IN THIS ISSUE:
Overview 2
On the cover of Virology: Prof. Johnson Mak  3
Paper in Endocrinology: Dr Yann Gibert  4
Research Focus: Prof. John Donald  5
Research Focus: Prof. Jagat Kanwar  6

OVERVIEW

The Centre for Molecular & Medical Research (C-MMR) investigates the molecular basis of health and disease – from basic gene discovery and molecular analysis through to pre-clinical and clinical research. Consisting of researchers from the School of Medicine and School of Life & Environmental Sciences, including strong partnerships with Barwon Health and CSIRO (AAHL), C-MMR focuses on four Research Themes: Infection & Immunity, Metabolic & Musculoskeletal Medicine, Cancer and Molecular Biosciences. In each of these areas, C-MMR encourages outstanding research that makes a difference, reflected in highly cited, high impact publications notably including papers in Nature, Science and Cell. C-MMR ranks 2nd in both National Competitive Grant income and HDR completions amongst Deakin’s Strategic Research Centres, and has contributed to ERA rankings of 5 (well above world standard) in Medical Microbiology, Medical Physiology, Pharmacology & Pharmaceutical Sciences and Zoology.
Professor Johnson Mak and his team are members of the School of Medicine who carry out their research at CSIRO AAHL, Geelong and CSIRO Manufacturing, Parkville. The research focus of the Mak lab is the human immunodeficiency virus type 1 (HIV1), and the Mak lab utilize multi-disciplinary approaches to dissect the late stage virus assembly process and the early steps of HIV entry. Some of the approaches utilized by the Mak lab are molecular virology, cellular biology and protein biochemistry, with techniques such as next generation sequencing, recombinant protein production, biophysical techniques, cryo-electron microscopy, super-resolution microscopy and proteomics.

Recently, a piece of work from the Mak lab was featured on the cover for the 60 anniversary December issue of Virology. This work describes a previous unknown step of HIV entry, known as pre-entry priming of HIV, which challenges some of the pre-conceived notions regarding viruses:


Viruses are considered neither live or dead, and it is understood that biological process within a virus must occur after it infects a cell. Using cryo-electron microscopy (cryo-EM) and single molecule fluorescence imaging, this work reported that HIV undergoes a previously unknown pre-entry priming size expansion event upon receptor engagement, challenging the dogma of viral entry. More specifically, this showed that cell-free viruses are able to perform biological process as seen with live organism. These discoveries open up the possibility that pre-entry priming process is a built-in mechanism for HIV to protect itself.

The Mak lab is currently actively pursuing this line of research by bringing together top Australian and International HIV researchers and using cutting edge technologies. Successful completion of the project may lead to revising our description of virus, and with the potential to open up new ways for the design and the development of HIV vaccine candidate.
Dr Yann Gibert, a Senior Lecturer at Deakin School of Medicine and the Head of the Metabolic Genetic Disease Laboratory is a pioneer in using the zebrafish as a vertebrate model to study lipid metabolism, obesity and bone homeostasis.

One of Dr Gibert’s recent projects was published in the prestigious journal Endocrinology (Fraher et al., 2015, Endocrinology 156:3596-609). This paper described for the first time an additive effect between the endocannabinoid pathway and the retinoic acid pathway in controlling lipid abundance during vertebrate embryogenesis potentially opening new venues for developing complementary therapeutics for the obesity epidemic.

Other research has studied lipid deposition and lipid usage during embryonic development in collaboration with Prof Andrew Sinclair that was published this year in Cell Reports, and bone homeostasis in SSRI exposed embryos in collaboration with Dr Lana Williams and members of IMPACT, published in Molecular Psychiatry in 2015. Dr Gibert’s group is also studying the endocannabinoid pathway and the retinoic acid pathway in controlling bone formation in zebrafish.
Background

Professor John Donald is the Deputy Head of School of the School of Life and Environmental Sciences with responsibility for the Waurn Ponds operations of the School, a position he has held since early 2011. Professor Donald obtained his PhD in 1987 from the Department of Zoology at the University of Melbourne, and then spent seven years at the University of Florida in Gainesville as a Postdoctoral Research Fellow. He came to Deakin in 1994 as an ARC-funded Australian Research Fellow, and in 1997 became a Lecturer. His research has used a diverse range of animal models and is broadly in the area of integrative animal physiology with primary focus on cardiovascular regulation, osmoregulation, and more recently, the control of appetite and energy balance. The primary theme is to reveal the physiological control systems in vertebrate animals from diverse environments in order to understand how they have evolved and contribute to the maintenance of homeostasis. The research has used a suite of molecular, cellular and physiological techniques, which permits an integrated analysis from gene to function. Professor Donald’s research has been supported by ARC and internal grant funding, and is published in the leading international journals for the discipline, with over 100 publications. Along the way, he has supervised 35 Honours and 15 PhD students. Professor Donald has a highly productive research collaboration with the University of Tokyo, which has generated an ARC Discovery grant, joint publications, and external competitive funding for exchange visits of researchers and research students, including a Visiting Professor role in 2009. Professor Donald is a member of the Editorial Board of the American Journal of Physiology: Regulatory, Integrative and Comparative Physiology.

