Targeting cancer with sesterterpenoids: the new potential antitumor drugs

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Abstract Cancer remains a major cause of death in the world to date. A variety of anticancer drugs have been used in clinical chemotherapy, acting on the particular oncogenic abnormalities that are responsible for malignant transformation and progression. Interestingly, some of these anticancer drugs are developed from natural sources such as plants, marine organisms, and microorganisms. Over the past decades, a family of naturally occurring molecules, namely sesterterpenoids, has been isolated from different organisms and they exhibit significant potential in the inhibition of tumor cells in vitro, while the molecular targets of these compounds and their functional mechanisms are still obscure. In this review, we summarize and discuss the functions of these sesterterpenoids in the inhibition of cancer cells. Moreover, we also highlight and discuss chemical structure–activity relationships of some compounds, demonstrating their pervasiveness and importance in cancer therapy.

Keywords Terpenoids · Sesterterpenoids · Cancer therapy · Structure–activity relationship

Introduction: overview of sesterterpenoids and their biological functions

Natural compounds sourced from different organisms exhibit immense structural diversity and possess extensively biological activities against malaria, inflammation, multiple types of cancer, and many infectious diseases. Many of these compounds have been used in clinical therapy, such as etoposide [1], vincristine [2], irinotecan [3], and paclitaxel [4]. As the largest subclass of natural products, accounting for more than 40,000 individual compounds, terpenoids also exhibit diverse biological functions, particularly in the prevention and therapy of multiple cancer types such as skin, lung, pancreatic, colon, and prostate cancer [5, 6]. Based on the number of isoprene units building their parent terpene scaffold, terpenoids can be generally categorized into hemiterpenoids (C5), monoterpenoids (C10), sesquiterpenoids (C15), diterpenoids (C20), sesterterpenoids (C25), triterpenoids (C30), tetraterpenoids (C40), and polyterpenoids (more than C40) [7, 8]. Among these terpenoids, pharmaceutical effects against tumor cells have been extensively reported in monoterpenoids and triterpenoids [9–11], which exhibit the ability to suppress the growth of cancer cells by inducing tumor cell differentiation and apoptosis, and inhibiting tumor angiogenesis, invasion, and metastasis [12–14]. In recent years, sesterterpenoids, a small subgroup of terpenoids, have been widely isolated from different organisms, and also exhibit diverse biological properties involving anti-inflammatory, antimicrobial, anti-feedant, antitubercular, and anti-biofilm formation [7, 8]. Some sesterterpenoids even possess multifunctional activities. For instance, manoalide has both anti-inflammatory and antimicrobial activities [7, 8]. Importantly, many sesterterpenoids can suppress the growth of cancer cells in vitro, and are therefore considered as...
promising candidates for anticancer drugs [7, 8, 15]. However, their functional mechanisms and molecular targets are barely known to date.

Sesterterpenoids commonly harbor C25 carbon skeletons in their molecular structures. However, some compounds that contain C21–C24 are also grouped into sesterterpenoids, termed as norsesterterpenoids [7, 8]. So far, nearly 1,000 sesterterpenoids have been isolated from terrestrial fungi, lichens, higher plants, insects, and various marine organisms, particularly sponges [8, 16]. Based on the carbocycle numbers contained in their molecular structures, sesterterpenoids can be broadly classified into 6 subgroups: linear, monocarbocyclic, bicarbocyclic, tricarbocyclic, tetracarbocyclic, and miscellaneous sesterterpenoids [7, 8, 17]. All of these six subclasses of sesterterpenoids have been reported to exhibit significant cytotoxicities against tumor cells.

