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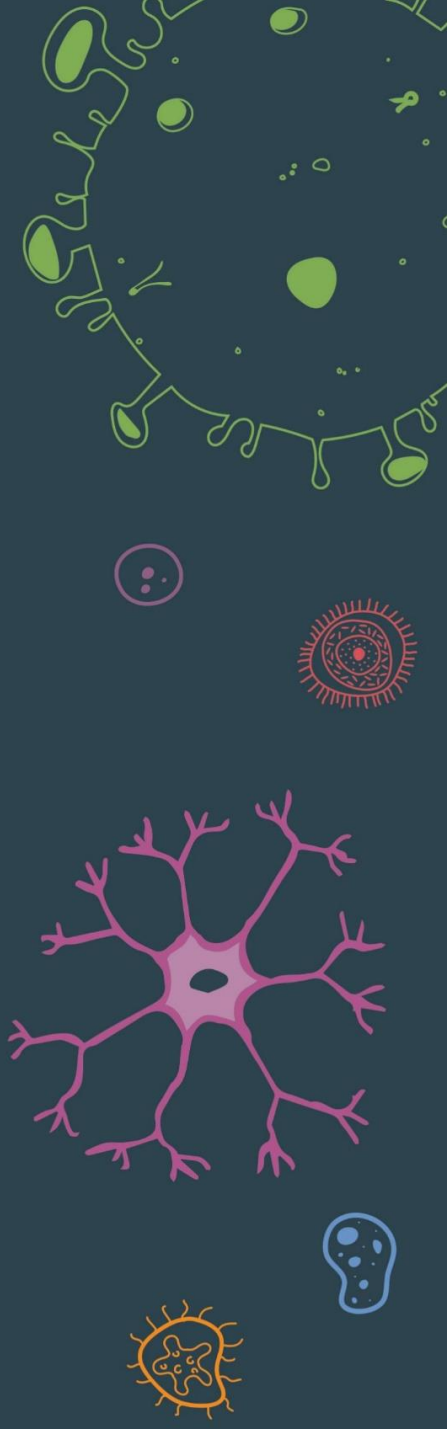
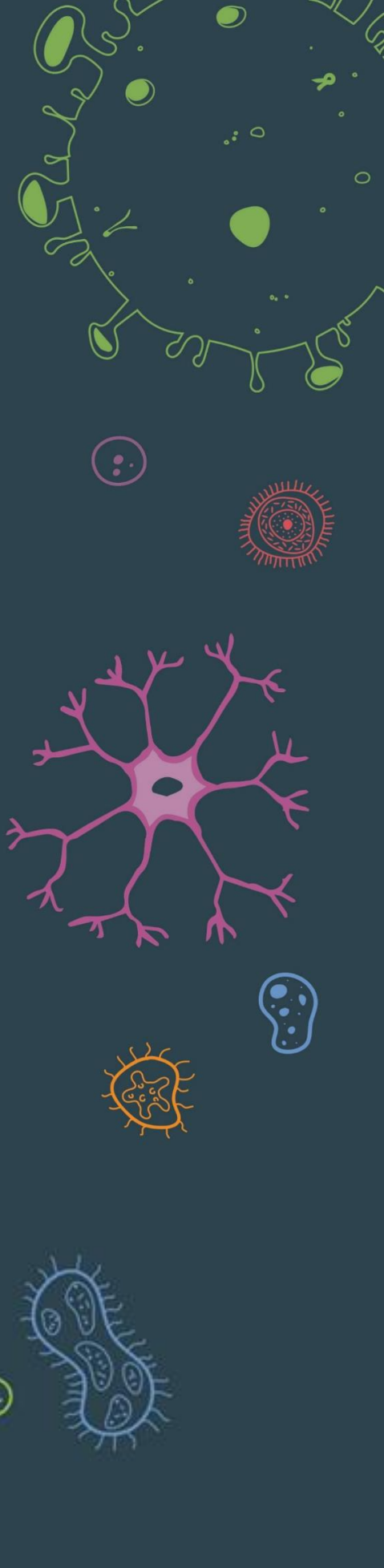


Cardiff University Biobank

Annual Report July 2018 - January 2020

Contents



> “The CUB vision is to provide high quality biosamples to research organisations”

Introduction

This is the first Cardiff University Biobank (CUB) annual report encompassing the first 18 months of CUB’s operation. Although CUB officially opened in October 2019 this report captures information from July 2018 since this was the month that CUB consented its first participants.

CUB currently has a number of active collections into which donors are being actively consented along with completed collections that have been adopted into CUB. In January 2020 CUB also began its first patient collection with other collections soon to be commencing.

CUB currently has three routes for samples to enter into the biobank. Donors can be directly recruited to the biobank where individuals are consented using CUB information sheets and consent forms. Samples can also be deposited into the biobank from existing and completed collections. Finally, the CUB is an active collaborator and has a current partnership with the Welsh Centre for Anatomical Education (WCAE).

Aims and Vision

The CUB vision is to provide high quality biosamples to research organisations throughout the UK, Europe and the rest of the world.

The CUB mission is to consistently meet customer expectations whilst strictly adhering to human tissue, data protection and biobanking standards and legislation. Our strategic direction is to successfully integrate the existing biobanks at Cardiff University into the CUB facility. We aim to maintain our certification and commitment to ISO 9001:2015 whilst expanding on current sample collections and creating new collections in areas not currently covered by the biobanks presently situated within Cardiff University.

CUB Academic Lead Report

It's now been a little over a year since CUB was launch by the Cabinet Secretary for Health and Social Services and it's been a very busy time in the biobank as you can read in this, our first, annual report. A few activities have been key for us this past year; starting new collections in new disease areas and also integrating with some of Cardiff University's existing tissue banks. This later activity was one of the original reasons for creating CUB in the first place and so it really is satisfying to see CUB now supporting these collections, making patient-donated samples available for research for many years to come. All this would not be possible without the generosity and altruism of many 1,000s of patients and donors, for which we offer a heartfelt 'thank you'.

Whilst such activities are key to the future sustainability of CUB, critical to the future success of any biobank is on-going access to patient samples through a strong, governance-driven working relationship with the NHS. To this end CUB has this past year, developed a strategic framework agreement with Cardiff and Vale University Health Board (CVUHB) to enable access to patient material to support mutually beneficial research projects. Thinking about the sustainability of biobanking, diversification of biobanking activity is a key component to try and achieve this aim. CUB has therefore been working with partners to develop collections of (a) residual animal tissues and (b) microbes to support UK and international research to drive improvements in human health.

In my discussions with colleagues and lay representatives over the years, we have often ruminated over the potential of Wales to coordinate its activities around biobanking and data linkage more effectively – "the whole is great than the sum of the parts" as Aristotle once said. Hence CUB has been and is actively involved in supporting the development of an all-Wales biobanking initiative. We were a key contributor to a Health and Care Research Wales (HCRW) task and finish group that reported on a coordinated biobanking approach. Furthermore, we are currently working with HCRW to develop an all-Wales Biobanking forum to further engage the wider Welsh biobanking community in order to deliver recommendations on Welsh biobanking for the Welsh Government.