Current research projects

The evolution of vasodilation with major focus on the role of nitric oxide in vertebrates

This research combines physiological, molecular and genomic approaches. Genomic analyses have been critical in elucidating the evolution of key proteins called nitric oxide synthases (NOS), which generate nitric oxide. There are three isoforms of NOS called NOS1, NOS2 and NOS3, respectively. In particular, the evolution of the nos3 gene, which is the primary endothelial NOS in mammals, is intriguing. The gene first appears in a bony fish lineage (spotted gar) but is lost in the teleost fishes. In tetrapods, NOS3 is present in amphibians, reptiles and mammals but is lost in most birds. The functional significance of this pattern of gene evolution in terms of nitric oxide control of blood vessels is currently being elucidated.

Professor Donald is also involved in a range of other research projects as a collaborator. For example, his laboratory recently cloned a second fads2 gene from rainbow trout that has $\Delta^5$ activity, which has important implications for understanding fatty acid biosynthesis in a commercially important aquaculture species (see below).

Recent key publications:


Background

Professor Jagat Kanwar leads the Nanomedicine-Laboratory of Immunology and Molecular Biomedical Research (N-LIMBR) group in the School of Medicine. He received his PhD in 1992 from Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, and was previously a Senior Scientist in the University of Auckland, New Zealand.

Professor Jagat Kanwar’s group is developing targeted nanomedicine based therapeutics for different types of cancers (colon, breast, liver, prostate and retinoblastoma), chronic inflammatory diseases including arthritis and eye diseases such as cataract, corneal haze. He has published widely and organised more than 15 conferences in the last 5 years, and been invited speaker for more than 30 keynote and plenary lectures. Many of his PhD students have won conference presentation awards and other prestigious awards such as Australian Endeavour Fellowships. He has won national and international competitive grants, including 2 NHMRC project grants and 2 Australia-India Strategic Research Fund (AISRF) grants.

Current Research Interests

Cancer Theranostics
Survivin inhibition has emerged as a powerful approach for inducing drug sensitivity and inhibiting metastasis. His group has shown that survivin inhibition, using more stable locked nucleic acid (LNA) modified siRNA to survivin and cell permeable dominant negative survivin (SurR9-C84A) protein, leads to the downregulation of multidrug resistant (MDR) markers including survivin and induced drug sensitivity in sorted colon cancer cells as well as cancer drug-resistant stem cells. His group also established orally administered nanocapsules/nanocarriers (NCs) encapsulated with superparamagnetic iron oxide (Fe3O4)-saturated bovine lactoferrin (bLf) and zinc-ferrite saturated bLf (ZnxFe3-xO4-bLf) as theranostics for real-time live imaging in colon, prostate and breast tumours developed and atherosclerosis.

Rheumatoid Arthritis
Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease that causes painful joint inflammation. RA is incurable and poses a significant health burden in terms of personal, social and economic losses in Australia and worldwide, with current anti-RA drugs having severe side-effects. There is, therefore, presently an unmet need for a safe drug that is disease modifying and targets joint inflammatory disease progression. Recently, his group designed, tested and patented biodegradable, non-toxic nanocapsules/nanocarriers (NCs) as a smart oral drug delivery system.

Eye Diseases Corneal Haze/Scarring and Cataract
The personal and socio-economic consequences of blindness and visual impairment continues to be important public health issues in developing and under developed countries. Corneal haze/scarring is caused by microbial infections, dry eyes, contact lenses, chemical trauma, physical agents surgery, and accidents, and is one of the leading cause of global blindness. After the award of NHMRC grant on "corneal haze", Prof Kanwar’s group developed in vitro and in vivo animal models for haze, glaucoma and age-related macular degeneration (AMD) and cataract. Recently, his group fabricated ultra-small algal chitosan nanoparticles (US CS NPs) for efficient delivery of Trichostatin-A (TSA) and cell permeable recombinant dominant-negative survivin protein tagged with poly-arginine (R9 carrier peptide) named SurR9-CB4A, and bovine lactoferrin (bLf) to ocular tissues through topical administration to prevent carbendazim-induced toxicity. US CS NPs could be further explored for their potential for delivering various ocular drugs through topical administration for other eye diseases including cataract, glaucoma and age-related macular degeneration.

Recent key publications:


Roy K, Kanwar RK, Kanwar JR. LNA aptamer based multimodal, Fe3O4-saturated lactoferrin (Fe3O4-bLf) nanocarriers for triple positive (EpCAM, CD133, CD44) colon tumour targeting and NIR, MRI and CT imaging. Biomaterials. 2015;71:84-99.


Our mission
A world-class medical research grouping with a unique research profile that will enhance Deakin’s reputation nationally and internationally.