QMB Abstracts

Q1: Novel thiomorpholino oligonucleotides (TMOs) as a robust next generation platform for spice switching antisense therapies.

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Synthetic nucleic acid therapeutics including antisense oligonucleotides (ASOs) and small interfering RNAs (siRNAs) continue to demonstrate their potential in RNA-targeting drug development, and several ASO drugs have been approved recently for clinical use. One successful ASO-based therapeutic approach is the modulation of splicing by targeting pre-messenger RNA (pre-mRNA) in the nucleus. Multiple FDA-approved ASO drugs use this strategy, including Exondys51, Vyondys53, Amondys45, and Viltepso to treat Duchenne muscular dystrophy (DMD); and Spinraza to treat spinal muscular atrophy (SMA). Phosphorodiamidate morpholino oligomer (PMO) chemistry currently utilized for DMD drugs has significant limitations as PMOs show rapid kidney clearance and poor cellular uptake that leads to high and costly dosages. Therefore, it is crucial to develop next-generation splice-switching oligonucleotide chemistries with improved efficacy, safety, and biodistribution.

We have recently developed and investigated the potential of novel thiomorpholino oligonucleotides (TMOs) to induce splice switching. We synthesized various TMOs and evaluated their efficacy to induce exon skipping in a Duchenne muscular dystrophy (DMD) *in vitro* model using H2K mdx mouse myotubes [1], and also, we have evaluated the efficacy in mdx mice *in vivo*. Our experiments demonstrated that TMOs can efficiently internalize and induce excellent exon 23 skipping potency compared with a conventional PMO control and other widely used charged nucleotide analogs. Based on the present study, we propose that TMOs represent a new, promising class of nucleic acid analogs for future RNA targeting oligonucleotide therapeutic development.

1. Le BT, Paul S, Jastrzebska K, Langer H, Caruthers MH, Veedu RN. *Thiomorpholino oligonucleotides as a robust class of next generation platforms for alternate mRNA splicing*, PNAS, 2022, 119, e2207956119

Q2: Circular RNAs drive oncogenic chromosomal translocations within the MLL recombinome in leukemia

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The first step of oncogenesis is the acquisition of a repertoire of genetic mutations to initiate and sustain the malignancy. An important example of this initiation phase in acute leukemias is the formation of a potent oncogene by chromosomal translocations between the mixed lineage leukemia (MLL) gene and one of 100 translocation partners, known as the MLL recombinome. Here, we show that circular RNAs (circRNAs)—a family of covalently closed, alternatively spliced RNA molecules—are enriched within the MLL recombinome and can bind DNA, forming circRNA:DNA hybrids (circR loops) at their cognate loci. These circR loops promote transcriptional pausing, proteasome inhibition, chromatin re-organization, and DNA breakage. Importantly, overexpressing circRNAs in mouse leukemia xenograft models results in co-localization of genomic loci, de novo generation of clinically relevant chromosomal translocations mimicking the MLL recombinome, and hastening of disease onset. Our findings provide fundamental insight into the acquisition of chromosomal translocations by endogenous RNA carcinogens in leukemia[1].

1. Conn, V.M. (2023). *Circular RNAs drive oncogenic chromosomal translocations within the MLL recombinome in leukemia*. Cancer Cell. May 16:S1535-6108(23)00169-1. doi: 10.1016/j.ccell.2023.05.002. Epub ahead of print. PMID: 37295428.

Q3: Therapeutic genome editing for severe monogenic skin conditions

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Introduction: CRISPR-based *ex vivo* gene therapy has emerged as a promising strategy for correcting patient-specific mutations to treat epidermolysis bullosa (EB). Recessive dystrophic EB (RDEB) is a devastating form of EB caused by biallelic, loss-of-function mutations in the *COL7A1* gene encoding type VII collagen (C7). As C7 is a critical component for adhesion between the dermal and epidermal skin layers, its reduction can lead to loss of skin integrity, blistering and other systemic complications. We have developed strategies that allow for precise correction of C7 mutations in patient derived skin cells. These strategies address the issues of historically low on-target editing efficiencies, off-target genotxocity and the lack of a suitable method to deliver gene-corrected cells to the patient which are currently hampering the field.
Methods: Primary RDEB keratinocytes and dermal fibroblasts from an individual with RDEB were electroporated with CRISPR editing components and subsequently analysed at the genomic DNA, mRNA and protein level. Gene repair and protein expression was detected in 50% of cells in a bulk cell population using a homology-directed repair (HDR) strategy, and in over 90% of cells using a non-homologous end joining (NHEJ) repair strategy. Unintended Cas9 editing at predicted off-target genomic sites was undetectable. CRISPR-edited cells were then used to engineer skin equivalents to assess skin integrity. Analysis of engineered skin equivalents confirmed restoration of functional C7 expression as demonstrated by its accurate deposition at the dermal-epidermal junction and the reversal of skin blistering *in vitro*.
Conclusion: CRISPR-based techniques were able to successfully correct mutations in *COL7A1* and restore skin integrity in engineered skin equivalents. We propose that these methods could be expanded to a wider range of EB causative mutations. Ultimately, we envision that engineered gene-edited, patient-specific skin sheets could be used to graft problematic areas of skin, providing significant benefit to the patient.

1. Stuffrein-Roberts, S., *Allelic expression patterns in psychatric candidate genes*. PhD Thesis in Pathology. 2008, University of Otago: Christchurch. p. 216.
2. Kikin, O., L. D'Antonio and P.S. Bagga (2006). *QGRS Mapper: a web-based server for predicting G-quadruplexes in nucleotide sequences*. Nucleic acids research. 34: W676-82.

Q4: The medicinal chemistry behind the discovery of Trofinetide/DAYBUE™, the first drug to treat Rett Syndrome

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Insulin-like growth factor (IGF-1) is a neurotrophic ("neuro nourish") factor located within the CNS in mammals that is responsible for growth and survival of neurons during development and maintaining adult neurons. In experimental animal models, IGF-1, produced endogenously in damaged regions of the brain, has potent anti-apoptotic effects on neurons and glial cells and is postulated to restrict progressive cell death. Much of the endogenous IGF-1 in the CNS is thought to be proteolytically cleaved into des-*N*(1-3)-IGF-1, a truncated IGF-1 comprised of 67 amino acids, and the *N*-terminal tripeptide Gly-Pro-Glu-OH (GPE). There is no direct evidence that GPE is naturally present or produced in the brain and although the mode of action of this tripeptide remains unknown, it has been reported that GPE inhibits glutamate binding to the N-methyl-D-aspartate (NMDA) receptors. GPE has been observed to act as a neuronal rescue factor following transient hypoxic-ischemic (HI, reduced blood/oxygen flow) brain injury for cerebral, cortical, striatal and hippocampal neurons.

