Voice – Vision on Information, Confidence and Engagement - Science for Patient Advocates

The following is a report from the Consumer Liaison Group members who were sponsored by NIHR CC to attend the course in September 2014:

- Sharon Paradine: Palliative and Supportive Care CSG
- Janette Rawlinson: Lung CSG
- Elspeth Banks: Psychosocial Oncology and Survivorship CSG

Introduction

The opportunity to access one of the 3 available NIHR CC sponsored places was first advertised in May 2014 for this, the second ICPV "VOICE" 5 day residential course. The event was held at Bart's Cancer Institute, Charterhouse Square London from 1 – 5 September 2014.

The aims of VOICE are to give participants an introduction to basic cancer biology and to epidemiology, statistics and reading scientific papers. The course was led by Professor Louise Jones, Professor John Marshall, Dr Richard Grose and many of their colleagues at Barts Cancer Institute. Their support was outstanding and their willingness to commit this significant time to delivering a first class course both in the classroom and the lab was acknowledged by all participants. We agreed that this experience would make a significant difference to our own future contributions and that the knowledge, understanding and skills acquired were transformative.

We were extremely well briefed and informed by ICPV's Dr Adrienne Morgan in the weeks leading up to the event. On our behalf Adrienne took on all of the onerous tasks of registering us as students, organising all accommodation and food and all administration linked to the event. The ongoing support of Adrienne and her husband Chris Finch throughout the course was a great benefit to all 15 of the course participants.

Arrival: Sunday 31 August

We arrived at Charterhouse and made our way to the student accommodation at Dawson Hall and were given a very warm welcome by Bec Hanley who was facilitating/co-ordinating the week.

The accommodation was basic but clean and comfortable. We each had a single room with a study desk and small fridge. In our rooms we found our study file for the week and a Bart's "goodie bag". Access to wifi was also helpful. We were taken on a brief tour to familiarise ourselves with our surroundings and the learning environment, given a briefing about the week ahead and introduced ourselves to one another. We were very much a mixed and diverse group of students in terms of age, experience and knowledge of science and had come from all corners of the UK. Once the "business" was done we enjoyed time together at a local Italian restaurant.

Day 1: Monday 1 September

Day one began with, as in the subsequent days, a breakfast served in our classroom in the Joseph Rotblat building. The standard format for each day was theory/lectures in the morning with practical work in the lab in the afternoon. Each session was never longer than 1 hour and we were encouraged to ask questions as they arose, following the premise that "no question is a silly question". We were provided with papers for each presentation and our folders contained an extremely useful glossary which was referred to constantly throughout the course.

Each day two students gave an overview of the previous day's presentations and labwork. It was constantly reiterated that we were not on the course to become future Nobel Prize winners but to learn enough to enhance our roles as patient advocates and to further build our confidence.

Monday morning Basic Cancer biology - What cancer cells do Professor John Marshall

Session 1 **What do normal cells look like and do**

During this session we were taken back to basics and learnt that there are more than 200 types of cells in the body, all sharing the same basic components before moving on to the structure of DNA and how it is replicated. In such a mixed ability group there was a wide range of understanding of his very complex subject. Participants with a science background found this to be an excellent "refresher"

Session 2 **What happens to normal cells to make them cancerous?**

This session was of particular interest and prompted debate and discussion. We explored:

- Sources and types of DNA damage
- Changes in the DNA resulting from damage/mutation
- Consequences of DNA mutation
- DNA repair mechanisms
- Oncogenes and tumour suppressor genes

Session 3 **Hallmarks of cancer and what cancers need to do to be successful**

This was a consolidation session and helped us to realise how much information we had absorbed. In addition to learning the difference between benign and malignant tumours this session highlighted that for cancer to be successful it needs to:

- Have self-sufficiency in growth signals
- Be insensitive to anti-growth signals
- To have limitless growth potential
- Have sustained angiogenesis (growth of new blood vessels)

Monday afternoon

This, our first session in the lab, proved to be an invaluable learning experience that would support us in all our labwork. As we donned our white lab coat, protective goggles and gloves it became clear that for some of us this was going to be something of a challenge. We worked in small groups with scientist mentors and spent the afternoon learning how to measure very small volumes of fluid accurately with a variety of laboratory tools, pipettes, centrifuge tubes etc. Dexterity and a steady hand were the order of the day.