So, a busy year with an even busier one ahead of us! Finally, can I thank all those colleagues, patients, donors and advisors that have enable CUB to get where it is today and remind everyone that CUB is a conduit between the patient/donor and the investigator, underpinning research that will make a tangible difference for the health of the people of Wales and beyond for many years to come.

Professor Phil Stephens
CUB Academic Lead

> "CUB is a conduit between the patient/donor and the investigator, underpinning research that will make a tangible difference"

Governance

Ethics submissions

CUB received its initial ethical approval in March 2018 (Wales REC 3 18/WA/0089). Since July 2018 CUB has submitted four substantial amendments to its ethics. All substantial amendments were given favourable opinions and are detailed as follows:

June 2018
This amendment was to allow the setup of two collections: the Elite Sports Person Collection and the inclusion of Internal donors (donors from Cardiff University) as part of the Healthy Volunteer Collection

November 2018
This amendment was to allow the set up of two new collections, a collaboration with the Welsh Centre for Anatomical Education and the collection of NHS diagnostic samples

May 2019
This amendment was to allow the collection of patient samples from children

November 2019
This amendment included a permission to contact procedure for external healthy volunteers and the collection of skin biopsy from patients as a non-diagnostic sample

Audit and Non-conformance

Audit

CUB conducts nine different types of audits. These are conducted for different regulatory reasons; to ensure compliance with the Human Tissue Act, to meet Health, Safety and Environmental standards, and to meet ISO standards. The audits CUB conducts are as follows:

- **Work Place Inspections** are inspections of all work areas as required to meet Health and safety legislation
- **Fire Safety** audits are inspections of all fire safety equipment as required to meet Health and safety legislation
- **Traceability** audits are monthly audits that trace samples from database to sample location and from sample location to database and are required to meet the HT Act
- **OECD** audits are audits against the Organisation for Economic Co-operation and Development Guidelines for Human Biobanks and Genetic Research Databases. Moving forward these audits will not be performed but audits against the new biobanking ISO standard (ISO20387:2018) will be undertaken instead
- **Vertical** audits are monthly audits that select a consent form and look at all records relating to it for completeness
- **Horizontal** audits select a record type and look at a percentage of all that record type for completeness
- **ISO 9001** audits are risk based and directly against the ISO 9001:2015 standard
- **HTA** audit is an annual internal audit directly against the HTA standard
- **Health, Safety and Environmental** audit is an annual internal audit to ensure CUB is working in line with the ISO4001 and OHSAS18001 standards

Audit

CUB conducted 143 audits in total between July 2018 and Jan 2020. Figure 1 shows the number of audits conducted by type. The largest number of audits conducted were traceability audits (22%) which is due to the fact that alongside the monthly traceability audits, ad hoc audits are conducted when collections move into CUB. For the rest of the audit types, the number of audits conducted were fairly similar apart from the HTA and Health and Safety audits as only one of each of these were conducted. This is due to these audits only being conducted on an annual basis.

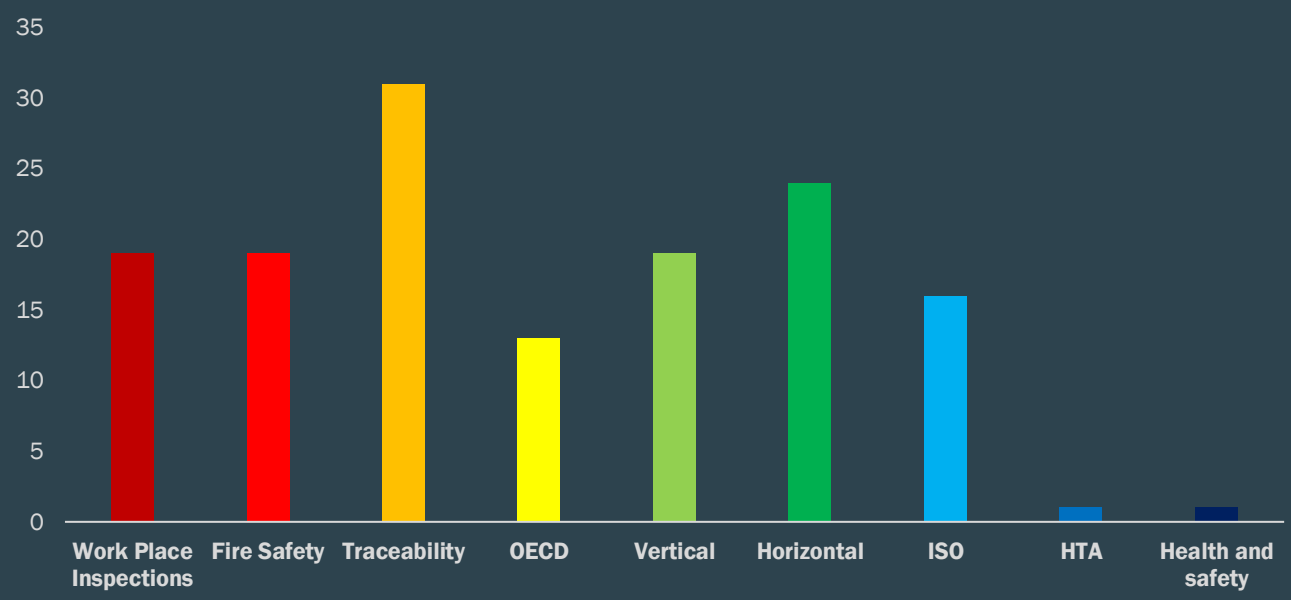


Figure 1 The Number of audits conducted by type between July 2018 and January 2020

Non-conformance

The majority of non-conformances raised within CUB were found through internal audit (54%) (see Figure 2). 87% of these non-conformances were closed by their target date. The second highest number of non-conformances were found in an ad hoc manner (39%) with 96% of these closed by their target date. Across all audit types, 88% of non-conformances were categorised as minor with 6% opportunity for improvement and 6% with no severity (see Figure 3). No non-conformances were categorised as major or critical.

