FACULTY OF HEALTH SCIENCES

2021 WEEKLY NEWSLETTER

Issue 1 | 4 - 8 January

Publication

1. Sang, W., Xie, L., Wang, G., Li, J., Zhang, Z., Li, B., Guo, S., **Deng, C.**, and **Dai, Y.** (2020) Oxygen-Enriched Metal-Phenolic X-Ray Nanoprocessor for Cancer Radio-Radiodynamic Therapy in Combination with Checkpoint Blockade Immunotherapy. *Adv Sci* **[2019IF = 15.84]**

2. Gurian, E., Di Silvestre, A., Mitri, E., Pascut, D., Tiribelli, C., Giuffre, M., Croce, L. S., **Sergo, V.**, and Bonifacio, A. (2020) Repeated Double Cross-Validation Applied to the PCA-LDA lassification of SERS Spectra: A Case Study with Serum Samples from Hepatocellular Carcinoma Patients. *Anal Bioanal Chem* **[2019IF = 3.637]**

1 Article Sharing

The team led by Prof. Yunlu DAI designed and synthesized an oxygen-enriched metal-phenolic X-ray nanoprocessor which improved the radiodynamic therapy and enhanced anti-tumor immune response by concentrating the energy generated by radiotherapy in the tumor microenvironment, and at the same time generating ROS to induce cancer cell damage. The study has been published in the top international academic journal *Advanced Science*.

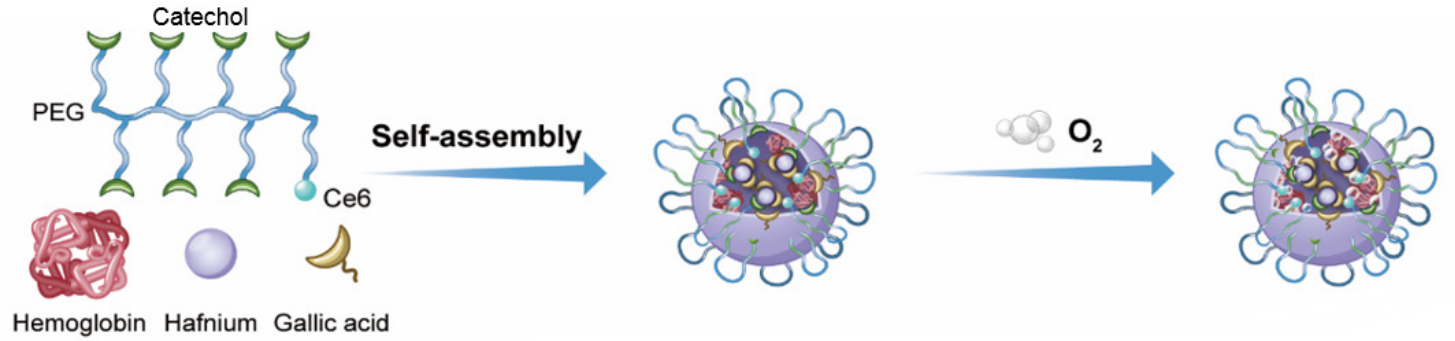
The efficacy of tumor radiotherapy has been clinically proven in various types of cancer for years. However, high-dose radiotoxicity and radiation resistance greatly limit the application of radiotherapy. The research team has developed an oxygen-enriched X-ray nanoprocessor: Hb@Hf-Ce6 nanoparticles, which can be used in combination with PD-1 antibody to improve the therapeutic effect of radiotherapy and radiodynamic therapy and promote anti-tumor immune response.