The lecture will describe research undertaken with Neuren Pharmaceuticals (ASX) on the synthesis of peptide mimetics of GPE as a platform for the discovery and development of the drug candidate NNZ2566/trofinetide to treat Rett Syndrome. Neuren then partnered with Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) who conducted phase 3 clinical trials of trofinetide/NNZ2566 for Rett Syndrome. The U.S. Food and Drug Administration (FDA) recently approved DAYBUE™ (trofinetide) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older.[1] DAYBUE™ is the first and only drug approved for the treatment of Rett syndrome.

1. https://www.businesswire.com/news/home/20230303005382/en/Acadia-Pharmaceuticals-Announces-U.S.-FDA-Approval-of-DAYBUE™-trofinetide-for-the-Treatment-of-Rett-Syndrome-in-Adult-and-Pediatric-Patients-Two-Years-of-Age-and-Older

Q5: Peptides and peptidomimetics as a potential treatment for hard-to-treat polymicrobial infections

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The global spread of multidrug-resistant bacterial pathogens poses one of the greatest threats to human health. Antibiotics are arguably the most successful medicines, however, effective treatment of bacterial infectious disease is severely under threat due to antibiotic failure and a declining rate of new antibiotic discovery. In addition, many infectious diseases are found to be polymicrobial, meaning that two or more species of microbes occupy the same infection site and interact in a cooperative or competitive manner. One critical emerging problem in health care facilities are skin and soft tissue infections, which are among the most common infections in Aotearoa/New Zealand. Here we show how peptides and peptoids (peptidomimetics) enhanced the activity of antibiotics and could be used to treat bacterial biofilms and high-density skin infections caused by the multidrug resistant pathogens *Pseudomonas aeruginosa* and *Staphylococcus aureus*. We employed a subcutaneous abscess mouse model to demonstrate that peptides can be used to pharmacologically treat infections and to reduce the severity of skin abscesses. Adjuvant therapy with clinical antibiotics further reduced abscess lesions and bacterial loads. Peptoids are isomerically related to peptides with side chains appended to the amide backbone nitrogen rather than the α-carbon atom and are more appealing as therapeutics due to their decreased susceptibility to proteolysis and relatively lower synthesis costs. We revealed the anti-biofilm activity of several structurally-related peptoids to treat *P. aeruginosa* and *S. aureus* biofilms, individually (monomicrobial) and combined (polymicrobial), under host-mimicking conditions. Ultimately, using our new *Pseudomonas-Staphylococcus* co-infection skin abscess mouse model, we showed that under these challenging conditions, peptoids were able to reduce the severity of the co-infection. In conclusion, we show that peptides and peptidomimetics have the potential to broaden our limited antibiotic arsenal for extremely difficult-to-treat infections caused by multidrug resistant pathogenic bacteria.

Q6: Community conversations: *The Science of Medicines – Whakatere Waka*

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Accessible, relevant, and engaging information about medicines that is grounded in science, not mis- or disinformation, is imperative in supporting whānau to have confident conversations and make informed decisions about their use of medicines.

Framed by a waka and wayfinding analogy, the *Science of Medicines: Whakatere Waka* is a community engagement initiative in which we have collated and created a suite of hands-on and interactive displays, demonstrations, and activities through which young people and their whānau can journey into the science of medicines. Each paddle of our waka steers to a different part of this journey: discovering where medicines come from; creating medicines; exploring how medicines work to prevent or treat illness; protecting ourselves and our planet by using medicines safely; and putting our minds together to realise future potential and tackle current and future challenges related to medicines and health.

We have taken *Science of Medicines: Whakatere Waka* to settings of everyday life for communities throughout Aotearoa and the Pacific Islands. Travelling to schools, festivals, marae, and community hubs, we have engaged nearly 10,000 people over the last 2 years.

Met with a huge appetite for conversations about medicines, this work has highlighted the importance of kanohi-ki-te-kanohi (face-to-face) engagement and ongoing dialogue with our communities. This presentation will share details and experiences from the design and delivery of the *Science of Medicines: Whakatere Waka* initiative, with a view to considering the central importance of community engagement in the development of new therapeutics.

Q7: AI as a Partner in Science

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Science generally, and in the case of biology in particular, has sought to model ever more complex systems ever more precisely and accurately. Processing limitations of human individuals and human teams limit our ability to do this effectively. We are now seeing signs of genuine intellectual power in AI systems, along with some limitations that make current systems unreliable as partners in scientific teams. However, these limitations are not irreducible, and are far more subject to engineering correction that human cognitive limitations. In this talk, I'll describe some ways that near-future AI may help us greatly accelerate the work of science, and what is being done to get it to that state.

Q8: GWAS and beyond: towards 'omics based precision medicine discovery for Māori and Pacific people

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Precision medicine — medical care tailored to an individual (including their genetics) — is set to revolutionise healthcare. However, the genetic studies and databases driving these advances, lack Māori and Pacific individuals. This creates a massive inequity and threatens to exacerbate the health inequities these populations face in Aoteoroa. In our previous work we have used GWAS from European people to hone in on regions of the genome that associate with metabolic conditions in Māori and Pacific people. Due to the cost of sequencing we have been restricted to candidate gene approaches, focusing on a handful of protein-coding and copy number variants including a Mendelian effect variant within the lipid associated gene CETP. However, for polygenic metabolic conditions like type 2 diabetes, chronic kidney disease and gout, GWAS find that less than 10% of associated regions of the genome have causal mechanisms implicating a protein-coding variant. Instead, the majority of the polygenic associations are outside of the coding regions, in non-genic regions which are linked to the regulation of genes (enhancers). So while coding variants represent the 'low hanging fruit' of potential precision medicine targets, researchers and therapeutic companies are now turning their attention to the untapped potential of the non-coding genome for drug discovery. Large 'omics databases like GTEx make it possible to translate these non-coding regions into function however these datasets do not contain Māori and Pacific data. Therefore without equivalent datasets for Māori and Pacific people a "status quo" precision medicine approach will exacerbate health inequities in Aoteoroa. To prevent this, it is critical that genetic approaches to precision medicine are undertaken in Aotearoa for Aotearoa. Thus we are beginning to apply an 'omics strategy in collaboration with Variant Bio to discover clinically relevant Māori and Pacific genetics and functionally translate the non-coding genome.

Q9: Algorithms for evolutionary and systems biology

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Recent advances in computer science enabled algorithms that are capable of learning from large-scale data. Striking and surprising was the discovery of algorithms demonstrating superhuman abilities at tasks that traditionally have been believed to be beyond artificial intelligence. With early examples of this phenomenon coming primarily from games (Atari, Chess, Go), the protein structure prediction problem is a notable example from molecular biology. Importantly, all these algorithms are data-driven, that is, they learn from data directly with little to no prior knowledge about the problem. However, currently this approach is only possible in data-rich domains with very low error tolerance, making its applications in molecular biology challenging. As a result, the model-driven approach, with its high error tolerance and moderate data sizes, is currently the gold standard in biological data science.

