

Guest editorial

Ganoderma lucidum in cancer research

Ganoderma lucidum, popular medicinal mushroom, has been used as a home remedy in traditional Chinese medicine (TCM) in many Asian countries during the past two millennia [1]. The regular consumption of *G. lucidum* in the form of tea or mushroom powder was believed to preserve the human vitality and to promote longevity [2]. *G. lucidum* has been also used for the prevention or treatment of a variety of diseases including cancer [3]. Western medicine started to accept natural product from the TCM and the popularity of herbal therapies for the treatment of cancer have been recently increasing in the United States [4]. Therefore, scientific justification based on the elucidation of mechanisms responsible for the biological effects of these natural products could help for their validation in alternative or adjuvant cancer therapies. The anticancer effects of *G. lucidum* were associated with triterpenes [5], polysaccharides [6,7], or immunomodulatory proteins [8], through the mechanisms involving inhibition of DNA polymerase [9], inhibition of post-translational modification of the Ras oncoprotein [10], or the stimulation of cytokine production [11]. Moreover, *G. lucidum*: (i) inhibits proliferation and invasive behavior of breast and prostate cancer cells through the down-regulation of expression of cyclin-D1 and suppression of secretion of urokinase-plasminogen activator (uPA) [12–14]; (ii) inhibits growth and induces apoptosis of breast and prostate cancer cells through the up-regulation of expression of p21 and Bax [15,16]; (iii) inhibits growth of hepatoma cells through the suppression of protein kinase C [17]; (iv) induces apoptosis of colon cancer cells by increasing the activity of caspase-3 [18]; (v) suppresses angiogenesis through the inhibition of secretion of vascular endothelial growth factor (VEGF) and transforming growth factor- β 1 (TGF- β 1) from prostate cancer cells [19].

In this issue of *Leukemia Research*, Müller et al. [20] evaluated the effects of *G. lucidum* on cancer cells of hematologic origin, and they found that *G. lucidum* inhibits proliferation and induces apoptosis in a variety of leukemia, lymphoma, and myeloma cells. Moreover, they showed that the inhibition of proliferation of acute myeloblastic leukemia HL-60 cells was associated with cell cycle arrest at G2/M phase and

apoptosis, whereas the inhibition of proliferation and apoptosis of lymphoma U937 was mediated by the up-regulation of expression of p21 and p27. Therefore, Müller et al. further increased our knowledge about the anticancer effects of *G. lucidum* on hematopoietic cells, and confirmed that *G. lucidum* inhibits distinct signaling pathways in different cancer cells. Finally, they used standardized *G. lucidum* extract containing 0.15% ganoderic acid C2. Although triterpenes or triterpenoid fractions from *G. lucidum* previously demonstrated anticancer effects in vitro as well as in vivo, it is uncertain if this amount of ganoderic acid could be responsible for the effect of *G. lucidum* on hematopoietic cells. Nevertheless, the standardization of *G. lucidum* is crucial for its characterization since the composition and amount of biologically active triterpenes depend on the places of the production, cultivation conditions, extraction procedures and the strains of *G. lucidum* [21]. As recently demonstrated, some extracts of *G. lucidum* markedly inhibited intracellular signaling and invasive behavior of cancer cells, whereas other extracts did not show any effect [22]. Thus, the standardization of *G. lucidum* is necessary for the acceptance of *G. lucidum* as a natural product suitable for the treatment of cancer.

The major obstacle for the acceptance of natural products in Western medicine is their complexity. However, this complexity can also bring significant advantages. For example, certain components in the natural products can reduce the cytotoxicity of the whole product, and the interaction between different biologically active components can be responsible for their in vivo effects [23]. In addition, different compounds can modulate unrelated signaling and therefore, can possess synergistic effect [24]. Thus, triterpenes in *G. lucidum* directly suppress growth and invasive behavior of cancer cells, whereas *G. lucidum* polysaccharides stimulate immune system resulting in the production of cytokines and activation of anti-cancer activities of immune cells [5,25]. In conclusion, although the data from the recent studies demonstrating the effect of *G. lucidum* on the molecular level are promising, preclinical and clinical studies with *G. lucidum* are necessary for the validation of this natural product in the prevention and/or therapy of cancer.

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