Hb@Hf-Ce6 nanoparticles are prepared based on the structure of metal polyphenol coordination, which integrate all functional molecules into nanoparticles to achieve multifunctional anti-tumor effects. The polyphenol structure modified by chlorin e6 (Ce6) is coordinated with high-Z radiotherapy sensitizers (hafnium, Hf), and the oxygen carrier hemoglobin (Hb) is chimeric in the c oordination structure to overcome the radiation tolerance associated with hypoxia. Specifically, under X-ray radiation, the radiation-induced physical process stimulated by Hf can stimulate the photosensitizer

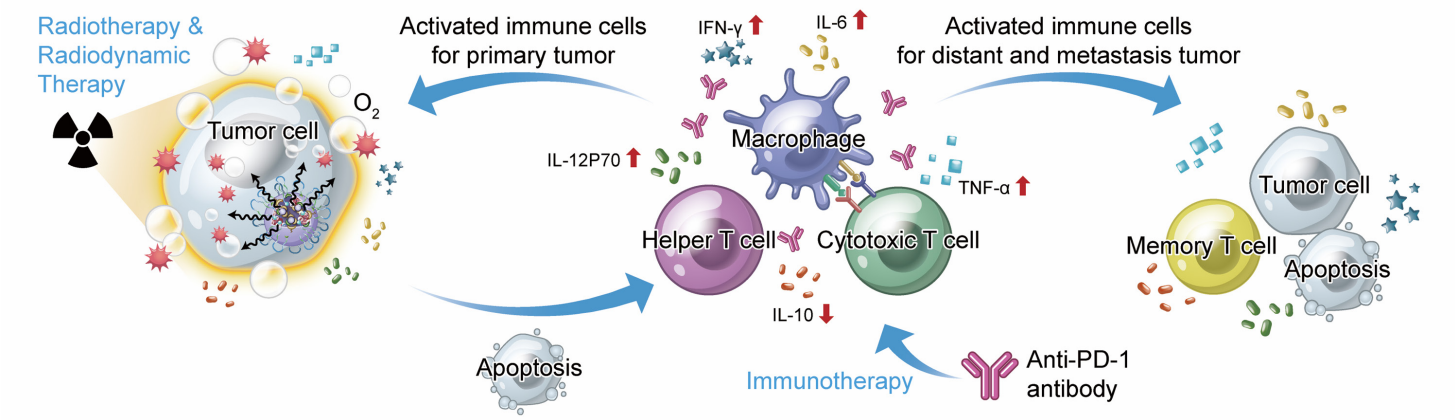
Ce6, thereby generating high levels of ROS to induce cancer cell damage.

In addition, combination therapy with immune checkpoint inhibitor has increased the immune response caused by radiotherapy and radiodynamic therapy. Hb@Hf-Ce6 nanoparticles can achieve high-efficiency and long-term inhibition of tumor growth and metastasis. Therefore, this combination therapy strategy induces a comprehensive anti-tumor immune response against cancer eradication and metastasis suppression. This study proposes a multifunctional metal polyphenol nanoplatform which can be combined with immunotherapy to realize efficient X-ray-mediated radiotherapy-radiodynamic therapy and provide new treatment options for cancer treatment.

Prof. Dai is the corresponding author of the study. His PhD student, Wei SANG and the post-doctoral fellow, Lisi XIE are the co-first authors. FHS Dean Chuxia DENG, the post-doctoral fellows, Bei LI and Jie LI, as well as PhD students, Guohao WANG, Zhan ZHANG and Sen GUO also made important contributions. This research was funded by the Science and Technology Development Fund, Macao SAR (File No. 0109/2018/A3 and 0011/019/AKP) and UM (File No. SRG2018-00130-FHS). The full version of the related paper can be viewed at: https://onlinelibrary.wiley.com/doi/10.1002/advs.202003338



Schematic illustration shows the synthesis of metal-phenolic nanoprocessor



Nanoparticles enhance immune response under X-ray irradiation

2 BCAT Meeting

In the BCAT meeting on 6 January, Prof. Garry WONG presented the influence of piRNAs on age-related neurodegenerative diseases such as Alzheimer's (AD) and Parkinson's diseases (PD). He introduced the main pathogenic proteins involved in these diseases, Amyloid beta and alpha-synuclein, respectively. He reviewed the imaging data showing the overlap of these proteins in brains of both AD and PD patients. He then described the construction of a *C. elegans* nematode double transgenic model neuronally over expressing both of these proteins. These animals showed the movement deficits, neuronal damage, and decreased life span. Moreover, he described the studies showing the dysregulation of the epigenetic marks in these animals and showed the results of an RNAi screen to identify the factors that contribute to the neuropathology. The discovery of piRNA biogenesis factors in mediating these effects led to the studies to investigate the role of piwi-RNAs (piRNA) from human brain samples of control and the PD patients. Furthermore, He showed and summarized the results from preliminary data exploration and hypothesis testing of noncoding RNA-seq data sets. The work has the implications for biomarker discovery and identification of novel pathways involved in proteotoxicity in AD and PD individually or in instances where their pathologies overlap.