In this talk, I will discuss these two algorithm design paradigms (data- and model-driven) in the context of evolutionary and systems biology. Specifically, I will demonstrate how choosing the right balance between the two can lead to more capable algorithms for reconstructing evolutionary dynamics of populations of cancer cells using spatial transcriptomics data, as well as mining for genetic interactions in genotype-phenotype data.

Q10: Utilisation of digital pathology and AI methods for the detection of MSI status in colorectal cancer

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The future of New Zealand cancer diagnostics will require innovative methods to meet increasing demands placed on it by an ageing population, the introduction of population-based screening programmes, and the requirement to reduce health inequities. Colorectal cancer (CRC) is a significant health problem in New Zealand with over 1200 deaths annually(1,2).

Microsatellite instability (MSI) involving a deficient DNA mismatch repair system is a recognized molecular pathway that describes a distinct biological type of CRC. MSI occurs in 10-20% of CRC with important clinical and surgical management implications. A patient's MSI or mismatch repair deficiency (dMMR) status is becoming increasingly important in the era of personalized medicine, as MSI/dMMR status appears predictive of immunotherapy response to immune checkpoint inhibitors. Due to clinical and hereditary implications and the opportunities to prevent CRC, universal screening for MSI/dMMR status in new CRC cases with no known family history is recommended.

Recent developments in the field of artificial intelligence (AI), have shown the ability to recognize tumour molecular subtypes and predict disease prognosis from analysing tissue histomorphology patterns.

We aim to utilise digital pathology and AI methods for the detection of MSI/dMMR status from whole-slide images of histological stained colorectal cancer cases. Whole-slide FFPE images of colorectal cancer cases (n=461) with MSI status information were downloaded from The Cancer Genome Atlas (TCGA). These cases were randomly split, 70:30 ratio, into a training and test dataset. A machine learning algorithm using a deep learning convolutional neural network (Resnet) was developed using transfer learning methods to predict MSI status. Preliminary results from training (AUROC=0.71) showed the potential to detect MSI status. This algorithm will be tested on an external independent dataset of New Zealand colorectal patients (n=250) obtained from He Taonga Tapu-Cancer Society Tissue Bank to determine AI algorithm performance and translatability to a New Zealand population.

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.

2. New Zealand Ministry of Health. Cancer : New registrations and deaths 2013. 2016. 19–93 p.

Q11: Residual Graph Attention Networks for Molecular Property Prediction

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Molecular property prediction plays a vital role in the process of discovering new drugs. Numerous computational methods have been proposed to predict various molecular properties. Although recent approaches have shown promising results in this task, it remains challenging and requires considerable time and effort. In addition to traditional machine learning and deep learning models that operate on regular data, several deep learning architectures have been introduced to handle graph-structured data and overcome the limitations of conventional methods. Utilising graph-structured data in modelling presents an alternative approach to effectively extracting relevant features, particularly when considering connectivity information.

In this study, we present ResGAT, a deep learning architecture specifically designed for molecular graph-structured data. ResGAT can be employed for both regression and classification problems and offers a flexible and customizable design to accommodate different types of data. Our implemented models using ResGAT demonstrate competitive performance compared to state-of-the-art architectures. To assess the reliability of ResGAT, we conducted experiments under two different data sampling conditions, and the results confirmed its robustness. Furthermore, we evaluated the stability of the models by repeating the experiments multiple times to quantify the variation in prediction efficiency.

Q12: Pseudouridine guides germline small RNA transport and epigenetic inheritance

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Chromosome dosage has substantial effects on reproductive isolation and speciation in plants and animals. The triploid block is a hybridization barrier between diploid seed parents and tetraploid pollen parents, in which the hybrid endosperm aborts in triploid seed. It was discovered at Cold Spring Harbor Laboratory in the 1920s by Albert Blakeslee, and is conserved in flowering plants. We speculated that small RNA in pollen could monitor chromosome dosage, as they depended on transposable elements repeated on every chromosome. Epigenetically activated "easiRNA" in pollen are transported from the vegetative nucleus to the sperm cells, and depend on the plant specific RNA Polymerase IV (Pol IV) and on the pollen specific miR845, that targets the primer binding site of LTR retrotransposons. We found that Pol IV-dependent easiRNAs mediate the triploid block, and target transposons near imprinted genes. Argonautes interact with Nuclear Histone-like Protein-2 (NHP-2) of the highly conserved Dyskerin complex required for pseudouridylation of rRNA, snRNA, and other non-coding and mRNA. We therefore developed three novel techniques to detect pseudouridine (Ψ) in short RNA sequences, demonstrating its presence in a handful of mouse and *Arabidopsis* microRNAs and their precursors. Much more substantial pseudouridylation was found in easiRNAs in pollen, and piRNAs in mouse testis. In pollen, pseudouridylated easiRNAs were enriched in sperm cells, and we found that *PAUSED/HEN5 (PSD)*, the plant homolog of Exportin-t, interacted genetically with Ψ and was required for transport of easiRNAs into sperm cells. We further showed that Exportin-t was required in individual pollen grains for the triploid block. *paused* and *hasty* had previously been identified as mutants in genetic screens for phenotypes associated with RNAi, and *HASTY* (which encodes Exportin-5) is required for systemic transport of artificial miRNA. In our study, small RNA sequencing from sperm cells were consistent with a model in which pseudouridylated miRNA and siRNA preferentially require *PSD*, while other miRNA use *HST* for transport between the vegetative nucleus and the sperm cells. miR159 is inherited in the endosperm and is heavily pseudouridylated in pollen, consistent with these results. Thus, Ψ has a conserved role in marking inherited small RNAs in the germline, which may help distinguish "self" from "non-self" small RNA derived from viruses.

Q13: Using natural transposon compliments in plant genomes to manipulate gene function

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Transposons are mobile genetic elements ubiquitous to the genomes of all of Life. Their presence and activity have greatly contributed to the size and complexity of Eukaryote genomes. While their biology, unchecked, is highly mutagenic, their involvement in a wide range of key phenotypes in plants, such as vernalisation, apomixis, sexual determination, and pigmentation, but to name a few, hints at possibilities for their use to generate valuable new phenotypic variation in ways not easily achievable with current technologies.

Our programme has focused on determining the conditions under which natural compliments of transposons can become active and the genomic and epi-genomic consequences of this activity on the host plant. We have been working in Grapevine, Nicotiana, Capsicum, Piosella (Mendel's Hawkweed) and Hop genomes to determine means to heighten natural transposon mobility levels, the genomic contexts of active transposon compliments and the role and identify of novel transposons in apomixis and sexual identity in Piosella and Hops respectively.