Monday evening: **Guest lecture "The trials and tribulations (and joys) of running a cancer research laboratory." Professor Clare Isacke, Institute of Cancer Research**

This lecture was truly spellbinding. Clare gave an honest and humorous personal insight into the reality of the responsibilities that accompanied the job. In addition to hearing of the sense that every day brought a new challenge, there was also financial and job insecurity, pressure to publish, staff support, long hours, disappointment and sometimes the need to cope with failure. However I think what stayed with us was an enduring sense of an absolute passion for science, dedication, the importance of the team and that scientists also like to have fun!

Day 2: Tuesday 2 September

Tuesday morning: Cancer Biology (How cancer cells do it) Dr Richard Grose

Session 1 **Signalling messages to cells**

Session 2 **How cells grow**

Session 3 **How cells survive or die**

These three sessions were interactive and took us systematically through the process of how normal cells communicate with each other. The take home messages were:

- Cells in our bodies need to talk to each other
- Cancer cells can hijack these communication pathways
- We can hit these pathways but cancer is a hard target
- We are developing smarter, cleaner drugs, against new targets, giving hope for future treatments

Learning how cells grow led us onto how various cancer therapies work and where within the cell cycle they are targeted. The final session covered cell death (apoptosis). We learnt about the p53 "Guardian of the genome", oncogenes, and how they drive cancer through the stimulation of cell birth or the inhibition of cell death. Tumour suppressor genes act protectively to block the cancer development.

Session 4 **How and why we use animals to study cancer**

This was an incredibly interesting session and a new subject for most of the group, prompting much interactive debate. Once again the session led us systematically through rationale for using mice in genetic science, the regulatory processes for maintaining integrity and practical examples of the work being conducted using the mice. Richard left us to ponder the following:

- Do we need to use animal models?
- What are the alternatives? – Patient derived xerografts? (a new emerging field, taking patient samples then growing in mice and returning to humans)

Tuesday afternoon: How do we study DNA? DNA extraction and polymerase chain reaction

Our second day in the lab enabled us to do what we've seen on many crime-related programmes – take our own DNA sample with a mouth swab! Using pipettes to measure various solutions to add with this sample to isolate the DNA, cut it into fragments and put it onto gel plates. This allowed us to reuse our new skills of mastering pipettes! The introduction to the session described how isolating cells was 'like identifying one word in a book in a library' or 'listening to one person's voice in a football stadium' to give us an idea of the scale of the task. We would be able to observe the results another day.

Tuesday evening

Adrienne organised for us to have a tour of Charterhouse. We heard the fascinating history of this former Carthusian priory, hospital and school with royal connections, its own chapel, burial plaques of historic figures including those of Baden Powell and William Makepeace Thackeray, and original cloisters.

Day 3: Wednesday 3 September

Wednesday morning: Different types of cancer

This morning brought us a selection of extremely different but equally passionate and enthusiastic presentations about head and neck, melanoma and prostate cancers from Krishna Suchak, Melissa Phillips, and Dan Berney. Their presentations included illustrations and samples – some of which we would recognise in our laboratory work throughout the week.

Krishna's comment about seeing 'different samples from patients coming back to the lab and making her feel sad so she wills them to do well' reminded us that these are not anonymous tissue samples being analysed but real people with lives impacted by investigations and their results.

It was surprisingly reassuring that the system is not so vast or anonymous that scientists lose touch with the reality of the work. Krishna and Melissa revealed lesser-known information about mouth ulcers, predisposition or prevalence amongst different community groups with increased risks and warnings to protect skin from sun and check out moles using ABCDE approach. Some notable facts were that similar mutations (BRAF) are in melanoma to other cancers so BRAF inhibitors now being used as frontline treatment and melanoma has a higher percentage of young patients and is increasing faster than any other cancer in UK and Europe . Both presenters stressed the importance of self-examination, early detection and swift treatment.