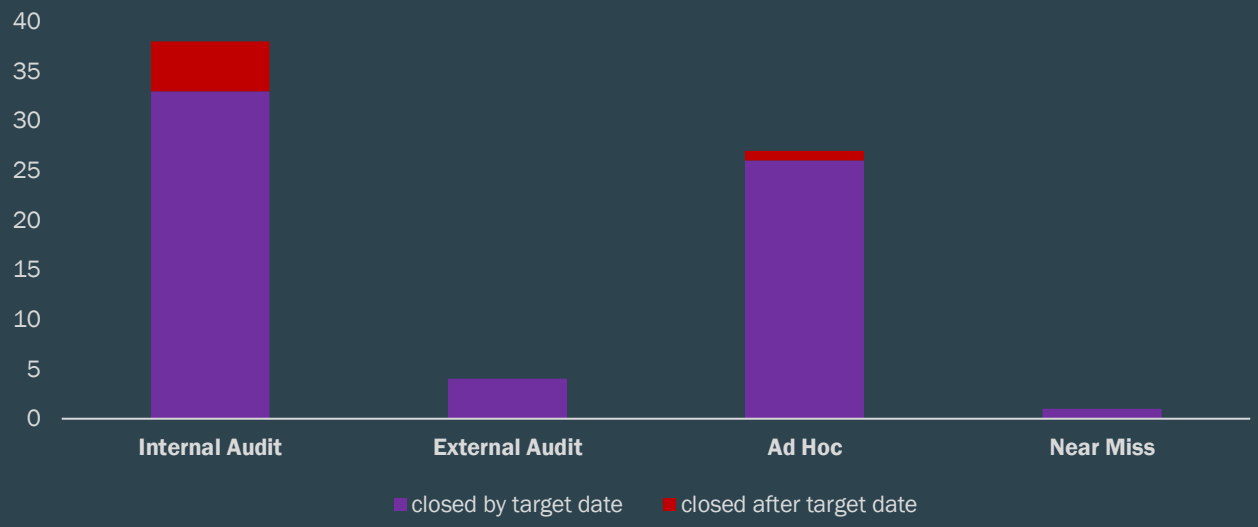


Figure 2 Number of Non-conformances raised by type

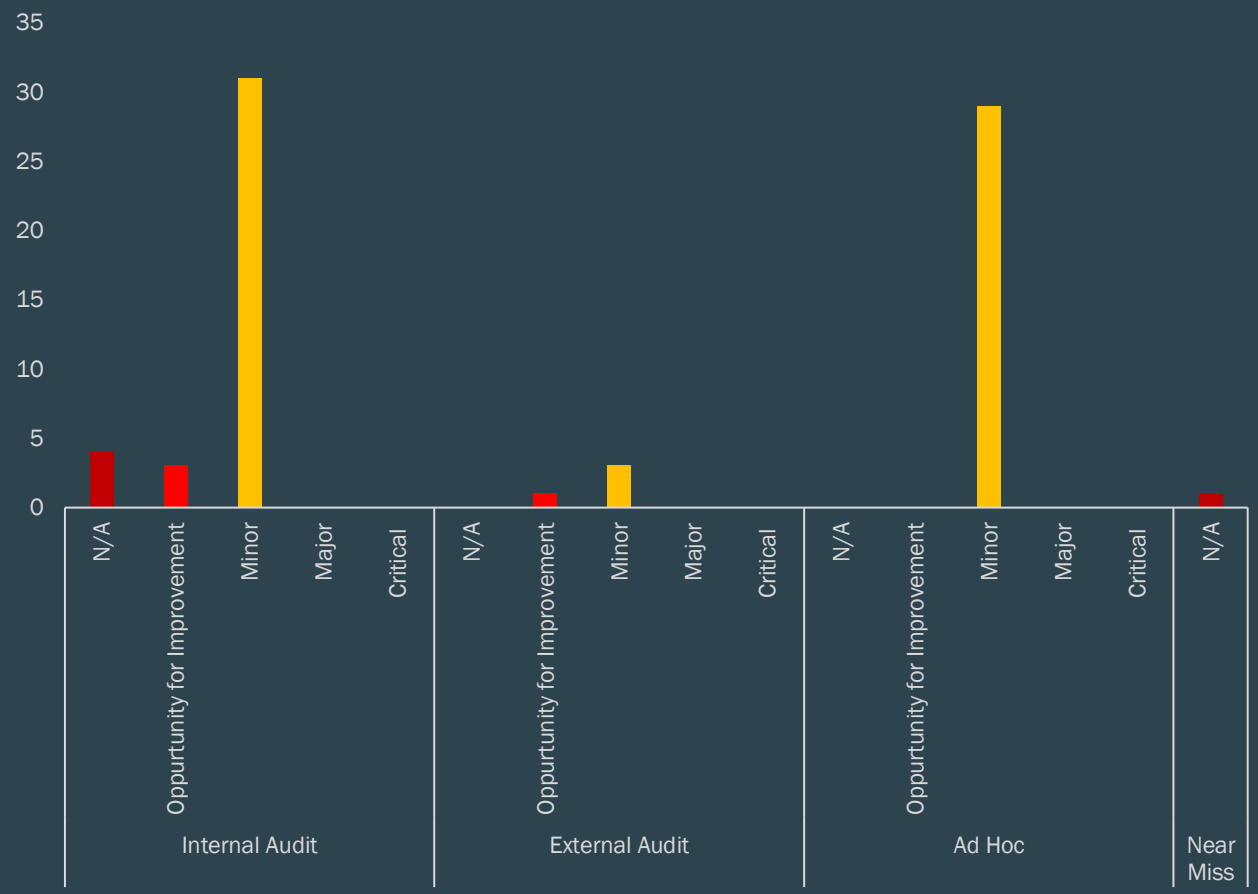


Figure 3 Number of Non-conformances raised by severity


Haier
Salvum

CUB Sample collections

The CUB has a number of different existing collections within the biobank, some of which are actively recruiting and some that are closed existing studies. All samples are supplied anonymously to approved projects.

Healthy Volunteer Collection

This collection consists of samples collected from donors that are classified as healthy. These samples are collected within the biobank using CUB's dedicated phlebotomy suite. The CUB is ethically approved to collect blood, urine and saliva samples with only blood and saliva currently being collected. After sample collection donors are asked to complete a questionnaire about their health and lifestyle. Samples from the healthy volunteer collection can be released as fresh samples and from storage.

Elite Sports Person Collection

This collection consists of samples collected from donors that are classified as elite sports persons. Samples collected from these donors are blood and saliva. Samples from the elite sports person collection can only be provided from storage.

Cystic Fibrosis Collection

This collection consists of samples collected from donors that are diagnosed with cystic fibrosis. Samples collected from these donors are blood and sputum. Samples from the cystic fibrosis collection can be released as fresh samples and from storage.

Anatomy

This collection is a collaboration between CUB and the WCAE. CUB collects samples from donations to the WCAE. These samples are all embalmed tissues. Samples from the anatomy collection can be collected bespokely if required or released from storage.

Acute Myeloid Leukaemia

This collection consists of samples from completed clinical trials from patients with acute myeloid leukaemia. Samples collected from these donors are primary cells (bone marrow mononuclear cells and peripheral blood mononuclear cells). Samples from the acute myeloid leukaemia collection can only be released from storage.

Neurofibromatosis-1

This collection consists of samples from patients with neurofibromatosis 1 (NF1). This collection is mainly frozen and formalin fixed paraffin embedded tissues. Samples from this collection can only be released from storage.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Donor Recruitment

CUB has commenced recruitment within a number of its collections since July 2018, which includes the healthy volunteer collection, elite sports person collection and the cystic fibrosis collection. Figure 4 depicts the number of donors recruited by month, which has mainly been within the healthy volunteer (47%) and elite sports person collections (45%) with a small number of participants recruited to the Cystic Fibrosis collection (8%). Recruitment over the last 18 months has been minimal with a peak in July 2018 which was the result of a recruitment clinic for the elite sports person collection. Recruitment between August 2018 and December 2019 has been to the healthy volunteer collection through regular clinics. From January 2020 onwards recruitment began to the Cystic Fibrosis collection which is CUB's first patient collection.

