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Editorial

Outstanding female cancer research paper awards of the *Taiwanese Association of Obstetrics and Gynecology*

The winners of the 2017 outstanding female cancer research paper of Hsu Chien-Tien Cancer Foundation have been announced. Similar to previous winners before [1–3], these new winners received their honors at the *Annual Meeting of the Taiwan Association of Obstetrics and Gynecology* (TAOG), which was held on 17 and 18 March 2018 in Kaohsiung, Taiwan.

The golden-award winner is Dr. Yu-Li Chen, who published an excellent mini-review entitled "Metronomic chemotherapy and immunotherapy in cancer treatment" [4]. The authors performed a well-written mini-review to introduce updated information of the use of metronomic treatment in the management of cancer patients [4]. This review addressed two important issues. One is the combination of metronomic chemotherapy regimen, for example cyclophosphamide and immunotherapy for the cancer treatment, which is a new and better choice for cancer patients although the drug dose, treatment, duration, and schedule of metronomic agent of chemotherapy administration is still uncertain. In addition, it is still unknown that this metronomic chemotherapy should be given concomitantly, before or after immunotherapies. The other issue is that host immunity is a critical step for the successful treatment for cancer. Therefore, immunotherapy alone or metronomic chemotherapy alone or combination of both therapies should focus on enhancement of activated host immune system or restoration of the immune compromised or immune tolerance status of the host [4]. In fact, in the 2012 June issue of the *Taiwanese Journal of Obstetrics and Gynecology* (TJOG), this metronomic treatment has already been introduced [5]. The only difference is that Dr. Chen's publication has shown a recent magic bullet, such as various kinds of immunotherapy agent and targeted therapy agent [6–8] as an element for the current understanding for metronomic therapy. Immune checkpoint inhibition with blocking antibodies targeting cytotoxic T-lymphocyte antigen-4 (CLTA-4) and the programmed cell death protein 1 (PD-1) or programmed cell death-ligand 1 (PD-L1) becomes a new treatment modality for various kinds of cancer [6]. There is still a big gap between the optimal use of these magic bullets or chemotherapy agent. Recent clinical trials or clinical practices of the combination are still based on the "standard" regimen or schedule of chemotherapy. This thinking process is based on the understanding of pharmacokinetics and pharmacodynamics of chemotherapy in the cancer treatment: maximal tolerance and maximal effectiveness. This concept might be significantly different from the "key elements" of metronomic chemotherapy, which recommends that the agent had better be used in low dose, short interval and continuous pattern [5]. This is a Dr. Chen's contribution.

The silver-award winner is Dr. Kuo-Chang Wen for his research to evaluate the importance of glycosylation change in cancers [9]. In the last year, we have provided a brief introduction for this topic [10]. Dr. Wen's contribution includes two parts. One is sialylated EGFR by α2,3-sialyltransferase type I (ST3Gal I), responsible for the addition of sialic acid (SA) to the core 1 glycan, contributing to tumor dissemination [9,10]. The other is a combination of soyasaponin I (SsaI: an inhibitor for α2,3 sialylation) and epidermal growth factor receptor (EGFR) inhibitor having the synergistic effect on inhibition of tumor invasion. This study confirmed the previous report addressing the importance role of ST3Gal I or other glycosylation changes on malignant transformation and cancer progression [11,12]. Previous report showed that MUC1 modulates the tumor immunological microenvironment through engagement of the lectin Siglec-9 (SA-binding immunoglobulin-like lectins 9) [11]. The aberrant O-linked glycosylation of MUC1 can alter the interaction of MUC1 with lectins of the immune system can influence tumor-immune system interplay [11]. The cyclooxygenase-2 (COX-2) can increase ST3Gal I expression, and the chronic inflammation induced by the binding of MUC1-sialylyltransferase (MUC1-ST) to Siglec-9^{+} myeloid cell would maintain continued expression of MUC1-ST glycoform via induced expression of COX-2, resulting in the positive feedback loop which might maintain the induction of tumor-associated macrophages and the continued modulation of the cancer microenvironment [11], which is beneficial in cancer growth and invasion. Glycosylation change of cancer cells can be mediated by formation of various tumor antigens serving as ligand for the cell adhesion molecules, including loss of E-cadherin, or N- or O-linked glycans, which involve adhesion of cancer cells to vascular endothelium and contributing to hematogenous metastases [12]. In addition, altered glycosylation is also related to cancer cell survival, drug resistance and immune escape [12].

The last reward winner is Professor Angel Chao, who evaluated the role of lysine-specific demethylase 1 (LSD1, KDM1A) in gynecological cancer [13]. Professor Chao found LSD1 is overexpressed and promotes tumorigenesis in ovarian cancer and uterine serous carcinoma, and can destabilize p62 (sequestasome 1-SQSTM1, a key role at the crossroads of autophagy, apoptosis and cancer, since p62 regulates nuclear factor (erythroid-derived 2)-like 2, tuberin-mammalian target of rapamycin (mTOR), and nuclear factor κB (NF-κB)) and inhibit autophagy in ovarian and uterine serous cancers [13]. Professor Chao found that combinations of LSD1 inhibition and autophagy blockade display additive inhibitory effect on cancer cell viability [13]. The authors highlighted the value on the

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anticancer effects of LSD1 inhibitors [13]. LSD1, the first identified histone demethylase, has dramatically revolutionized research in the field of epigenetics. However, the role of LSD1 is complicated, involving a wide range of biological operations, such as development, cellular differentiation, embryonic pluripotency, and disease (for example, cancer), and LSD1 can be considered as a double-edged sword. Inhibition of LSD1 also involves the normal epigenetic changes in physiological processes [14].

From all three winners' studies [4,9,13], we found that multimodality treatment, such as a combination of various kinds of agents, including convention or metronomic chemotherapy, immunomodulation therapy, or targeted therapy is a trend for the current treatment choice for cancers. This concept provides a better chance to "cure" cancers. A fully understanding of intracellular or extracellular changes of tumors, mediated through the power technology, such as whole genomic sequence, or functionome study might provide a comprehensive view of the deregulated function of the cancer [15]. As a president of the *Taiwan Association of Obstetrics and Gynecology*, and an Editor-in-Chief and a Deputy Editor of the TJOG, we are pleased to congratulate all doctors on their winning of the *Outstanding Female Cancer Research Article Awards*. We encourage our audience to continue your research works to battle against the lethal diseases of women: female cancers.

Conflicts of interest

All authors declare no conflict of interest.

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