ACADEMIC ACTIVITIES

Publication(s) of the week

1. Lyu, P., and Kwok, H. F. (2018) High-throughput Strategy Accelerates the Progress of Marine Anticancer Peptide Drug Development. *Recent Pat Anticancer Drug Discov*
2. Debono, J., Bos, M. H. A., Nouwens, A., Ge, L., Frank, N., Kwok, H. F., and Fry, B. (2018) Habu coagulotoxicity: Clinical implications of the functional diversification of Protobothrops snake venoms upon blood clotting factors. *Toxicol In Vitro*
3. Wang, Y. Y., Feng, Y., Wang, F., Huang, W., Ng, C. H., Ungvari, G. S., Wang, G., and Xiang, Y. T. (2018) Comparing two short versions of the 32-item Hypomania Checklist (HCL-32) for patients with bipolar disorder. *Perspect Psychiatr Care*
4. Kamato, D., Burch, M., Zhou, Y., Mohamed, R., Stow, J. L., Osman, N., Zheng, W., and Little, P. J. (2018) Individual Smad2 linker region phosphorylation sites determine the expression of proteoglycan and glycosaminoglycan synthesizing genes. *Cell Signal* **53**, 365-373
5. Xu, X., Chen, E., Mo, L., Zhang, L., Shao, F., Miao, K., Liu, J., Su, S. M., Valecha, M., In Chan, U., Zheng, H., Chen, M., Chen, W., Chen, Q., Fu, H., Aladjem, M. I., He, Y., and Deng, C. X. (2018) BRCA1 represses DNA replication initiation through antagonizing estrogen signaling and maintains genome stability in parallel with WEE1-MCM2 signaling during pregnancy. *Hum Mol Genet*
6. Miao, K., Zhang, X., Su, S. M., Zeng, J., Huang, Z., Chan, U. I., Xu, X., and Deng, C. X. (2018) Optimizing CRISPR/Cas9 technology for precise correction of the Fgfr3-Gly374Arg mutation in achondroplasia in mice. *J Biol Chem*

Publication highlight

Recent news on the use of human embryo gene editing has initiated a huge debates worldwide on the ethical and governance issues. This week, FHS published a paper on the optimization of CRISPR technology for editing the genome to correct a mutation in mice.

J Biol Chem. 2018 Nov 28. pii: jbc.RA118.006496. doi: 10.1074/jbc.RA118.006496. [Epub ahead of print]

Optimizing CRISPR/Cas9 technology for precise correction of the Fgfr3-Gly374Arg mutation in achondroplasia in mice.

Miao K[1], Zhang X[1], Su SM[1], Zeng J[1], Huang Z[1], Chan UI[1], Xu X[1], Deng CX[1].

Abstract

CRISPR/Cas9 is a powerful technology widely used for genome editing, with the potential to be used for correcting a wide variety of deleterious disease-causing mutations. However, the technique tends to generate more indels (insertions and deletions) than precise modifications at the target sites, which might not resolve the mutation and could instead exacerbate the initial genetic disruption. We sought to develop an improved protocol for CRISPR/Cas9 that would correct mutations without unintended consequences. As a case study, we focused on achondroplasia, a common genetic form of dwarfism defined by missense mutation in the Fgfr3 gene that results in glycine-to-arginine substitution at position 374 in mice in fibroblast growth factor receptor 3 (Fgfr3-Gly374Arg), which corresponds to Gly380Arg in humans. First, we designed a GFP reporter system that can evaluate the cutting efficiency and specificity of sgRNAs. Using the sgRNA selected based on our GFP reporter system, we conducted targeted therapy of achondroplasia in mice. We found that we achieved higher frequency of precise correction of Fgfr3-Gly374Arg mutation using Cas9 protein rather than Cas9 mRNA. We further demonstrated that targeting oligos of 100nt and 200nt precisely corrected the mutation at equal efficiency. We showed that our strategy completely suppressed phenotypes of achondroplasia and whole genome sequencing detected no off-target effects. These data indicate that improved protocols can enable the precise CRISPR/Cas9 mediated correction of individual mutations with high fidelity.