We have identified that only a very small number of families and loci where they are located, are currently active in all of the genomes we have studied. Moreover, we have identified species within the Nicotiana and Capsicum group that show very recent bursts (< 7000 years) of GYPSY and COPIA mobility respectively and that a previously uncharacterised family of type I DNA transposons appear to be responsible for the acquisition of apomixis in Piosella. In this presentation I will highlight our current ongoing work in grapevine to produce a population of vines with novel retrotransposon insertions, our efforts to identify the genomic contexts of recently mobile GYPSY and COPIA transposons in Nicotiana benthamiana and Capsicum species and the role of transposons in the acquisition of apomixis and sexual determination in plants.

Q14: Double-stranded RNA targeting putative pathogenicity determinants for control of the invasive basidiomycete *Austropuccinia psidii*

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Austropuccinia psidii, the causal agent of myrtle rust disease, must infect and manipulate living host plants to complete its infection cycle. The genome of the 'pandemic' biotype of *A. psidii,* which infects over 480 different plant species, has been sequenced and phased. Similar to other obligate biotrophic pathogens, the *A. psidii* genome contains a suite of effector genes: in this species, almost 370 sequences representing approximately 2% of the total predicted genes. Effector proteins are relatively small (c. 20 kDa) and contribute to the pathogen's manipulation of the host cell, including suppression of pathogen recognition and defence mechanisms. Double-stranded RNA targeting essential *A. psidii* genes, has been demonstrated to significantly reduce/stop *A. psidii* infection of host plants when co-applied topically with urediniospores[1]. To investigate how this pathogen manipulates and colonises its hosts, we have collected and analysed pathogen and host RNA transcripts from infected mānuka (*Leptospermum scoparium)* plants in time-course experiments. These plants have pre-determined resistance phenotypes to infection[2]. Numerous differentially expressed potential pathogenicity determinants have been identified from these experiments, as well as a range of differentially expressed plant transcripts as the host responds to the fungal challenge. The pathogen transcripts included putative effectors as well as putative 'cellulase' (plant cell wall-degrading) enzymes. Some of these pathogenicity determinants have been found in RNA samples taken 20 minutes after inoculation, suggesting the encoded proteins are essential in the initial phase of colonising the host plant. Progress on initial RNA interference experiments targeting the pathogens effector transcripts will be presented.

1 Degnan RM, et al. (2023). *Exogenous double-stranded RNA inhibits the infection physiology of rust fungi to reduce symptoms in planta.* Molecular Plant Pathology, 24:191-207.

2 Smith GR, et al. (2020). *Resistance of New Zealand provenance Leptospermum scoparium, Kunzea robusta, Kunzea linearis, and Metrosideros excelsa to Austropuccinia psidii.* Plant Disease, 104(6):1771-1780.

Q15: Insect Odorant Receptor Biosensors for non-invasive disease detection

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Infectious disease detection is still a largely lab bound process requiring expensive, complex and slow tools, commonly relying on sampling nucleic acids and proteins. These challenges mean that diagnostics are often unavailable in the countries with the highest disease burden and can't be effectively used to reduce transmission. Animals such as dogs, rats, and bees can be trained to use their sense of smell to detect disease (e.g., cancer, TB, COVID-19) rapidly, at high sensitivity and with high accuracy. This implies infected individuals can be identified non-invasively by volatile organic compound (VOC) signatures. However, animals are not scalable as they are expensive to train and difficult to incorporate in clinical diagnosis.

We have recently received funding from the Bill & Melinda Gates foundation to pursue the development of novel biosensors which utilise insect olfactory receptors (ORs) to detect the VOC signatures of disease states (TB, Malaria, COVID). This biomimicry approach offers the potential for a highly sensitive universal screen that could be used at any point of care. We need to develop a robust understanding of how ORs detect volatile compounds that serve as signatures or markers of global health disease states to enable the development of new diagnostics.

The core of our technology is the ability to recombinantly produce functional insect ORs and couple them to sensor technologies. To date we have successfully cloned 50 receptors from multiple insect species and functionally validated them on five different platforms. Based on these data we have developed algorithms to design receptor arrays, which will allow us to detect VOC signatures using a combinatorial approach. We will discuss our strategy and initial data for the detection of biomarkers associated with TB. The ability to rapidly detect and definitively diagnose TB will provide significant improvements to mortality globally and slow/reduce antibiotic resistance.

Q16: PRODUCTION OF HIGH VALUE BIOLOGICS USING PLANTS

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The production of high-value antibodies and proteins using plant-based systems has emerged as a revolutionary approach in biopharmaceutical manufacturing. Helico Bio, a pioneering biotechnology platform, presents an innovative solution to meet the growing demand for cost-effective and scalable production of biologics. Leveraging transgenic green-leaf plants as versatile bioreactors, we have harnessed the inherent potential of plants to serve as efficient factories for therapeutic proteins.

Our research showcases the successful engineering of specific host plants to produce a diverse array of high-value antibodies and proteins, offering an attractive alternative to traditional production methods. Through a combination of advanced computational modelling and plant transformation techniques, we achieve remarkable expression yields with minimal waste, contributing to the sustainability of the process.

Furthermore, we present our proprietary technology's applicability in producing complex biopharmaceuticals, including monoclonal antibodies and other bioactive molecules. Our results demonstrate the potential of plant-based systems to revolutionize biologics manufacturing, providing a scalable and economically viable platform that addresses the challenges of cost, scalability, and sustainability faced by the industry.

Q17: Breeding technologies for delivering crops for the future

Baldwin, Samantha, and the Hua Ki Te Ao Horticulture Goes Urban Direction team, The New Zealand Institute for Plant and Food Research Limited

Our rapidly changing environment, increasing human population size and finite resources, dictate that we need to produce more food with increasingly restricted resources. One potential mitigation strategy is genetic improvement of current or future crop species to become more sustainable, fit future growing systems, and meet a range of nutritional needs. At Plant & Food Research we recognise that a future growing system could include indoor growing of perennial fruits and vines close to consumption. This will require rapid re-domestication of crops targeting traits such as altered plant architecture, flowering, pollination and fruit maturity, that enable more compact production both in space and time than is currently achievable outdoors. Unlike leafy greens, that are more readily grown in vertical farms, perennial crops have unique opportunities and challenges that will require greater integration of knowledge from across different species and a toolbox of genetic technologies to be available. Examples of the knowledge required and technologies being developed or implemented will be discussed.