**Linear sesterterpenoids and their cytotoxicities against tumor cells**

Although the structures of linear sesterterpenoids are very simple, many of them possess significant cytotoxicities against human tumor cells, with unknown mechanisms of action. Four C22 furanosesterterpenoids isolated from the *Ircinia* species of sponges, including irciformonins C (1), D (2), 15-acetylirciformin B (3), and 10-acetylirciformin B (4) [18], have been reported to significantly inhibit different human cancer cells, in which compounds (1) and (2) suppress the growth of colon tumor cells, and compounds (3) and (4) display notable cytotoxic activities against K562, DLD-1, HepG2, and Hep3B cancer cells [8, 19]. Some haslenes (5–7) (from *Haslea ostrearia*) that house C25 highly branched isoprenoid (HBI) alkenes appear to possess cytostatic effects on human lung cancer cells in vitro [20, 21]. Four furanosesterterpenes isolated from the marine sponge *Ircinia oros*, ircinin-1 (8) [22], (7E, 12E, 18R, 20Z)-variabilin (9) [23], (8E, 13Z, 18R, 20Z)-strobilinin (10) [23], and (7E, 13Z, 18R, 20Z)-felixinin (11) [23], have been demonstrated to show cytotoxicities against SK–MEL-2 human cancer cells by inducing cell cycle arrest and apoptosis [8, 22]. Supplementation with ircinin-1 (8) can lead to G1 phase arrest during cell cycle progression, and this process is associated with a marked decrease in protein levels of cyclin D, CDK4 and CDK6 [22]. Ircinin-1 can also induce the release of cytochrome c, activation of caspase-3 and caspase-9, and upregulation of Fas and Fas-L [22].

Moreover, furospinosulin-1 (12), a marine-sponge-derived furanosesterterpene, exhibits activity against DU145 human prostate cancer cells by inhibiting cell proliferation [24]. Subsequent study has demonstrated that furospinosulin-1 could suppress the expression of insulin-like growth factor-2 (IGF-2) [24], which is a hypoxia-inducible angiogenic factor and is selectively induced under hypoxic conditions through inhibiting the binding of nuclear proteins to the Sp1 consensus sequence in the IGF-2 promoter region [24] (Fig. 1).

![Structures of linear sesterterpenoids 1–12](image-url)
Monobocyclic sesterterpenoids and their cytotoxicities against tumor cells

A variety of monobocyclic sesterterpenoid compounds have also been demonstrated to exhibit significant cytotoxicities. However, little is known about their functional mechanisms. 24-n-Propyl-O-manoalide (13), a derivative of manoalide, was isolated from Luffariella species [25] and showed significant cytotoxicity against HCT-116 cancer cells [25]. Some monobocyclic sesterterpenoids isolated from Diacarnus cf. spinopoculum, including ent-muqubilin A (14), ent-epimuqubilin A (15), nuapapuin B (16), epi-nuapapuin B (17), muqubilin B (18), and epi-muqubilin B (19), possess cytotoxicities against NCI-60 cells [8, 26]. The diacarnoxides A (20) and B (21), isolated from Diacarnus levii, display cytotoxicities against T47D breast tumor cells by inhibiting HIF-1 (hypoxia-inducible factor) activation under hypoxic conditions [27]. It should be noticed here that the activity of HIF-1 is involved in angiogenesis required for tumor cell growth, and thus HIF-1 inhibitors are now under investigation for anticancer effects [28]. The alysinoplides A–C (22–24) identified in Aplysinopsis digitata have cytotoxicities against P-388 mouse leukemia cells [29]. Luffariolides A–J (25–33), obtained from Luffariella species of marine sponge, exhibit significant cytotoxicities against murine lymphoma L1210 cells. Of them, luffariolides A (25), B (26), E (29), and F (30) show the most significant activities [15, 30, 31] (Fig. 2).

Bicarbocyclic sesterterpenoids and their cytotoxicities against tumor cells

Sesterterpenoids with a bicarbocyclic skeleton in many compounds show structures reminiscent of the clerodane and labdane diterpenoids [7, 8]. Kohamaic acid A (34) [32], a compound isolated from Ircinia species of marine sponge, functions as a powerful inhibitor of DNA...
polymerases [32], which are specialized for DNA replication and repair, and can help cancer cells tolerate DNA damage [33]. Some of these enzymes have been developed as viable targets for therapeutic strategies of cancer [33]. The derivatives of kohamaic acid A have also been shown to prevent the growth of HL-60 human cancer cells through inhibition of DNA replication and repair processes [34]. Several sesterterpenes, including thorectandrols A–D (35–38) [35, 36] and palauolol (39) [37], share similar chemical structures and also display cytotoxicities against a variety of cancer cell lines [38]. Palauolol shows significant inhibitory activity against MCF-7, SNB-19, COLO-205, KM12, MOLT-4, H460, A549, LOX, and MALME-3 tumor cell lines, whereas thorectandrols A–D only display weak activities against some of them [38]. Two other sesterterpenoids (40 and 41), which were isolated from the Coscinoderma species of sponge, exhibit moderate cytotoxicities against K562 cells [39] (Fig. 3).