KEYWORDS:

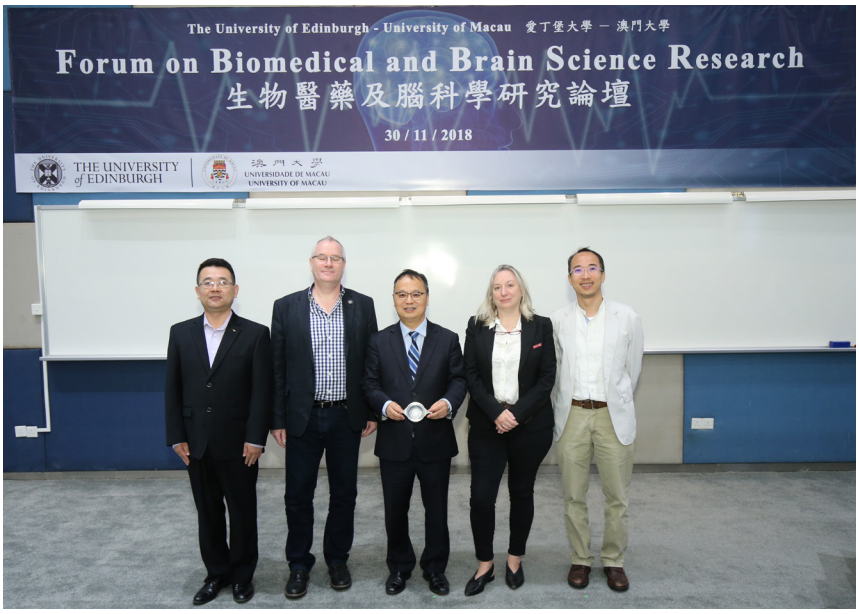
CRISPR/Cas; bone; fibroblast growth factor receptor (FGFR); gene therapy; genetic disease

健康科學學院
Faculdade de Ciências da Saúde
Faculty of Health Sciences

NEWSLETTER ISSUE 47
26 - 30 NOVEMBER 2018

The University of Edinburgh – University of Macau Forum on Biomedical and Brain Science Research

The "Forum on Biomedical and Brain Science Research" jointly organized by The University of Edinburgh and University of Macau was held at University of Macau on 30 November. Two professors from the University of Edinburgh, Professor Susan WELBURN, Professor of Moelcular Epidemiology and Executive Dean of Zhejiang University-University of Edinburgh Institute, and Professor Mike SHIPTON, Dean of Biomedical Sciences and Professor of Physiology of Edinburgh Medical School, together with Professor Zhen YUAN and Professor Simon Ming-Yuen LEE from FHS and ICMS respectively, delivered talks and led the discussions at the forum to explore the relationship between biomedicine and brain science.



Seminar Series

New Gold-based Anti-Cancer Drugs and Biodegradable Porous Polymers - Prof. Murray BAKER

Prof. Murray BAKER, Professor of The University of Western Australia, presented a talk on “New Gold-based Anti-Cancer Drugs and Biodegradable Porous Polymers” on 27 November.

Prof. BAKER shared two areas, N-heterocyclic carbene (NHC) analogues of the gold-phosphine drug auranofin and Poly(2-hydroxyethyl methacrylate) (PHEMA) in this seminar.

Firstly, Prof. BAKER discovered the exciting prospects including compounds exhibiting promising anti-mitochondrial, anti-cancer activity and fluorescence of gold-NHC compounds. He had done many researches of gold drugs incorporating NHCs and found that NHCs are much easier to synthesize than their phosphine counterparts. This is good for the drug design and optimisation of reactivity profile, lipophilicity, and other properties.

Secondly, Prof. BAKER wants to find a way to break the traditional routes of porous polymers biodegradation. Multistep processes and toxic solvents or insoluble salts as additives are involved in the traditional way. Prof. BAKER has discovered PHEMA which is easily synthesized in a non-biodegradable but porous form. The method “polymerisation-induced phase-separation” used does not need toxic solvents or other additives. Finally, Prof. BAKER found a way which use biodegradable crosslinking agents and controlled polymerisation techniques to synthesize PHEMA in both porous and biodegradable forms.

PhD ORAL DEFENSE

PhD Oral Defense by Shichao WANG of Prof. Xuanjun ZHANG’s group

Mr. Shichao WANG, supervised by Prof. Xuanjun ZHANG, has completed his PhD Oral Defense on 30 November. The title of his thesis was “Fluorescent and photoacoustic probes for *in vitro* or *in vivo* detection of ROS/RNS and Cu(II) in mouse brain with Alzheimer’s Disease”.

Mr. WANG presneted the design and synthesis of the probes for detection of reactive oxygen/nitrogen species (ROS/RNS) and the performed induced metal.