Dan's presentation took a novel (literally) effective approach choosing to challenge the current treatment and screening regime for prostate cancer on the theme of Dante's comedy. Who knew that anchoring the

thoughts, treatments, options to literary examples would resonate so strongly to help us understand the dilemmas facing those involved? Lewis Carrolls' 'Red Queen hypothesis' helped us work through the relevance of current options. Learning of the need to separate 'tigers' from 'pussy cats', we were left in no doubt about the current ethical dilemma and the need for a new approach, detection and treatment methods.

All 3 presenters left us pondering whether screening and identification of certain cancers leads to unnecessary treatment - the consequences of which may be worse than if left alone. Time and again we heard about cancer heterogeneity and prevalance helping us appreciate cancer's complexity and the need for ongoing research into different treatment regimes as well as greater understanding on cause, effect, treatment and effects of treatment on quality of life.

Wednesday afternoon: Observing and handling cancer cells

The afternoon lab session tested more than our scientific ability – we used microscopes to observe and count cancer cells on slides of samples tested with various agents. Good eyesight was essential as was the ability to use a click counter and calculator! We saw cell membrane, nucleus and cytoplasm clearly visible under the microscope. It brought home the repetitive nature of lab work, taking dishes to and from the incubator, reassessing them under microscopes, recording data, measuring fluids to test and repeating several times. Several of us had new found respect for those working in such conditions.

Wednesday evening

Having been invited to join Barts celebrate the Barts Cancer Institute 10th anniversary with a river cruise, most of us set off by taxi to catch a large river cruiser, many bedecked in borrowed props dressed up for a 'Great Gatsby' theme leaving us to try and recognise delegates and staff – some of whom resembled others in their blonde or dark wigs. Dave Chuter won the prize as a 'Peter Stringfellow' lookalike and Professor Louise Jones in a dark bobbed wig was almost unrecognisable. Dapper trilbys, braces, flapper dresses, beads, feathers and beaded dresses transformed the scientists, academics and delegates! An evening's entertainment ensued with several having caricatures drawn, magic tricks performed at the tables, wonderful food and drink including individual iced celebration cakes and the highlight seeing Tower Bridge opened for us– toasting with bubbly as we did so, allowing us a peek at some of the Tall Ships gathering for the Tall Ships weekend.

Those who didn't join the cruise went to see the memorable sculptured poppies installation at the Tower of London where a moving brief service at sundown commemorates several names being read out from a selection of those killed on that day 100 years ago and a soldier playing 'The Last Post'.

Another educational and entertaining full day.

Day 4: Thursday 4 September

Thursday morning: Different types of cancer

Continuing with the theme of the previous day, Alastair Ironside, Louise Jones and Diana Eccles led us through oesophageal and lung cancers, breast cancer and genetic testing risk assessment and screening.

We learned that oesophageal cancer is the second most common cancer in adults and of the rapid increase in the most common type - adenocarcinoma - over the past 40 years. Those diagnosed with Barrett's Oesophagus are 11 times more likely to develop adenocarcinoma. Progress is being made in new surgical techniques and chemotherapy regimens. Importantly there is a developing understanding of genetic changes in this cancer and new biological therapies such as growth factor blockers, PARP inhibitors, monoclonal antibodies and vaccines.

An interesting aspect of the presentation on lung cancer was this question "What don't we know?" We don't know:

- How best to prevent lung cancer
- The best way to identify high risk individuals and screen for early stage lung cancer
- Why don't all smokers get lung cancer? (and conversely why do non-smokers get lung cancer?)
- Why doesn't the same type of lung cancer always respond the same way to treatment?

- How can we avoid treatment-related side effects?

In considering faulty genes and the development of lung cancer we learned of the role of the p53 tumour suppressor gene (not for the first time in the course), the role of the sNRSF gene in small cell lung cancer and how our genes determine how smoking affects our lungs. A European study – EPIC – is looking for links between diet and lung cancer.