**Tricarbocyclic sesterterpenoids and their cytotoxicities against tumor cells**

Many sesterterpenoids that possess tricarbocyclic skeleton have also been found to show cytotoxicities. Ophiobolins, including ophiobolin A (42), 6-epi-ophiobolin A (43), 3-anhydro-6-epi-ophiobolin A (44), and ophiobolin I (45), were isolated from Bipolaris species [40]. All of them have cytotoxic activities against A-549, HT-29, and Mec-20 human tumor cells [40]. Mechanistic analysis indicates that ophiobolin A suppresses proliferation and migration of cancer cells, and it triggers a paraptosis-like cell death through disrupting internal potassium ion homeostasis [41]. Both 43 and 44 exhibit significant cytotoxicities, whereas ophiobolin I only shows weak activity against tumor cells in comparison with compound 43 [7].

Aurorals (46–47) isolated from the sponge Rhabdastrella globostellata were found to exhibit cytotoxicities against KB cells [42]. Seven sesterterpenoids isolated from Petrosaspongia nigra, namely petrosaspongolides C–H (50–55) and L (56), exhibit cytotoxicities against NSCLC-N6 human bronchopulmonary non-small-cell-lung carcinoma cells [43]. The scalarane-related sesterterpene hyatolides A (57) identified in the sponge Hyatella intestinalis has shown activity as a growth inhibitor of several tumor cell lines such as MDA-MB-231, A-549, and HT-29 [44]. Five isomalabaricane-derived natural products from Rhabdastrella globostellata, namely globostelletins C–G (58–62), display different activities against human tumor cell lines such as A549, BGC-823, HCT-8, Bel-7402, and A2780 [45]. A globostelletin-derived compound, namely rhabdastrellic acid A (63), has shown to have potent inhibition against HL-60 cells by inducing apoptosis in M/G2 phase [46]. Further studies indicate that rhabdastrellic acid A can inhibit proliferation of Hep3B and A549 tumor cells and induce autophagy-associated cell death through blocking the Akt pathway [46]. This process can be negated by transfection with constitutively active Akt plasmid [46] (Fig. 4).

**Tetracarbocyclic sesterterpenoids and their cytotoxicities against tumor cells**

Tetracarbocyclic sesterterpenoids are emerging as a class of attractive compounds exhibiting significant activities against tumor cells. Scalaranes, the most common sesterterpenoids, have been reported to possess broad and significant cytotoxicities against cancer cells [47]. Among them, three scalaranes isolated from Haloragis erecta, namely salmahyrtisol B (64), 3-acetyl- and 19-acetyl-sesterstatin (65 and 66), show significant cytotoxicities against P-388, A-549, and HT-29 tumor cells [47]. A pentacyclic sesterterpene isolated from Haloragis erecta, namely sesterstatin 6 (67), shows significant cytotoxicity against murine leukemia (P-388) and some human tumor cell lines, including BXPC-3, KAT-4, SW1736, NCI-H460, FADU,
and DU-145 [48]. Hyaatelactam (68), isolated from Hyatella intestinalis, has been shown to inhibit HT-29 tumor cells [44]. Hippospongide B (69), which was isolated from a Hippospongia species of sponge, exhibits significant cytotoxicity against DLD-1, HCT-116, T-47D, and K562 tumor cells [49]. Seven other novel scalarane sesterterpenes isolated from Psammocinia species, namely 12-deacetoxy-23-hydroxyscalaradial (70), 12-deacetoxy scalaradial (71), 12-dehydroxy-23-hydroxyhyrtiolide (72), 12-O-acetyl-16-deacetoxy-23-acetoxy scalarafuran (73), 12-deacetoxy-23-hydroxyheteronemin (74), 12-deacetoxy-23-O-acetoxyheteronemin (75), and 12-deacetoxy-23-acetoxy-19-O-acetylscalarin (76), exhibit cytotoxicities against human renal cancer cell lines (A498, ACHN), pancreatic cancer cell lines (MIA-paca, PANC-1), and noncancerous monkey cell line (CV-1) in vitro [50].