健康科學學院
Faculdade de Ciências da Saúde
Faculty of Health Sciences

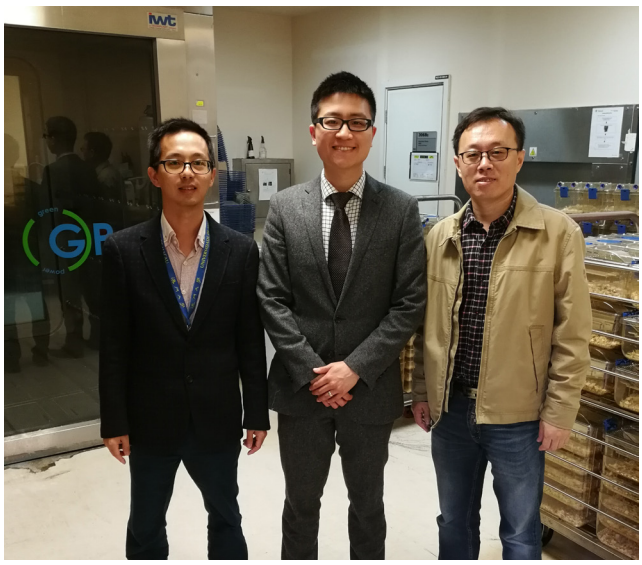
NEWSLETTER ISSUE 47
26 - 30 NOVEMBER 2018

GUEST VIST

This week, Prof. Susan Welburn and Prof. Mike Shipston from The University of Edinburgh, Dr. Wui IP from Stanford University School of Medicine visited animal facilities, fish room and core facilities of FHS. The current research projects and the research prospects were also presented to the guests.



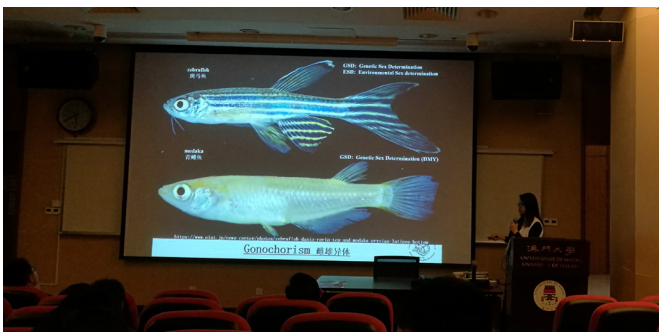


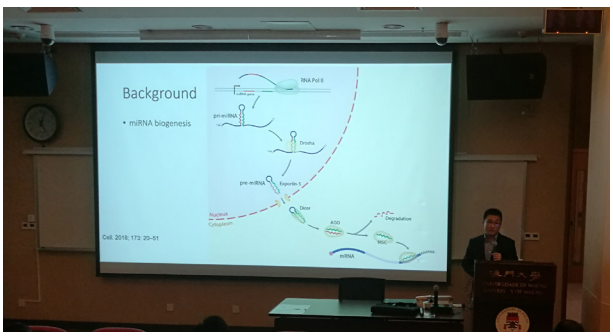



STUDENT ACTIVITIES

FHS Postdoc Student Seminar - Presented by Prof. Wei GE's group and Prof. Garry WONG's group

This week, the FHS Postdoc Student Seminar series continues. On 29 November, Ms. Mingming QIN of Prof. Wei GE's group presented "Roles of Figla/figlain Juvenile Ovary Development and Follicle Formation during Zebrafish Gonadogenesis" and Mr. Liang CHEN of Prof. Garry WONG's group presented "miRNA Arm Switching Identifies Novel Tumour Biomarkers". The next seminar will be held on 13 December, presented by the groups of Prof. Yutao XIANG and Prof. Jun ZHENG.





健 康 科 學 學 院
Faculdade de Ciências da Saúde
Faculty of Health Sciences

UPCOMING

DECEMBER

Mon	Tues	Wed	Thurs	Fri
3	**4**	**5** **Oral Defense** Xiaoyan WANG Supervisor : Prof. Ren-he XU Time: 15:00 Venue: N6-2022	**6** **Seminar Series** Skin Regeneration: Stem Cells and their Niches Speaker: Yaojiong WU Host: Prof. Ren-he XU Time: 09:30-10:30 Venue: E12-G004	**7**
10 The first working day after the Feast of Immaculate Conception	**11** **AC Meeting** Time: 14:30 to 16:30 Venue: E12-G004	**12** **Seminar Series** The Exosome-Mediated Autocrine and Paracrine Role of Plasma Gelsolin in Ovarian Cancer Chemoresistance Speaker: Benjamin Tsang Host: Prof. Wei GE and Prof. Lijun DI Time: 11:00-12:00 Venue: E12-G004 **Year-end Tea Gathering** Time: 15:00-16:30 Venue: E12-Learning Common	**13** **FHS Postdoc/ Student Seminar Series** Host: Prof. Yutao XIANG and Prof. Jun ZHENG Time: 17:00-18:00 Venue: E12-G003	**14**
17 **Seminar Series** RNA editing with CRISPR-Cas13 Speaker: David Cox Host: Prof. Ren-he XU Time: 14:30-15:30 Venue: E12-G004	**18**	**19**	**20** Macau SAR Establishment Day	**21**

For more information or submission of articles to be featured, please contact Ms. Mathilde CHEANG at mathildec@umac.mo or 8822 4909