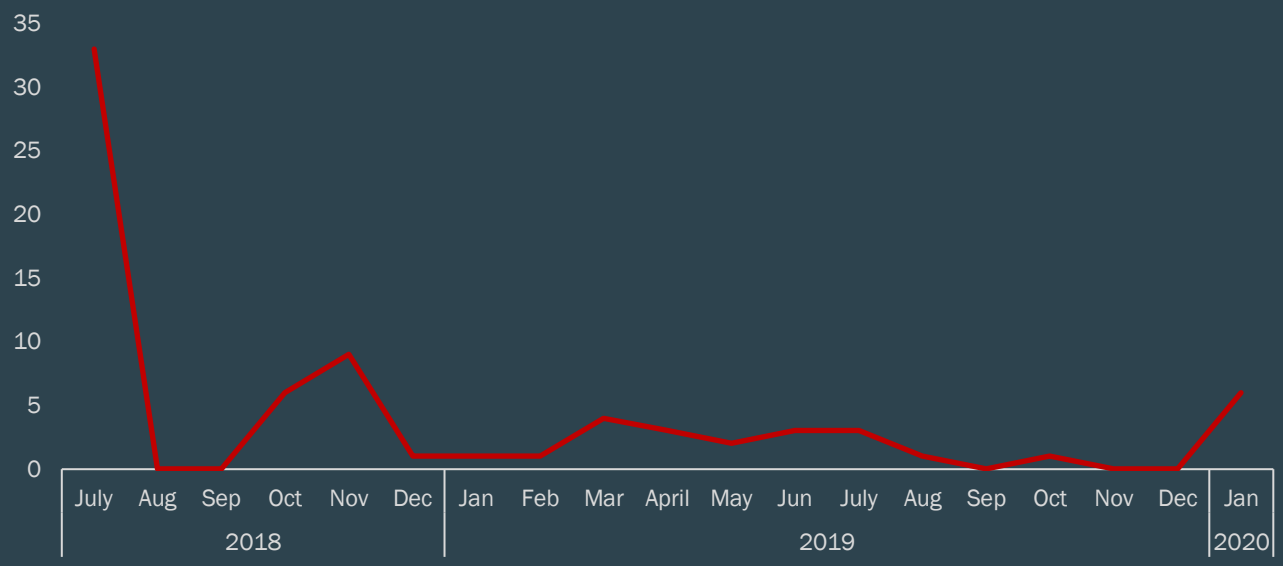


Figure 4 Number of donors recruited by month between July 2018 and January 2020

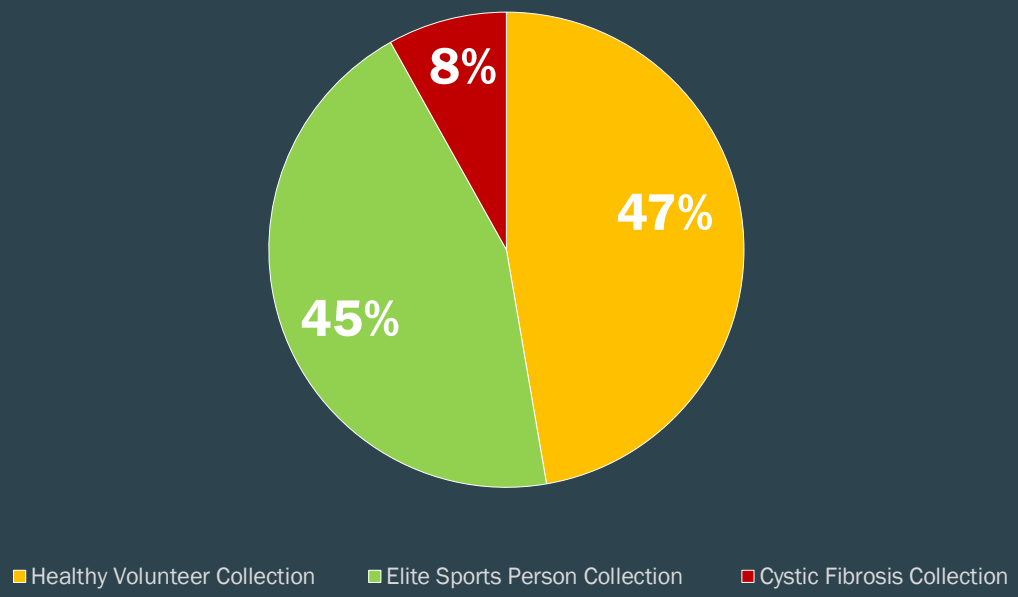


Figure 5 Percentage of donors recruited split by collection

Age and gender splits show that most participants were in the 20-29 age bracket (51%) and male (64%) rather than female (36%) (Figures 6 and 7). This is likely due to the fact that currently all participants within the Elite Sports Person collection to date have been male and under the age of 30. The second largest age group is 30-39 (24%) with recruitment fairly evenly split across the other age groups (16-19 [2%], 40-49 [11%], 50-59 [8%], 60+ [4%]). That fact that most donors are recruited in the 20-49 age group is likely because most of CUB's recruitment up until January 2020 has been from Cardiff University staff who are of working age.

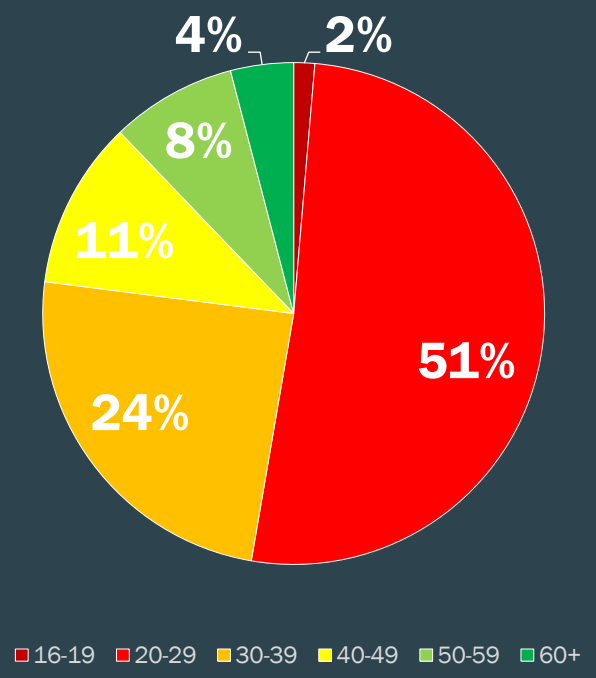


Figure 6 Percentage of donors recruited by age

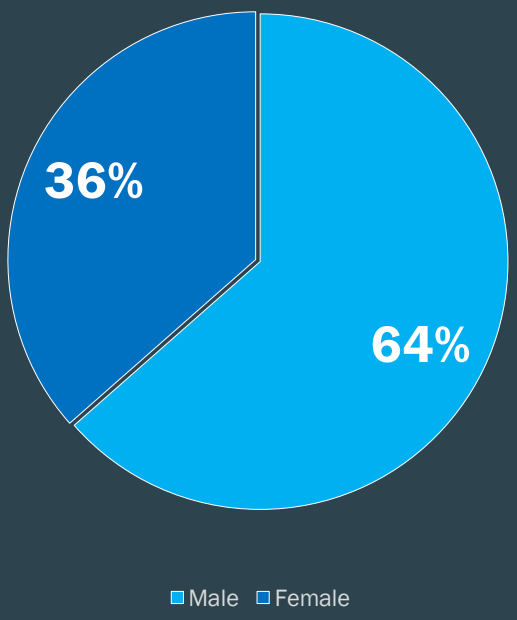


Figure 7 Percentage of donors recruited by gender


H36
H37
H38
H39
H40

Sample Storage

CUB currently has samples stored from a number of active collections and completed studies.