Hyaatelone A (77), 19,20-di-O-acetylhyatelone B (78), and 20-O-acetylhyatolide C (79) possess cytotoxicities against MDA-MB-231, A-549, and HT-29 tumor cells [44]. Beside anti-feedant and anti-inflammatory properties, scalarenedial (80) also displays cytotoxicity against HL-60 cells [51]. 12-O-Deacetyl norscalaradial (81), isolated from the sponge Hyatella intestinalis, exhibits activity to inhibit the growth of MDA-MB-231, A-549, and HT-29 tumor cells [44]. Sesterterpene polyols, the mangicols A–G (82–88), which possess unprecedented spirotricyclic skeletal components, show only weak-to-modest cytotoxicities against a variety of cancer cell lines in vitro, especially for NCI-60 cells [52]. Heteronemin (89), a sponge

sesterterpenoid isolated from Hyrtios species, inhibits TNF-α-induced NF-κB (nuclear factor kappa-B) activation through proteasome inhibition and induces apoptotic cell death [53, 54]. Heteronemin can affect a variety of cellular processes including cell cycle, apoptosis, the mitogen-activated protein kinases (MAPKs) pathway and the NF-κB signaling cascade, thereby contributing to tumor cell growth inhibition [53, 54], PHC-2–PHC-7 (90–95), which were isolated from Phyllospongia chondrodes, can increase hemoglobin production in human chronic myelogenous leukemia cell line K562 by inducing erythroid differentiation [55]. Neomangicols A (96) and B (97) are cytotoxic to HCT-116 human colon carcinoma in vitro [56].

Moreover, scalaradial (80) and cacospongionolide A (98) should be particularly noted; they are isolated from Cacospongia scalaris and Fasciospongia cavernosa marine sponges, respectively, and can significantly inhibit the growth of T47D, A431, HeLa, and HCT116 cells with different mechanisms [57]. Detailed studies indicate that treatment of T47D cells with scalaradial or cacospongionolide can lead to increased DNA migration and fragmentation [57]. Incubation of HCT116 and HeLa cells with scalaradial or cacospongionolide results in increased pro-apoptotic protein levels and the loss of mitochondrial transmembrane [57], implying the activation of apoptosis signaling. These results suggest that scalaradial and cacospongionolide may represent new promising compounds for inhibiting cancer cell proliferation (Fig. 5).
Fig. 5 Structures of tetracarbocyclic sesterterpenoids 64–98
Miscellaneous sesterterpenoids and their cytotoxicities against tumor cells

Studies also demonstrate that miscellaneous sesterterpenoids exhibit significant cytotoxicities against tumor cells. Salmahyrtisol A (99), which was isolated from *Hyrtios erecta*, exhibits significant cytotoxicity against murine leukemia (P-388), A-549, and HT-29 human cancer cells [58]. Terpestacin (100), a miscellaneous compound, was isolated from a *Phomopsis* species of fungus [59]. Mechanistic study indicates that terpestacin suppresses tumor angiogenesis by targeting UQCRB of mitochondrial complex III in the mitochondrial respiratory chain, thereby causing the inhibition of hypoxia-induced reactive oxygen species and cellular oxygen sensing [59, 60] (Fig. 6).

Chemical structure–activity relationships

Some sesterterpenes share similar chemical structures but exhibit distinct cytotoxic activities against cancer cells. Thus, it will be interesting and helpful to investigate the relationship between chemical structure and activity. Although many sesterterpenes have been found to show cytotoxicities to tumor cells, it is impossible to compare their activities meaningfully since different cancer cell lines were used for different compounds in cytotoxic assays. Here, we track some sesterterpenes isolated by Dr. Liu’s group (from South China Sea Institute of Oceanology) in the past years, and try to find factors affecting their activities (Table 1), thereby providing guidance for modifying the chemical structure of sesterterpenes and obtaining derivatives with more bioactivity in the future.

C-21 structures and cytotoxicities against tumor cells

Sarcotin A, a compound isolated from *Sarcotragus* species, possesses a pair of epimers, C-21R (101) and C-21S (102) [61]. Cytotoxicity analysis indicates that the C-21R epimer is much more cytotoxic than the C-21S epimer. Consistent with this, sarcotin B (103) and isopalinurin (104), and the other two furanosesterterpenes (105 and 106) from *Psammoscinia* species also show much higher cytotoxicity to cancer cells in their C-21R epimers than their respective C-21S epimers [62] (Fig. 7).

