselves, which can go on to infect further cancer cells once the initially infected cells "bursts" or "lyses". Secondly, the way the viruses kill the cells (by bursting them) produces an immune response which enhances the body's immune systems own ability to recognise and kill the tumour. Finally, the DNA of the virotherapy can be further engineered to include other anti-cancer agents, such as immune-therapies and/or antibodies, such as Herceptin. Essentially, if correctly designed, virotherapies have the potential to turn tumours into immunogenic factories producing anti-cancer agents to facilitate their own destruction.

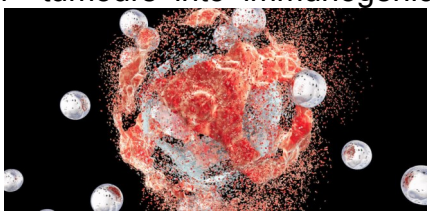

Image Credit: GENEONLINE

To date however, the potential of virotherapies has yet to be fully realised. This is largely because viruses, in their native state, can't discriminate between a cancerous cell and a healthy cell. In a new publication, researchers from Cardiff University have made significant inroads to address this problem. Starting with a common respiratory virus, (adenovirus serotype 5, Ad5), they engineered each of the three major capsid (shell of the virus) proteins to prevent all known means of virus infection of normal, healthy cells. The resultant virus, $Ad5_{NULL}$ was unable to infect any cells, since it can't attach to any cells.

To make the virus able to selectively infect tumour cells, the virus was further engineered to include a small piece of protein, called A20, into one of the virus shell proteins. This small piece of protein binds strongly and selectivity to a cellular protein (called αvβ6), which is present in certain aggressive cancers, including about a third of ovarian tumours that become resistant to platinum based chemotherapies. The resultant virotherapy, termed $Ad5_{NULL}$-A20 was shown experimentally to be

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extremely selective for cancer cells with αvβ6. Importantly, in animal models, tissues and organs which would normally be infected using unmodified Ad5 were completely clear of infection with the refined virus, whilst in an animal model of αvβ6 positive ovarian cancers, mice treated with the refined virotherapy all survived for the full duration of the study (100 days) whilst untreated control mice or mice treated with an unrefined virus all deceased by day 40-50.

The first author on the paper, Hanni Uusi-Kerttula, said "We've taken a common, well-studied virus and basically given it a complete makeover, so that it can no longer attach to non-cancerous cells but instead seeks out a specific marker protein called αvβ6, which is unique to certain cancer cells, allowing it to invade them. The virus selectively infects tumour cells, producing millions more copies of itself, eventually bursting the cells, and allowing the copies to spread to surrounding cancerous cells. This activity also activates the body's natural immune system, helping it to recognise and destroy the malignant cells.

We were delighted with the selectivity we observed, and the efficacy we found in our pre-clinical animal model".

Alan Parker, the senior author of the study said: "this is an exciting advance, offering real potential for patients with ovarian cancers, as well as other cancer types that express αvβ6 integrin, such as pancreatic cancer, lung cancer, and aggressive forms of breast cancer. It is likely that additional modifications to the virus may enhance the therapeutic effects further, for example, by engineering the refined virus to overexpress immunotherapies to stimulate the host immune system to fight back against the cancer. We look forward to developing this further with our exceptional network of collaborators and funding agencies to translate our exciting pre-clinical findings into meaningful, well executed and timely first-in-human clinical trials."

EU General Data Protection Regulation

In May 2018 a new data regulation, the GDPR, was implemented in the EU. The new regulation will reshape the way data is handled across all sectors, not just healthcare, and is being touted as 'the most important change in data privacy regulation in 20 years'. It is designed to:

- Harmonize data privacy laws across Europe,
- Protect and empower all EU citizens data privacy
- Reshape the way organisations across the region approach data privacy.*

The Health Research Authority (HRA) is the body nominated in the UK to publish guidance on the implementation of the GDPR and the UK's new Data Protection Act 2018 for health and care research+. The GDPR requires each activity of processing data to have a legal basis under this legislation, in addition to the common law basis. The guidance from the HRA to universities and the NHS is that the legal basis for processing data under the GDPR should be a 'task in the public interest'.

The Wales Cancer Bank process does not need to change in order to be compliant – patients will still be consented to ask permission to access samples and medical records. What will change is the way data is handled if patients choose to withdraw consent. *(over)*

GDPR contd.

Only a handful of patients have ever withdrawn consent but for those that do, their samples will be destroyed but data will now be kept so that researchers who may have already used samples can still include those samples and data in their research and not have to take them out. If lots of data has to be withdrawn it can hugely affect the validity of research projects and this is one reason that 'task in the public interest' is now the legal basis for processing data.

Additional information in the updated patient information sheet gives further details about the GDPR and what it means for new patients consenting to donate their samples and data. If you have already donated samples and want to find out more, there is a data privacy notice on the WCB website: *https://www.walescancerbank.com/data-privacy-notice.htm*

* *https://eugdpr.org/*
\+ *https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/*

WCB Team

Emma Watson joined the Wales Cancer Bank team earlier this year. She introduces herself below.

Hello, my name is Emma Watson. I graduated from Dublin Institute of Technology in 2004 with a BSc in Biomedical Science majoring in Histopathology. In 2008 I completed an MSc in Biomedical Science specialising in cellular pathology from University of Ulster, Colerain.

I have six years of experience working in a routine diagnostic Histopathology Laboratory at University College Hospital Galway and later at the Bon Secours Hospital in Cork. I also spent two years working at the routine diagnostic Microbiology laboratory at Waterford Regional Hospital before returning to Histopathology in a senior role at Waterford Regional Hospital Histopathology Laboratory.

I moved with my family to Wales in June 2017 and joined the Wales Cancer Bank in May 2018. I am very excited to be part of this team and hope my knowledge and previous experience can contribute toward the advancement of cancer research.

Get in Touch……..

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