3 PhD Oral Defence

PhD Oral Defence by Kefang LIU of Prof. Chuxia DENG's group

Mr. Kefang LIU supervised by Prof. Chuxia DENG completed his PhD oral defence on 4 January. His thesis title is "Structural and Functional Study of Tumor Immunotherapy-Related Molecules, PD-1, PD-L1, and PDGF-DD".

Mr. Liu claimed that the antibodies blockade immunotherapy has been shown promising effect in clinical practice. Therefore, he has demonstrated varied N-glycan composition in PD-1, and discovered that the camrelizumab, an IgG4 MAb approved by the National Medical Products Administration of China, directly binding to the glycosylation of N58 site. He also found that the blockade efficiency of camrelizumab blocking PD-L1

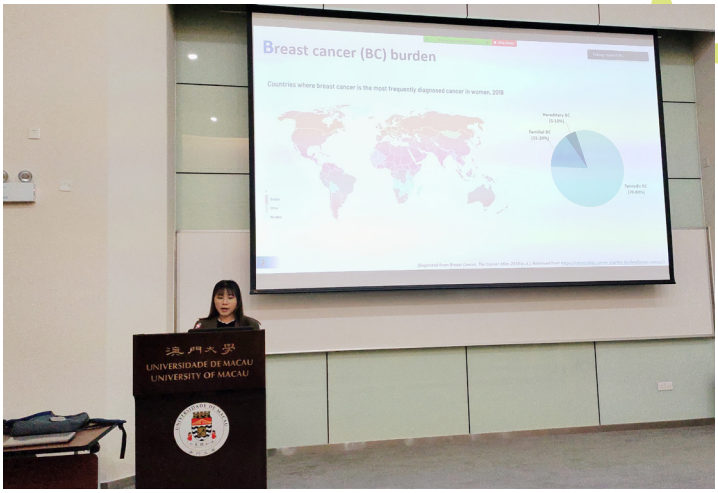
binding to N58 glycosylation-deficient PD-1 was substantially reduced. Moreover, he has cooperated with Bruno E. Correia's team to determine the complex structures of two in *de novo* PD-L1 binders to PD-L1. They have successfully determined the structure of PDGF-DD. He concluded that the results have increased the understanding of the roles of glycosylation in the binding of PD-1-specific MAbs for tumor treatment, and have provided the useful information for verifying protein design method and broadened the knowledge on PDGFs family.

4 FHS Postdoc Student Seminar

Presented by Prof. San Min WANG's group and Prof. Douglas ZHANG's group

On 7 January, Ms. Zixin QIN of Prof. San Min WANG's group presented "The Study of BRCA Variation by Genetic Population Screening" and Mr. Xiangqing HOU of Prof. Douglas ZHANG's group presented "Short-term Exposure to Ambient Air Pollution and Hospital Visits for Allergic Sensitization: A Time-Stratified Case-Crossover Study in Southern China from 2012 to 2019".

The next seminar will be held on 21 January, and presented by the group member of Prof. Zhen YUAN via Zoom again.



UPCOMING EVENTS

Jan		
Mon	**11**	**18**
Tue	**12**	**19**
Wed	**13** **AC Meeting** Time: 15:00-17:00 Venue: N21-G013	**20** **BCAT Meeting** Speaker: Prof. Wakam CHANG Time: 17:00-18:00 Venue: E12-G004
Thu	**14**	**21** **FHS Postdoc/ Student Seminar** Session: Bioimaging Host: Prof. Zhen YUAN Time: 17:00-18:00 Venue: N22-G002 and Zoom
Fri	**15** **Oral Defence** Ran KE Supervisor: Prof. Leo Tsz On LEE Time: 15:00 Venue: E12-1015	**22**

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