Figure 8 shows the aliquots currently stored in CUB as of January 2020 split by sample type and collection.

The largest number of aliquots stored are of primary cells (51% of all samples stored) with tissue the second largest (16% of all samples stored) and whole blood the third largest (15% of all samples stored).

The smallest number of aliquots for any sample collection is currently sputum (0.2% of all samples stored). This is due to the fact that sputum is currently only being collected for the cystic fibrosis collection which has been in progress since the beginning of January 2020.

> “51% of all samples stored are primary cells”

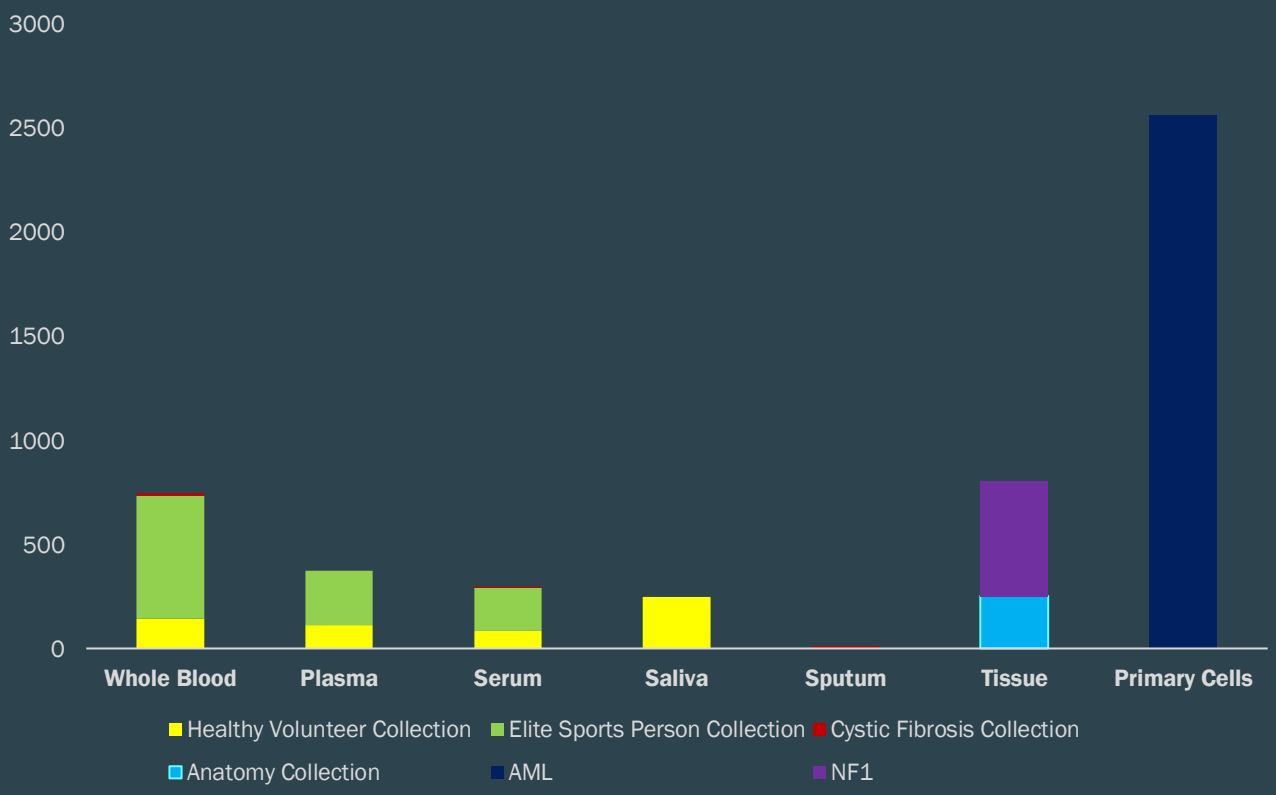


Figure 8 Number of aliquots stored by sample type and collection

Sample Application

Application process and turnaround times

CUB is currently accepting applications to access samples from academic institutions and commercial companies in the UK and abroad. CUB has a two-stage application process for access to fresh and stored samples. The first stage is a brief preliminary application to ensure the proposed project fits in with CUB's ethical approval. Once the preliminary application has been approved the applicant will be asked to complete a full application form.

Full applications are reviewed by the CUB scientific committee. This committee is independent of CUB and consists of lay, scientists, ethicists and clinicians. As part of our commitment to ISO 9001:2015 CUB's application target time is 30 working days. At present our average turnaround time for applications is 18 working days.

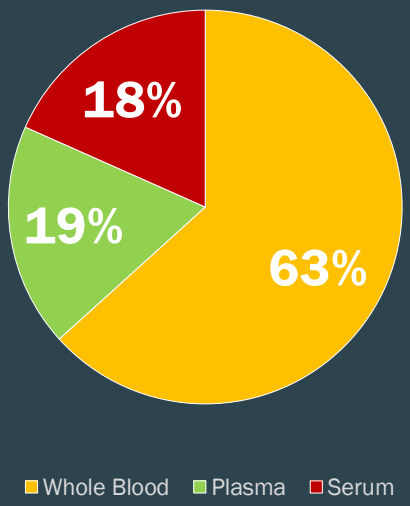
Applications and supply of biosamples

Since July 2018 CUB has received six applications to access fresh and stored samples. This low number of applications is due to the strategic focus on building collections and moving existing collections into CUB within the first years of operation. All applications received have been approved and the lay summary of each application can be seen in Appendix A.

> "CUB is currently accepting applications to access samples from academic institutions and commercial companies in the UK and abroad"

Sample Release

CUB has only released a small number of samples over the first 18 months of operation. Samples released to date have all been from the Healthy Volunteer Collection. 65% of samples released have been whole blood (see figure 9) and the majority of these have been released as fresh samples rather than from storage. Figure 10 shows the release of samples split by month. The release of samples was concentrated in the middle of 2019 with the highest number of samples released in May 2019. This is due to the release of samples from storage to an approved project.



