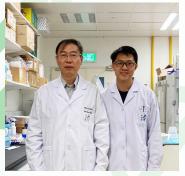


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Article Sharing

Major Breakthrough in Cancer Drug Resistance Research

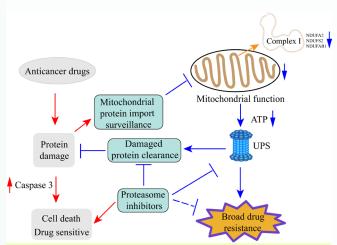


Prof. Chuxia DENG and his team have discovered the connection between the ubiquitinated proteasome system and drug resistance. The team has found that the inhibition of proteasome activity can block broad drug resistance in multiple types of cancer. The findings could help address drug resistance in cancer patients, and the study has been published in the internationally renowned journal *Advanced Science*.

A major reason for the persistently high cancer mortality rate is the body's automatic development of drug resistance. When cancer cells are treated

with several drugs simultaneously or successively, they may become multidrug resistant, making this type of cancer very difficult to treat, such as primary drug resistance of tumor cells and acquired drug resistance. Many tumours, even if initially well treated with chemotherapy, gradually become drug resistant and difficult to control. In addition, many cancers treated with one drug often develop cross-resistance, or broad drug resistance, to many other new drugs with different structures and mechanisms of action, leaving many leading medical institutions scratching their heads.





The inhibition of proteasome activity can block broad spectrum drug resistance in many types of cancers.

The team has found that enhanced proteasome activity and lower mitochondrial activity can contribute to drug resistance in cisplatin through genome-wide RNAi screening and evolutionary drug resistance model. Cisplatin is one of the most widely used chemotherapy drugs in the treatment of different types of cancers. Further studies have indicated that cisplatin treatment induces protein damage, which activates the mitochondrial protein input monitoring pathway. The activation leads to a decrease in mitochondrial activity and enhances proteasome activity, thereby increasing the clearance rate of damaged proteins and saving cell viability. In addition, the team has confirmed that enhanced proteolysis and

lower mitochondrial activity are common mechanisms for resistance to up to 40 cancer drugs, and that proteasome inhibitor therapy reverses resistance to 27 of these drugs through screening against a library of 69 drugs and screening of patients' organs. The results have further shown that cisplatin and bortezomib in nanoparticle form can further enhance anti-tumour effects and reduce the side effects associated with drug combination therapy.

In identifying all human genes potentially associated with drug resistance through whole genome RNAi screening, the team has identified 45 genes associated with cisplatin resistance and 104 genes associated with cisplatin sensitivity. Using multiple models, the researchers have demonstrated that targeting the cellular functions involved in these candidate genes can overcome a broad spectrum of drug resistance. These studies show that despite the different structures, cellular targets, and mechanisms of action of different cancer drugs, cancer cells activate similar defense systems to maintain cell survival. In addition, it has been shown that enhanced proteolysis is a common mechanism for these drug resistances and that by targeting this universal defense system, it is possible to reverse multidrug resistance. These findings have important implications for translational medicine.

The study was led by Prof. Deng and Dr. Fangyuan SHAO is the first author. The study was funded by the Science and Technology Development Fund, Macao SAR (reg. number: 094/2015/A3, 048/2019/A1, and 0011/2019/AKP) and UM (reg. number: CPG2020-00004-FHS, MYRG2016-00139-FHS, MYRG2016-00132-FHS, and MYRG2017-00113-FHS). The full version of the related paper can be viewed at: https://onlinelibrary.wiley.com/doi/full/10.1002/advs.202001914





Visit

Zhejiang Delegation visits FHS

A Zhejiang delegation led by Mr. Xinle Yu, Deputy Director of Zhejiang Provincial Health Commission, paid a visit to FHS on 29 October. They were warmly received by Prof. Chuxia DENG. Prof. Deng oriented the guests of the latest developments, academic programmes, research achievements, cultivation of high-calibre students and internationalization of FHS.





Visit to Kiang Wu Hospital

On 28 October, Prof. Guokai CHEN led over 20 undergraduate students in the class of Endocrinology and Metabolic Diseases (HSCI3001) to visit the Clinical Laboratory and the Department of Pathology of Kiang Wu Hospital. Dr. Frank K.L. NGAI, the Head of the Clinical Lab, guided them through the tour, and the doctors and technicians in the lab showed them the process of analysis for medical diagnosis.











FHS Community Story iGEM Series II - The iGEM Team Holds Various Activities to Ameliorate Their Project



The students visit the Chimelong Ocean Kingdom.



The team conducts an online interview with the laboratory manager in laboratory of Ocean Park Hong Kong.

The UM iGEM team from FHS and FST has conducted users' interviews with Chimelong Ocean Kingdom and Ocean Park Hong Kong recently that enhanced their project for the International Genetically Engineered Machine (iGEM) competition.

The UM team focuses on modifying microorganism to degrade biofilm in aquariums. The team conducted users' interviews with Chimelong Ocean Kingdom and Hong Kong Ocean Park respectively for obtaining more information about the real situation and difficulties that the end-users are facing. It appears that the aquariums require immense amount of manpower and resources to clean exhibits and pools that maintains the marine life quality. The rapid growth and strong adhesion of the biofilms make the work for the aquarium scuba divers difficult. The hazards associated with a more time-consuming cleaning of the facilities include bounce diving (frequent ascending and descending), water pressure burden on the aquarium scuba divers and an exhalation of large amount of air bubbles that can be lethal for jellyfish.