Q18: Flowering time control for forage and food: Gene editing of *SOC1* genes in the reference legume Medicago abolishes flowering

Putterill, J.[1], Peng, Y.[1,2], Poulet, A.[3] , Zhao, M[1,2], Jaudal, M.[1,2], Tham, F.[1], Zhang, L.[1]

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The ability to flower at optimal times is a crucial trait in plant adaptation and crop productivity. Thus, genetic variants with altered flowering time were key to expansion of the geographical range of important crops such as soybean and rice. Deliberate environmental or genetic interventions can also be used to modify flowering time; to shorten the time to flowering for plant breeding, induce flowering eg. for important dates of the year, or to avoid heat waves or drought, minimise the effects of warm winters, or conversely to delay it for greater vegetative yield for forage or biofuels. A recent study will be presented. The reference temperate legume *Medicago truncatula*, related to the important forage alfalfa, is induced to flower by vernalization (extended cold) followed by warm long spring days. However, it lacks the key genes *FLC* and *CO* that regulate these processes in Arabidopsis. Despite this, Medicago possesses homologs of an important target of these regulators, called *SOC1*. Comparing and contrasting with Arabidopsis and soybean, work will be presented on RNA-seq and CRISPR-Cas9 gene editing directed towards functional analysis of three duplicated *MtSOC1s.* This revealed their roles in architecture and flowering, including via an unexpected non-flowering phenotype in triple mutants. The implication of our study is that the three *MtSOC1s* play an overlapping role in Medicago growth and flowering; sharing some functionality with Arabidopsis *SOC1*, but also divergent functions that together are critical for the transition to flowering in Medicago and indicate possible applications in forage production.

Early Career Researcher Talks

Broad-spectrum antiviral potential of PI3K inhibitors

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[2]Maurice Wilkins Centre for Molecular Biodiscovery, NZ,

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The phosphatidylinositol-3-kinase (PI3K) signaling pathway is central to many cellular functions including cell growth, survival, metabolism and the antiviral immune response. Persistent activation of the PI3K pathway has been linked to cancer, and several PI3K inhibitors have been successfully developed as anti-cancer therapies. Viruses are obligate parasites that have co-evolved with their hosts to hijack many cellular pathways including PI3K to support the viral lifecycle and to evade immune clearance. Some PI3K inhibitors have published antiviral activities against several viruses including Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which caused the COVID-19 pandemic. In this study, we examined the potential to repurpose a selection of PI3K inhibitors already in various stages of development at the Auckland Cancer Society Research Centre (ACSRC) to reveal antiviral activities. Eight PI3K inhibitors were examined in vitro for antiviral efficacy against human betacoronavirus OC43 (causes the common cold), four variants of SARS-CoV2 as well as influenza A virus and herpes simplex virus using plaque reduction and foci forming assays. Two of the eight compounds demonstrated low micromolar potency against all the viruses examined, demonstrating broad-spectrum antiviral activities across three unrelated viral families. When examined in combination studies with clinically approved SARS-CoV-2 antivirals Remdesivir and Nirmatrelvir (Paxlovid) against the Omicron variant, one lead compound showed strong drug synergy with both approved antivirals, allowing significant dose reductions to achieve the same antiviral effects, which reduces risks of side effects and prevents antiviral resistance arising over time. This study demonstrates the therapeutic potential of repurposing PI3K inhibitors for treating viral infections, which could offer a broad-spectrum antiviral solution for viral threats such as SARS-CoV-2 as well as novel or re-emerging viral pathogens.

Faecal Microbiota Transplant-mediated alteration of the phageome composition in a clinical trial for obesity

Zuppi, M.[1], Vatanen, T[1,2], Wilson, B.C.[1], Golovina, E.[1], Cutfield, W.S.[1], Vickers, M.H[1], O'Sullivan, J.M.[1]

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Faecal microbiome transplant (FMT) is a medical procedure used to treat diseases associated with the gut microbiome. FMT aims at altering the gastrointestinal environment of its recipients through the introduction of donor faecal microbiome. Gastrointestinal phages are implicated with human health and successful engraftment of donor phages has been correlated with FMT treatment efficacy. Phages can impact the environment they inhabit by modulating bacterial communities, either through predation or by enhancing their fitness. These interactions can be described through population dynamics. In this study, we have investigated the effects of FMT on the phageome composition of participants within the Gut Bugs Trial (GBT), a placebo control clinical trial that investigated the efficacy of FMT in the treatment of adolescent obesity-related symptoms. Stool samples in the GBT were collected at baseline (prior to the transplant) and up to six months after the transplant (*i.e.,* 6 weeks, 12 weeks, and 26 weeks). Microbial DNA was sequenced using Illumina technology, and phage sequences were identified and characterised *in silico*. Donor phages engrafted stably in recipients following the FMT, and remained identifiable for the study time course. Phage engraftment was donor specific, and engraftment efficacy was positively correlated with donor phageome diversity. Engraftment of donor phages increased the abundance of temperate phages within FMT recipients and their phageome variability and diversity. An increase in variability and diversity was also observed in the bacteriome [1], suggesting that FMT altered microbial dynamics. Overall, FMT proved effective in modulating the gastrointestinal environment of the obese adolescents that participated in the Gut Bugs Trial, by altering their phageome composition in a donor-specific manner and by promoting shifts in microbial dynamics.

1. Wilson, B.C., Vatanen, T., Jayasinghe, T.N. et al. (2021). *Strain engraftment competition and functional augmentation in a multi-donor fecal microbiota transplantation trial for obesity*. Microbiome 9, 107.

Bioprinting Spheroid-Based 3D In Vitro Disease Models: Screening PatientSpecific Tissue in Healthy and Osteoarthritic Microenvironments

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Patient diversity and limited lateral integration with host cartilage are often overlooked in cartilage tissue engineering (TE) strategies. In this study, we aim to enhance the clinical translatability of TE strategies by screening the patient population, and by probing lateral integration between cartilage spheroids utilising a 3D disease model. Cartilage spheroids were fabricated via high-throughput centrifugation of human articular chondrocytes (hACs). Donor diversity was identified by screening the chondrogenic differentiation capacity of 14 Aotearoa chondrocyte donors with distinct donor demographics (ethnicity, age, sex). To evaluate lateral integration, two cartilage spheroids (healthy/diseased/TE) were

bio-assembled adjacently in 3D-printed thermoplastic cages (1x3x1mm)1 . Diseased spheroids were created by exposing healthy tissues to inflammatory cytokines (TNF-α/IL-1β). TE cartilage spheroids were generated by encapsulating clinically relevant cells in biomaterials. After 14 days (of fusion), tissue formation within the spheroids and at the tissue-tissue interface was characterised (GAG,DNA,Safranin-O,IHC:Col I/II). Single- and multi-demographic analysis revealed that ethnicity, sex and age impact chondrogenic differentiation capacity of chondrocytes, causing demographic-dependent potential for cell-based cartilage repair strategies. TE cartilage spheroids have shown potential to enhance lateral integration by inducing multi-directional cellular migration which supports hyaline cartilage tissue formation at the tissue-tissue interface1 . Diseased cartilage spheroids were successfully developed ranging from mild to severe changes in the cartilage matrix. Lateral integration was significantly impacted in diseased microenvironments, evident by reduced tissue fusion and lack of hyaline cartilage tissue formation at the tissue-tissue interface. The disease model allows us to systematically screen the potential of biomaterials on tissue integration in health and disease, ideally with patient-specific cells. Ultimately, repair capacity and lateral integration of novel TE constructs can be personalised, screened, and optimised prior to (pre)clinical studies.