> “65% of samples released have been whole blood”

Figure 9 Percentage of samples shipped by type

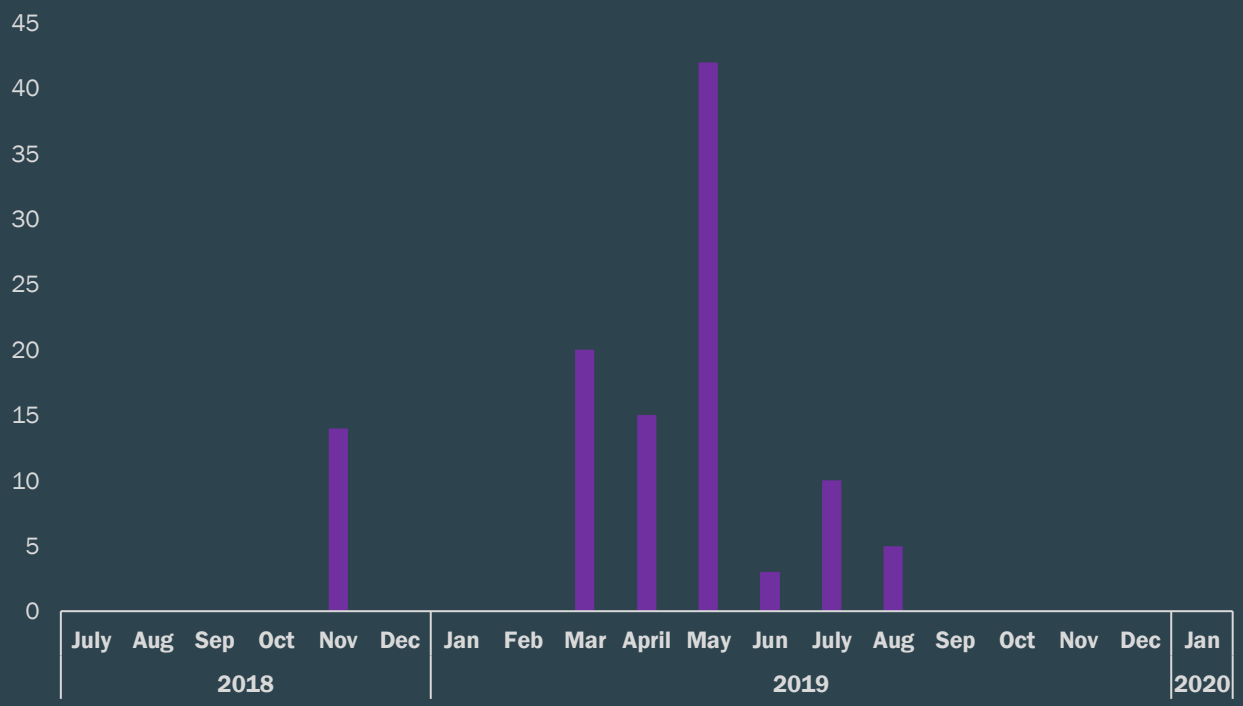


Figure 10 Number of samples shipped by month between July 2018 and January 2020

Donor Feedback

As part of our commitment to continual improvement the CUB proactively seek feedback from the healthy volunteer donors that visit the CUB facility. The CUB utilises an anonymous feedback survey to improve the experience of our donors. Donors are asked a number of questions about their donation experience (see figure 11) with 94% of donors stating they were very satisfied, 5% somewhat satisfied and 1% neither satisfied nor dissatisfied. There were no donors that were dissatisfied with their donation experience. 75% of donors when asked were extremely likely to visit CUB for further donations with 25% very likely to attend again (see figure 12).