They introduced their idea of building the biofilm degrading system to the theme parks, and this system bases upon a bioengineered *Escherichia coli* (*E. coli*), which can be commonly found in the environment. In their proposal, they plan to bioengineer this bacterium by introducing a detection switch and a chopper. The detection switch generates a protein called LuxR that senses the presence of biofilm in the environment to trigger the production of enzymatic protein, DspB, that chops the biofilm into smaller soluble pieces of microorganisms. Therefore, these two newly introduced functions work collaboratively to eliminate the deposit of the biofilm in the aquatic system. They have succeeded in bioengineering the genetic material with both the functions of detection and degradation for the bacterium. With this new genetic material, the bioengineered E. coli can continuously produce the chopping enzyme, DspB, when there is biofilm, leading to the disassembly and detachment of the biofilm from the surfaces in the aquatic system. Indeed, to make this a better system, they plan to further introduce two more enzymes that facilitate the elimination by killing the soluble microorganism pieces from the degraded biofilm through breaking down their survival-essential DNA and proteins.

Both theme parks are interested in the students' design and have given valuable feedbacks for their further improvement. Chimelong Ocean Kingdom raised their concerns about the survival of the engineered bacteria in different environment and their recycling. Ocean Park Hong Kong wondered if the engineered bacteria would clean up the bacteria in their biological filters located in dark area as these beneficial bacteria are used to remove toxic wastes in the aquariums. To solve these problems, the team designed a magnetic system and a light-sensitive system to modify their idea for the recycling of the engineered bacteria and preventing the degradation of the beneficial bacteria in the biological filters. The students also proposed using common bacteria for being modified as engineered bacteria to survive in different environments.



In addition, in order to arouse the interest of Macao high school students in synthetic biology, the team delivered a science talk for the secondary students in Macao Sam Yuk Middle School (English Section). During the talk, the team introduced iGEM and the details of their iGEM project. The activity not only raised the high school students' awareness in pushing the boundaries of synthetic biology by tackling everyday issues that the world is facing but also enriched the team's communication, interpersonal and presentation skills which will be an advantage for the students in the upcoming giant jamboree of the iGEM competition.



The team holds a high school talk at Sam Yuk Middle School (English Section).

Prof. Yutao XIANG wins a medal in the UM Table Tennis Competition

Prof. Yutao XIANG was the 2nd Runner-up in the table tennis competition held on 19 and 22 October of the "2020 UM Sports Fest". The sports fest was jointly organized by OSA (Office of Sports Affairs) and UMSU SPA (UM Students' Union, Sports Association).

Congratulations to Prof. Xiang!





A OCT - 7 NOV

Prof. Yutao XIANG Shares Psychiatry Talk in UM Residential College

On 29 October, Prof. Yutao XIANG presented a talk of "Clinical Studies in Psychiatry during the COVID-19 Pandemic" in the MLC MedX Lecture Series Opening Seminar of Ma Man Kei and Lo Pak Sam College (MLC).





PhD Oral Defence

PhD Oral Defence by Ruiqiang XIE of Prof. Jun ZHENG's group

Mr. Ruiqiang XIE supervised by Prof. Jun ZHENG completed his PhD oral defence on 30 October. His thesis title is "Analysis on Antibiotic Resistance and Virulence Features in *Acinetobacter baumannii*".



Mr. Xie introduced that *Acinetobacter baumannii* is one of the most challenging nosocomial pathogens due to the emergence and spread of the antibiotic resistance. His study has provided the first analysis of the global prevalence of antibiotic resistance in *A. baumannii* infections. He has discovered a faster increase in antibiotic resistance in the OECD countries than in the non-OECD countries during the past 11 years (2006-2016). Moreover, he has used k-shell decomposition to analyze the integrated co-functional network of A. baumannii, and has discovered that the genes for antibiotic resistance tended to have higher k-shell values and

located in the internal layer of the network, whereas the virulence genes tended to have lower k-shell values and located in the external layer of the network.



UPCOMING

Oct / Nov					
Mon	Tue	Wed	Thu	Fri	٦
	2 3	4	5		6
Holiday All Soul's Da	Oral Defence	BCAT Meeting Speaker: Prof. Douglas ZHANG Time: 17:00-18:00 Venue: E12-G004	FHS Postdoc/ Student Seminar Session: Cancer Research Host: Prof. Xiaoling XU and Prof. Qi ZHAO Time: 17:00-18:00 Venue: N22-G002 and Zoom	Oral Defence Xiaoxiao ZHOU Supervisor: Prof. Guokai CHEN Time: 10:00 Venue: E12-4004	7
	9 10	11	12	13	3
1	6 17 Qualifying Exam		19 FHS Postdoc/ Student	20	0
	The Application of Multiplex Electro- chemiluminescence Immunoassay in Oncology Research Speaker: MSD Asia Pac Field Application Scientists Host: Prof. Hanming SHEN Time: 15:00-16:00 Venue: N22-G002 & ZOOM	Speaker: Prof. Edwin CHEUNG Time: 17:00-18:00 Venue: E12-G004	Seminar Session: Cancer Research Host: Prof. Tzu-Ming LIU and Prof. Kathy Qian LUO Time: 17:00-18:00 Venue: N22-G002 and Zoom		
2	3 24	25	26	27	7

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