1. Veenendaal, L. et al (2022). 3D-bioassembly of VH-Spheroids for Cartilage Regeneration: in Vitro Evaluation of Chondrogenesis, Fusion and Lateral Integration. Advanced Materials Interfaces, 9(31), 2200882

Identification of lncRNAs as potential novel therapeutic targets in triple negative breast cancer

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Triple negative breast cancer (TNBC) treatment lacks targeted therapies. Recently, our laboratory and others described long non-coding RNAs (lncRNAs) as new drivers of TNBC progression, which represent an exciting new avenue for its treatment. LncRNAs are the most versatile and diverse class of non-coding RNAs with roles in the progression of TNBC development, including cell proliferation, development, differentiation, apoptosis, metastasis and drug resistance. LncRNAs have greater tissue-specific expression compared to proteins and can be targeted using nucleotide sequence specific RNA therapeutics, leading to reduced systemic toxicities when used as a cancer target. Using a combined approach of computational analysis of patient RNA-sequencing data and CRISPR functional screening, we identified hundreds of lncRNAs as novel drivers of TNBC. We prioritized one lncRNA target (*lncTNBC3*) with high clinical translational potential, where expression correlated with patient outcomes. Effects of *lncTNBC3* knockdown were tested using CRISPR systems and anti-sense oligonucleotides. Both forms of knockdown reduced the proliferation potential of cells. In order to gain an insight into the mechanism via which *lncTNBC3* functions, RNA sequencing was carried out on CRISPR- and ASO-treated cells, revealing that *lncTNBC3* functions in the cell cycle and DNA repair pathways. Cell cycle analysis revealed a ~20% increase in G2/M cell cycle arrest in CRISPR-treated cells. In conclusion, we have identified a promising novel lncRNA target with a role in stimulating proliferation of TNBC cells which correlates with TNBC patient survival.

A novel amyloid formation mechanism: oxidation-induced transition of the tumour suppressor protein p16 into amyloid fibrils

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Amyloids are protein structures associated with disease as well as diverse biological functions. These large, fibril-like structures are characterized by cross-beta sheet motifs and are stabilized by numerous hydrogen bonds. Typically, protein amyloids form spontaneously and the onset of this structural conversion is poorly understood. We recently discovered that the tumour suppressor protein p16 can fold into amyloid fibrils (1). In strong contrast, the amyloid formation of p16 is sparked by an oxidation event and such a mechanism has not been described earlier.

Intriguingly, the transition of p16 into amyloid is also accompanied by a major change in function. The monomeric, unoxidized p16 blocks cyclin-dependent kinases, thereby suppressing tumour formation, but we found that the oxidized amyloid conformation is unable to inhibit these kinases. We are currently studying the molecular characteristics of this transition and we observed that the transition into amyloid is reversible upon reduction of the disulfide bond. This suggests regulatory and functional control over this kinase inhibitor by redox processes.

We are further studying the oxidation-induced amyloid transition on the cellular level. We find that relatively low levels of oxidants convert the protein into the amyloid state and experiments with fluorescence-labelled protein show a rapid relocalisation into specific cellular compartments. When testing different biological oxidants for their potential to convert p16 into amyloid, we find that peroxymonocarbonate and hypothiocyanous acid are amongst the most efficient.

We present a novel mechanism of protein regulation where specific oxidation events lead to a dramatic functional and structural change. We anticipate that this mechanism may occur with other proteins beyond CDK inhibitors.

1. Göbl, C., Morris, V. K., van Dam, L., Visscher, M., Polderman, P. E., Hartlmüller, C., Dansen, T. B. (2020). *Cysteine oxidation triggers amyloid fibril formation of the tumor suppressor p16^{INK4A}.* Redox Biology, 28, 101316. doi: 10.1016/j.redox.2019.101316

Q19: Biofabrication Strategies for the Generation of Bone Tissue Interfaces

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Critical size bone tissue defects can have severe implications on patient health.[1] These defects are accompanied by damage to surrounding tissues, including periosteum, cartilage, ligament, or tendon. Clinical strategies for bone defect repair utilize autografts, but these methods are limited by donor site morbidity, lack of availability, and considerable medical costs. Tissue engineering (TE) strategies aim to provide a regenerative alternative by combining scaffolds, cells, and bioactive signals. Extrusion bioprinting allows for superior control over design of these three critical components and is particularly useful in the case of replicating heterogeneous bone tissue interfaces.[2] We have investigated several biofabrication strategies to generate heterogenous bone tissue interfaces, including (1) computational modeling to understand the effect of material patterning ratios on scaffold mechanics (2) multi- material printing for interfacial tissues, and (3) 4D printing to generate microscale tissues along with macroscale tissue counterparts.

A 3D stationary solid mechanics model was developed in COMSOL to recapitulate the osteochondral unit using a mechanically interlocking design. The model was used to simulate the effects print patterns on the mechanics of the scaffold under lateral shear, which was validated with in vitro experimentation.[3] For the development of the 4D printing strategy, charge interactions between anionic gelatin methacrylate and cationic poly-L-lysine (PLL) were harnessed to induce a “shrinking” effect- effectively enhancing the resolution of extrusion printed structures.[4] The effects of molecular weight, concentration, and incubation time of the PLL on printed sample dimensions, material properties, and cytocompatibility were investigated.

COMSOL modeling suggested that interlocking interfaces patterns can redirect shear stress from a single tissue throughout the entire tissue interface. Extrusion printing generated complex, heterogeneous tissue interfaces and 4D printing strategies enhanced resolution of these structures. These studies indicate that pre and post fabrication approaches produce bone tissue interface scaffolds with optimal mechanics and biological properties.

1. Cooper, G.M., et al. (2010) *Testing the critical size in calvarial bone defects: revisiting the concept of a critical-size defect.* Plast Reconstr Surg. 125(6):1685-1692.
2. Murphy SV, and Atala A. (2014) *3D bioprinting of tissues and organs*. Nat Biotechnol. 32(8):773-85.
3. Choe, R., et al. (2022) *Computational investigation of interface printing patterns within 3D printed multilayered scaffolds for osteochondral tissue engineering.* Biofabrication. 14:025015.
4. Gong, J. et al. (2020) *Complexation-induced resolution enhancement of 3D-printed hydrogel constructs.* Nat Commun. 11:1267.