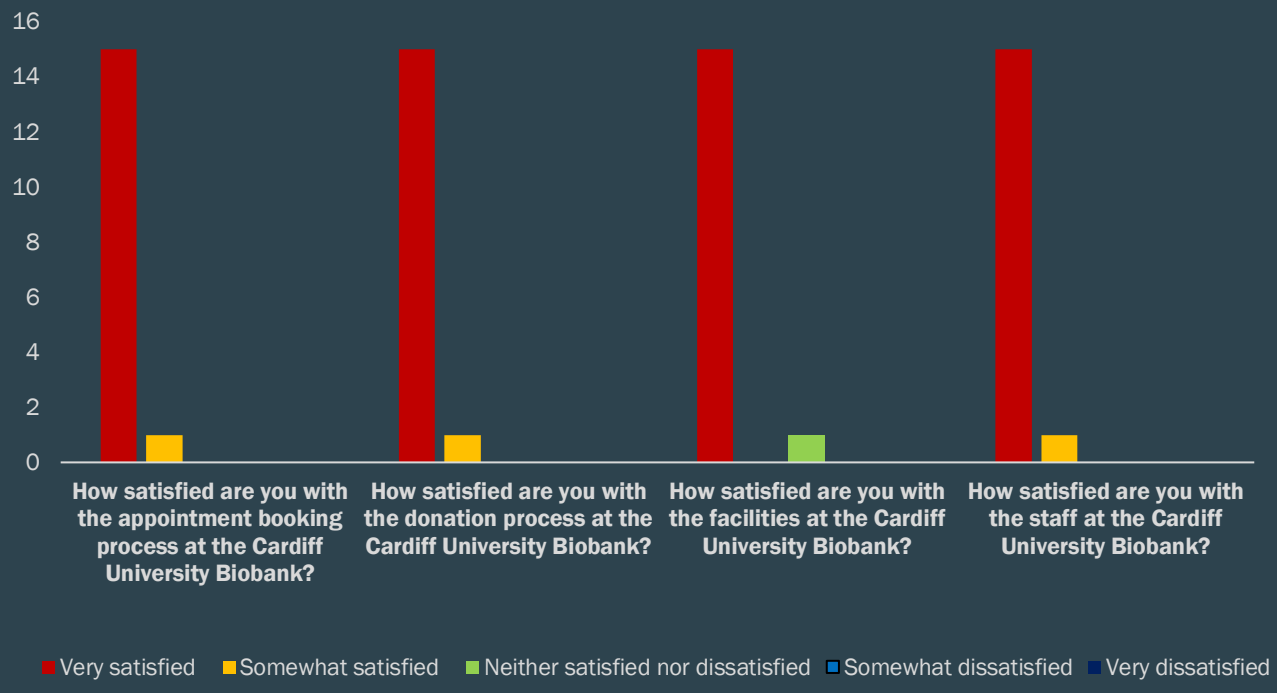


Figure 11 Donor Feedback Survey Responses

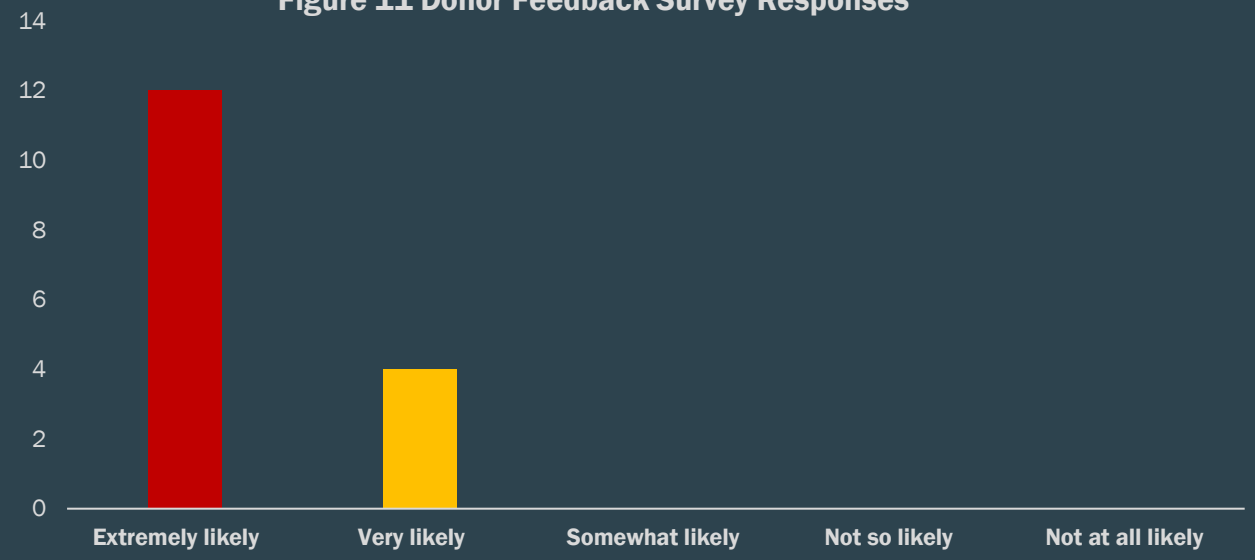


Figure 12 How likely would you be to visit the Cardiff University Biobank for further donations?

ISO 9001 and ISO 20387

ISO 9001:2015 is an internationally recognised quality management system (QMS) standard, with an estimate of over 1 million certificates issued in 178 countries. The ISO 9001 standard utilises a common, flexible structure that allows it to be adapted to a variety of industries and business requirements. There are many advantages of the standard including helping with process improvement, operational efficiency, training and competence, brand and reputation, internal auditing and risk management.

CUB recognised early that certification to the ISO 9001 standard will ensure customer satisfaction, reduced operating costs, improved stakeholder relationships, legal compliance, improved risk management, proven quality management credentials and the ability to conduct business commercially. In addition to the benefits listed the CUB also observed that certification to the international standard was uncommon within the UK biobanking environment and would act as a unique selling point.

In October 2018 the CUB completed a pre-assessment with the British Standards Institute which gave a positive recommendation to proceed to a formal assessment. In April 2019 after two successful stage 1 and 2 assessment audits the CUB was formally issued with certification to ISO 9001:2015.

In late 2018 the ISO 20387:2018 standard (general requirements for biobanking) was released providing the first internationally recognised framework for biobanking. Building upon the successful achievement of ISO 9001 certification the CUB will now aim to build upon its QMS and align with all aspects of the ISO 20387 standard. This will allow the CUB to standardise its processes against the international biobanking community whilst managing industry specific risk and maximising opportunity.

> “... the ISO 9001 standard will ensure customer satisfaction, reduced operating costs, improved stakeholder relationships, legal compliance, improved risk management, proven quality management credentials”

Quotations for Future Research

Since becoming operational CUB has been providing quotations for services for grant applications and project planning. Since July 2018 CUB has been consistently providing on average at least one quote per month (see figure 13) between July 2018 and Jan 2020. This level of quotation is both a positive indication in the interest of the CUB and of potential income in the future.

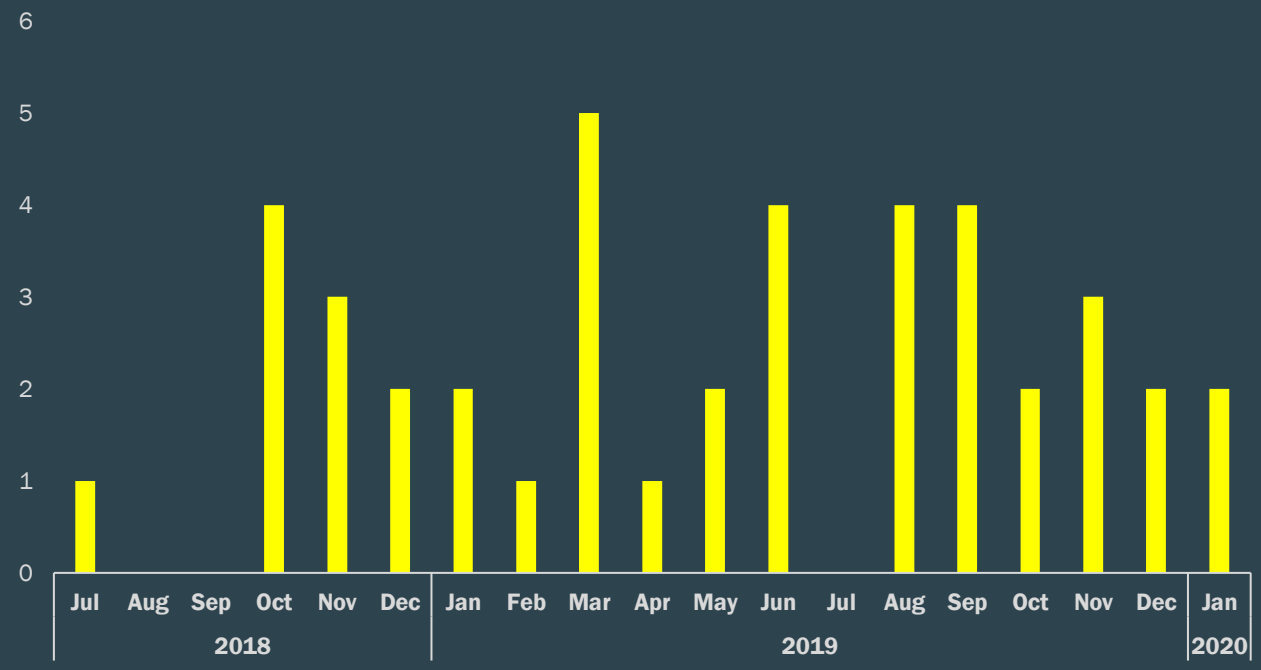


Figure 13 Quotations issued CUB between July 2018 and Jan 2020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and are interested in taking
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Communications

CUB utilises a number of communication methods in order to ensure that both internal and external users are provided with a regular update of CUB activity. The CUB has a dedicated website as well as an active social media account on Twitter. In addition, CUB also regularly releases an e-newsletter for researchers. In order to measure communication activity and impact CUB started to analyse website and basic social media data in August 2018. Figure 14 shows the average monthly users of the CUB website since August 2018.