Louise reminded us of genetic factors such as the clustering of breast cancer in families and the familial relative risk. Inherited mutations account for 7-10% of breast cancers but not all familial clustering of breast cancer is explained by known mutations. We learned about the different types of carcinoma such as ductal, lobular, tubular and mucinous, their frequency and 10 year survival. The message in relation to molecular classification is that:

- There are more "types" of breast cancer than we previously recognised
- The importance is there is variable behaviour within current classification types and
- We don't yet know how to use these complex classifications

Mammographic density is a major risk factor for breast cancer in a large number of women but the question is how can we use this knowledge to screen for high risk or prevention? We don't know how this predisposes to the development of cancer. One in three breast cancers detected by mammogram screening may actually be harmless, as suggested in a recent study. However, as it is not possible to distinguish between lethal and harmless cancers so all are treated.

Louise posed three key questions in relation to breast cancer:

- What do we mean by heterogeneity (where cancer is caused or contributed to, by several different factors which is one reason why the treatment of cancer is so complex) of cancer?
- How can we use molecular advances for clinical effect?
- What are the future priorities for future research?

Diana introduced us to the basic principles of cancer genetics and we learned about tumours acquiring many somatic mutations – a few critical "driver" and many "passenger" mutations. Somatic mutation is influenced by both genes and environment. She posed hereditary breast and ovarian cancer as examples of clinical dilemmas in genetic testing for predisposition to cancer, advising that in the case of genetic testing for BRCA mutations genetic counselling reduces distress, improves risk perception and reduces an individual's intention to have genetic testing. Anecdotal case studies illustrated the dilemma faced by many. The need for caution was underlined and the key message was that, like any medical test, genetic testing must be appropriately directed and interpreted in the light of the clinical picture to safely interpret findings.

Thursday afternoon: Bedside to bench, tissue and biomarkers.

Back in the lab, Louise led us through this practical session where we observed the dissection and examination of a human breast. This session was managed with great sensitivity and dignity. In observing the process we were able to view tumour tissue versus normal tissue. Breast tissue was prepared for analysis and tissue banking. It was a privilege to be present for this session.

The next lab session saw us guided through the process of immunohistochemistry and its use as a diagnostic tool. This was a fascinating process as we worked through the 17 steps of immunohistochemical staining presented to us. I could not have envisaged at the start of the week that, by day 4, I would have the skills and the confidence to be able to interpret and follow through the (complex) instructions. A great sense of achievement.

Thursday evening: Course dinner

Tutors and students enjoyed the opportunity to dine together and to share experiences of the week thus far. Elspeth was delighted to deliver a vote of thanks to everyone who had contributed to the success of this outstanding course, recognising the dedication and enthusiasm of "our" research scientists in their work towards improving outcomes for us all.

Day 5: Friday 5 September

Friday morning: How to read scientific papers – Professor John Marshall

This was a new session on the Voice programme, one which we found to be really informative. John took us though:

- The anatomy of a research paper
- Discussion of a paper published in the Journal of the National Cancer Institute and
- Should you believe everything you hear?

We learned the importance of author names and affiliations and the significance of where your name appears on the list. For example the first and last authors are normally the most significant as the first normally does the work and the last funds it! John highlighted the importance of the abstract – a brief summary of 200-300 words – as it is often the only part of the paper that is read by browsers, so it must be clear, concise and informative. The most important is the Results section, comprising figures, tables and text. Results are described, never discussed.

Other considerations include which journal do you hope to publish in? This affects how much data and what type of data goes into the manuscript. Are some journals better than others? How many citations come out of a specific journal? This is an impact factor. How many words does the journal allow? Will it go out to review and who takes this decision?

John helped us to interpret a journal article before which we were given a crash course in integrins. These are central to enabling tumour cells to move and metastasise. This was a fascinating session, providing new insights for many in the group.

Friday afternoon

Bec Hanley led us through the course evaluation, asking if the objectives we set ourselves at the start of the week had been overtaken. The response was a resounding yes.

Thanks to NIHR CC for enabling our participation in this event.