Q20: Digital Twins in Critical Care: Current State-of-the-Art and Future Potential

Chase, J.G.[1], Zhou, C.[1], Knopp, J.L.[1], Holder-Pearson, L.R.[1], Murphy, L.[1], Moeller, K.[2], Desaive, T.[3], Benyo, B.[4], Chiew, Y.S.[4], Näswall, K.[1], Malinen, S.[1], Wong, J.H.K.[1], Shaw, G.M.[6]

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[6]Dept of Intensive Care, Christchurch Hospital, Christchurch, NZ.

Healthcare is facing a devastating tsunami of rising demand multiplied by increasing chronic disease and aging demographics, which is unmatched by society's ability to pay. Intensive care unit (ICU) medicine in particular is under assault from the twin forces of aging demographics and epidemically increasing chronic disease. There is no means to meet growing demand without a significant change in productivity or raising significant new revenue to support the current economic model of care.

Digital technologies and automation brought significant productivity gains to many industries, and manufacturing in particular, but not to medicine. In manufacturing, digital twins, model-based optimisation of manufacturing systems, are a rapidly growing means of enhancing productivity and quality. This concept intersects well with the model-based decision support and control beginning to emerge in clinical use, which, in turn converges with emerging digital health data initiatives. Together there is the potential to create semi- to full- automation of core elements of ICU care with today's technology.

Automation using validated, in silico digital twin models offers the opportunity to personalise care, and improve its quality and productivity to meet growing demand. It is thus the opportunity to realise significant productivity gains, without reducing quality of care, as well as the opportunity to bring the gains seen in so many other industries into medicine.

This presentation covers digital twins from the perspective of a manufacturing concept translated into clinical care. It is based on our team's development, validation, and clinical implementation of digital twin models as standards of care. More specifically, it identifies the key elements required to implement digital-twin-based automation, and presents the state-of-the-art in the digital twin models and internet-of-things (IoT) technologies required to create a vision of an automated ICU bed space for core care in glycemic control, mechanical ventilation, and cardiovascular management.

Q21: Efforts to improve reproducibility and reusability in physiological models and measurements

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A scientific understanding of our world relies on the application of systematic methodology based on evidence. Scientific methodology includes objective measurements, testable hypotheses, and reproducibility. Traditional approaches to convey our scientific understanding include peer-reviewed publication in journals and presentation in meetings. However, such approaches are not without shortcomings. For example, very few physiological models are reproducible, being published with errors in their description, incomplete information, and results that are inconsistent with the accompanying mathematics. This presentation will discuss some recent efforts to improve reproducibility in physiological models and measurements[1,2] by making them more findable, accessible, interoperable, and reusable[3].

1. Physiome repository 2. Physiome journal 3. Wilkinson, M., Dumontier, M., Aalbersberg, I. et al. *The FAIR Guiding Principles for scientific data management and stewardship.* Scientific Data 3, 160018 (2016). https://doi.org/10.1038/sdata.2016.18

Q22: Concept to Clinic: Translating Biomaterials into Medical Devices

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Essential attributes, in particular physical, mechanical and biological functionalities that adapts to create smart biomaterials and devices in developing product/technology for healthcare applications will feature in this presentation. I shall also discuss a novel synthesis and reconstituted process that evidences green and sustainable methods that we have developed to create smart biomaterials and devices consisting of functional polymers and biopolymers. Fundamental understanding of the structural details at micro-/nanoscale levels, functions and properties of biomaterials. The applied research includes the reconstitution or fabrication of biomaterials into devices and their desired characteristic properties that exhibited remarkable performance toward medical and healthcare applications. However, there are major challenges (e.g. technological viability, ethical, and regulatory) when translating this into real products/technology (e.g. medical devices) on the way to market.
In this presentation, I shall try to highlight and share a number of specific devices assigning their fundamental and applied studies outputs or outcomes that were developed by my research team, and the challenges that we encountered during this translation process. Critical challenges in designing and/or developing devices associated with cost, documentation (including regulatory) pathways and end-user applications will also be emphasised.

1. Rajabi, m., McConnell, m., Cabral, J., Ali, M.A. (2023). *Chitosan hydrogels in 3D printing for biomedical applications, Carbohydrate Polymers*, Journal of Biomedical Materials Research Part A. p. 1-14.

2. Ghosh, A., Ali, M. A., Selvanesan, L., Dias, G.J. (2010). *Structure–function characteristics of the biomaterials based on milk-derived proteins.* International journal of biological macromolecules. 46(4). p. 404.

3. Shavandi, A., Bekhit, A. El-Din. A, Sun, Z., Gould, M., Ali, M.A. (2015). *A novel squid pen chitosan/hydroxyapatite/β-tricalcium phosphate composite for bone tissue engineering.* Materials Sci. &Eng. C: 55. p.373.

4. Kelly, R.J., Sigurjonsson, G.F., Marsh, C., Smith, R.A., Ali, M. A., *Porous keratin constructs, wound healing assemblies and methods using the same.* US patent 12127694.

Q23: Application of nanocellulose in health and agriculture industries

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Cellulose represents the most abundant renewable polymer on Earth. Its earliest human use dates back thousands of years, with extensive utility today in products such as paper, cellophane, packaging, textiles, and dietary fibres. During the last decade, there has been a large amount of work surrounding the conversion of a broad range of biomass sources into nanocellulose, which includes cellulose nanocrystals and nanofibres.

Nanocellulose materials form an exciting sub-class of a broader family of polysaccharide-based nanomaterials. Nanocellulose can be derived from plants (e.g. wood, grass, cotton), marine animals (e.g. crustacean shells, tunicates, algae or 'sea squirts'), and bacteria. Nanocellulose boasts desirable mechanical properties such as high specific stiffness and strength, and excellent chemical and thermal stabilities combined with low weight and biodegradability, which make them ideal candidates for a range of different applications. While nanocelluloses derived from various sources share a common molecular backbone, their structure, properties, surface chemistry, cost and practical uses can vary enormously depending upon the plant or animal sources and method of extraction or isolation.

This presentation gives an overview of the fundamental aspects of nanocellulose production and applications in several different industries including nanocomposites, health, and agriculture. Specifically, it demonstrates the nanocellulose application for medical devices, and as an efficient carrier for agrochemical delivery to plants.