Average of 121 website visits per month

Figure 14 Average monthly users of the CUB website

Communications

Since August 2018 CUB has continued to build its social media presence. In August 2018 CUB had 196 twitter followers which had doubled by July 2019 (see figure 15). In January 2020 CUB had 495 followers, which is on average an increase of 17 new twitter followers every month

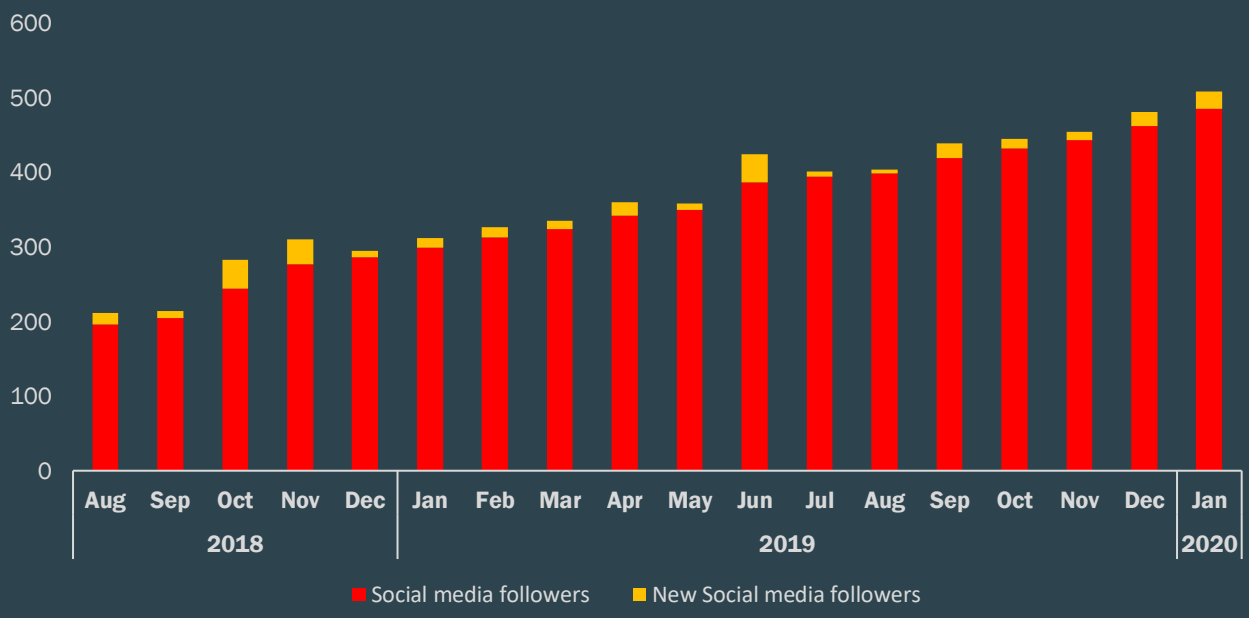

Figure 15 Number of total and new followers to CUB social media

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Appendix A

Lay summaries

Prof Aled Clayton, Cardiff University

Using surface acoustic waves to sort cancer cells and nanovesicles in blood; a potential tool for cancer diagnosis

This project is about making a small device (about the size of a postage stamp) that can be loaded with fresh patient's blood, and act as a gentle sieve. It will separate the complex assortment of different blood cell types, based on their different sizes and how easy they are to squeeze. It will use a special property of sound waves to force the cells to separate.

Whilst this is a useful tool for studying blood in general, we will apply it to an important area of medicine- to aid in the early detection of cancer. In many patients, cancer cells escape into the blood, and detecting and studying these blood borne cancer cells can give doctors useful information about the individual's disease. Our device is a way of achieving this, in a very simple, cheap way- which could even sit at the patient's bedside giving immediate information – without time consuming and complex laboratory analyses.

Support from CU Biobank, will provide healthy donor blood samples for us to test, and improve the device.

Prof Phil Stephens, Cardiff University

Effects of Oral Progenitor cells on Immune Cell Function

Researchers at the School of Dentistry, Cardiff university are interested in the biological function of inflammatory cells within the blood and how they can be manipulated during skin wound healing. Inflammatory cells help clean the wound space of debris, bacteria and viruses and any foreign cells. A type of inflammatory cell called a macrophage moves into the wound during healing and initially up-regulates the tissue repair process but then 'switches' and changes to a cell which dampens the wound healing response down. Typically, it is the first type of macrophage that causes the formation of skin scars whereas the second type reduces the amount of scar tissue. We know that stem cells are highly effective in controlling inflammatory cells. Hence, what we will investigate is whether stem cell secretions (from stem cells inside your mouth – where we know the wounds heal with no scarring) can drive production of more of the second type of macrophage and hence reduce scarring. This is part of our longer term objective to develop scar resolving/prevention therapies for patients suffering with this debilitating condition.

Dr Ryan Moseley, Cardiff University

Evaluation of the modulatory effects of plant-derived saps on neutrophil and macrophage responses associated with impaired healing, tropical ulcers

Chronic wounds, such as venous and diabetic ulcers, are becoming a significant problem for healthcare providers, especially with the increasing ageing population and number of people with diabetes worldwide. Described as skin wounds that don't heal, these represent major cause of pain and disability, especially amongst the aged. We know that the cells responsible for causing inflammation and fighting infection persist within chronic wounds, which means that the other events which help wounds to heal don't occur as they should. Therefore, by switching off these cells, we hopefully will allow wound healing to take place as normal. Our colleagues at the Royal Botanical Gardens Kew have collected a number of different plants from Papua New Guinea, where the natives use these plants to treat wounds similar to venous and diabetic ulcers, with good healing outcomes. Therefore, we wish to assess whether these plants have any anti-inflammatory effects on the cells responsible for causing inflammation and fighting infection in chronic wounds. In doing so, we hope to eventually develop these plant-derived chemicals as new therapies for the treatment of chronic wounds.

change during the progression of the disease. From here, these samples will undergo chemical analysis, looking at any changes that may occur to the mineral or organic content of the bone. These two forms of analysis will be compared to see if they can inform each other.

Dr James McLaren, Cardiff University

Profiling superantigen-induced immunosuppression of unconventional T cells during sepsis

The aim is to use the healthy blood samples to profile the biological mechanisms by which bacterial superantigens drive suppression in T cell populations, notably anti-microbial T cells, in in vitro assays. The logic is that this information will be correlated to what we see in patients with sepsis, notably those with confirmed S. aureus infections.

Dr Charlene Greenwood, Keele University

High Resolution Mapping of Osteoarthritic Tissue

Osteoarthritis (OA) is the most common musculoskeletal disease occurring in the UK, effecting approximately 8.75 million individuals [1]. There is currently no cure or preventative treatment for OA which often results in radical procedures such as total knee replacement; in the UK, 98% of total knee replacements were for OA [2].

The initiation and progression of osteoarthritis is not fully understood, preventing the development of effective diagnoses and therapies. The main radiographic characteristics of OA are loss of articular cartilage and disturbed bone growth, including the formation of osteophytes (bony spurs). Initially, the loss of cartilage was believed to be the initiating tissue of OA; however recently, researchers have turned their attention to the bone for further insights. This has led to conflicting research throughout animal and human studies [3–8]. With such variation in conclusions, - usually as a result of differing OA induction methods and animal models, there is a need to consolidate these within human tissue.

This work will focus on determining the morphological and physicochemical changes in knee and hip joints with OA. From here, using imaging techniques, the microarchitecture of osteoarthritic bone, including the osteophytes, will be examined to determine how it may change during the progression of the disease. From here, these samples will undergo chemical analysis, looking at any changes that may occur to the mineral or organic content of the bone. These two forms of analysis will be compared to see if they can inform each other.