1. N Amiralian, PK Annamalai, P Memmott, DJ Martin (2015). *Isolation of cellulose nanofibrils from Triodia pungens via different mechanical methods.* Cellulose 22, 2483-2498.
2. A Hosseinmardi, PK Annamalai, L Wang, D Martin, N Amiralian (2017). *Reinforcement of natural rubber latex using lignocellulosic nanofibers isolated from spinifex grass.* Nanoscale 9 (27), 9510-9519.
3. P Cao, N Amiralian, J Wang, B Sun, A Popat, F Xie, ZP Xu, Y Li, L Li (2023). *Engineering nano-cellulose bio-composites to improve protein delivery for oral vaccination.* Biomaterials Advances. 149, 213400.

Q24: 3D structures of electrospun nanofibers

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Electrospinning provides a scalable method for the production of nanofibres, from a variety of synthetic and bioderived polymeric materials. The ability to tailor the fibre properties of the polymer materials such as wettability, smoothness, diameter and surface area-to-volume means this technique is of great interest in both nanotechnology and biomedical applications. As an example, chitosan is a biopolymer derived from waste from the seafood industry, and is widely used in biomedical applications due to its antimicrobial, hemostatic and biocompatible properties. Electrospinning of chitosan nanofibres allows for enhanced performance in wound care, drug delivery and tissue engineering1 . Our recent research has focused on forming 3D structures of electrospun biopolymer nanofibres, instead of the flat 2D sheets typically manufactured by this technique. A brief overview of the structures that can be created will be presented, with discussion of the biomedical applications which may be possible with these materials.

1. AL-Jbour, N.D., M.D Beg, J. Gimbun, and A.K.M. Moshiul Alam (2019). *An Overview of Chitosan Nanofibers and their Applications in the Drug Delivery Process*. Current Drug Delivery. 16(4)

Q25: From Fish to Fight: Nitroreductases as versatile tools in cell ablation & cancer therapy

Abigail Sharrock[1]

[1]Victoria University of Wellington, NZ.

Abby Sharrock obtained her PhD from Victoria University of Wellington in 2019, focusing on engineering bacterial nitroreductase enzymes for improved cancer gene therapy and targeted cellular ablation. For the past four years she has worked as a Postdoctoral Research Fellow in Professor David Ackerley's Microbial Biotechnology lab. To date, Abby has published 17 research articles, a recent highlight being her 2022 first-author Nature Methods paper describing an improved enzyme for conditional cellular ablation that has already been widely adopted by the zebrafish research community. In 2022, she was also awarded the inaugural Research for Life Postdoctoral Fellowship to support her ongoing research into the development of nitroreductase-based next-generation cancer therapies.

Q26: The role of host ecology in shaping the virome

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[1]University of Otago, NZ.

New Zealand is a unique place to study the evolution of viruses. Separated from Gondwana around 84 million years ago, many of New Zealand's native hosts have lived in isolation, likely harbouring novel and highly divergent viruses. New Zealand's fauna therefore provides a powerful natural experiment to evaluate the key genetic and ecological parameters that affect viral evolution. Specifically, the unusual amalgam of native and invasive species, with well-documented history of invasive introduction, provide a unique opportunity to determine the factors that contribute to viral host-jumping over ecological timescales. We sample animal hosts such as birds, fish, reptiles and mammals to uncover what viruses they harbour, determine how their viruses have evolved over time and how their ecology and life history may promote viral host-jumping. Overall, we aim to reveal more of the unexplored virosphere, uncover potential disease-causing viruses affecting wildlife, and identify factors that shape the virome.

Summary of Abstracts for the Poster Session

No.	Title	Presenter	Institutions
Q25	Generating genome-scale cell free DNA methylome in solid cancers	A/P Aniruddha Chattejee	University of Otago
Q26	Identification of the genes at S and Z reveals the molecular basis and evolution of grass self-incompatibility	Dr. Herridge	University of Otago
Q27	Assessing the dynamics of horizontal gene transfer after faecal microbiota transplantation in obese adolescents	Anna Behling	University of Auckland
Q28	Understanding a novel oxidation-induced amyloid formation mechanism of a tumour suppressor protein	Pierre de Cordovez	University of Otago
Q29	Repurposed drugs for preventing meningioma invasion	Matt Munro	Gillies McIndoe Research Institute
Q30	Faecal microbiome transplants leave footprints in the plasma metabolome	F. Day	University of Auckand
Q31	Investigating the role of CNDP2 in heart disease	M. Ocariza	Christchurch Heart Institute
Q32	Investigating the role of *lncTNBC1* in Triple-Negative Breast Cancer growth	Kiri Burich	University of Otago
Q33	Investigation of long non-coding RNAs as potential tumor suppressors in triple-negative breast cancer	J. Grans	University of Otago
Q34	Network Analysis Links Melanoma Germline Risk Loci to Somatic Driver Genes Through Novel Genetic Pathways	Michael Pudjihartono	University of Auckland
Q35	Network analysis uncovers gene-regulatory intersections between juvenile arthritis and comorbid traits	N. Pudjihartono	University of Auckland

Q36	Defining factors underpinning clinically useful gene editing rates	Benjamin Buttle	University of Auckland
Q37	CRISPR-Cas detection of *Legionella* in human blood samples	E. Chernysheva	University of Otago
Q38	Infection-experienced haematopoietic stem and progenitor cells generate neutrophils with enhanced mitochondrial bactericidal activity	Dr. H. Darroch	University of Auckland
Q39	Understanding the molecular role of Polynesian-specific mitochondrial variants in metabolic disease	R. Atiola	University of Auckland
Q40	Investigating the therapeutic potential long non-coding RNAs in glioblastoma	A. Bennie	University of Otago
Q41	How STAG proteins influence cohesins role in cell fate determination	D. Lynch	University of Otago
Q42	Using a zebrafish stem cell model to understand the molecular basis of cohesinopathies	A. Labudina	University of Otago
Q43	Cybersickness Prevention and Alleviation via Machine Learning-Guided High-Definition Transcranial Direct Current Stimulation	Alexander Yang	University of Otago
Q44	Development of cell-instructive gelatin-based bioresins for lithography-based biofabrication of tissue engineered constructs	M. Ishii	University of Otago
Q45	Identification of lncRNAs involved in paclitaxel sensitisation in triple negative breast cancer	Kaitlyn Tippett	University of Otago
Q46	Gelatin incorporation in VEGF-loaded PVA-Tyramine hydrogels to enhance cellular interaction and vascular infiltration	T. Konig	University of Otago
Q47	The Foster method: Rapid and non-invasive detection of clinically significant American Foulbrood	J. MacKay	DNAture diagnostics & research

	disease levels in honeybees using eDNA sampling and a dual-target qPCR assay, with its potential for other hive pathogens		
Q48	Phylogenetic distribution of plastic-degrading microorganisms	V. Gambarini	University of Auckland
Q49	Developing next generation adipose tissue grafts for soft tissue reconstruction	V. De Jong	University of Otago