\(\gamma\)-Hydroxybutenolide moiety and cytotoxicities against tumor cells

Some cacospongionolides (98, 107–108) share similar chemical structures with thorectandrols, but exhibit significantly higher cytotoxicities than thorectandrols. Their structure comparison suggests a possible relationship between the \(\gamma\)-hydroxybutenolide moiety and cytotoxicity [57, 63]. Furthermore, some sesterterpenes including a norsesterterpenoid compound (109), sarcotin I (110) and sarcotin J (111) [61, 64], share similar chemical structures with compound 101. However, their cytotoxicities against cancer cells are weaker than compound 101, which contains a \(\gamma\)-hydroxybutenolide moiety. These results clearly demonstrate that the \(\gamma\)-hydroxybutenolide moiety is necessary for the activities of sesterterpenes, and the opening ring of \(\gamma\)-hydroxybutenolide may also cause the decrease in cytotoxicity (Fig. 8).

Furan moiety and cytotoxicities against tumor cells

The furan moiety also displays a relevance to cytotoxicity. Comparison of the chemical structures and cytotoxicities of compounds 109 and 112–113 indicates that sesterterpenes containing a furan moiety have increased cytotoxicity when the furan moiety is oxygenated to form unsaturated lactone or dihydrofuran [63, 64]. Moreover, sesterterpenes 8 and 114–117 containing two furan moieties show higher cytotoxicities than those compounds (118–120) that contain only one furan moiety [65]. That is to say, the more furan rings means stronger cytotoxicities, and the oxidation of a furan ring at an appropriate degree might also improve the cytotoxicities of sesterterpenes (Fig. 9).

Pyrrrole moiety and cytotoxicities against tumor cells

The pyrrolosesterterpenes are chemically unique compounds, and incorporate a pyrrole ring to replace the furan ring. The pyrrole moiety also displays correlation with cytotoxicity in sesterterpenes. Comparison of the chemical structures and activities of compound 118 and sesterterpenes 121–126 indicates increased cytotoxicity in compounds harboring a pyrrole moiety [61]. However, sesterterpenes carrying a \(\beta\)-substituted lactam ring (127) instead of the \(\alpha\)-substituted one exhibit dramatically decreased activity [61]. Moreover, an alkyl moiety attached
on the N-atom of the pyrrole ring is also required for cytotoxicity. For instance, some sesterterpenes (128–131), in which the alkyl moieties are substituted by carboxylic acids sodium, show completely absent cytotoxicity [64] (Fig. 10).

### Double bonds and cytotoxicities against tumor cells

The double bonds within the sesterterpenes also have significant effects on cytotoxicity, and the effect is complicated. For instance, comparison of cytotoxicities of two furanosesterterpenes (9 and 10) isolated from a *Psammocinia* species of marine sponge [60] clearly indicates that compound 10 which carries a double bond in $\Delta^{12,13}$ has much higher cytotoxicity than 9 [60]. Furthermore, the configuration of double bonds also plays important roles for the activities of compounds. Some $E$-difuranosesterterpenes (115 and 117) have been reported to display lower activities than their respective $Z$-difuranosesterterpenes (114 and 116) [65]. The different position of double bonds may lead to different activities. For instance, compounds 105 and 106 share similar structures, but have different positions of double bonds. Interestingly, compound 105 exhibits higher cytotoxicity than 106 in SK-MEL-2, SK-OV-3, and XF498

### Table 1 Cytotoxic activities of compounds

| Compound | Tumor cell lines | Reference |
|----------|-----------------|-----------|
|          | A549 | SK-MEL-2 | SK-OV-3 | HCT15 | XF498 |
| 101      | 29.7 | >30      | 22.1    | 27.2  | 24.8  | [61] |
| 102      | 12.3 | 5.6      | 9.6     | 6.5   | 9.8   | [61] |
| 103      | 10.1 | 7.8      | 11.3    | 9.0   | 8.9   | [61] |
| 104      | 5.2  | 4.4      | 10.2    | 5.4   | 5.1   | [61] |
| 105      | >30  | 10.7     | 16.5    | >30   | 10.0  | [62] |
| 106      | 24.1 | 19.0     | 18.6    | 23.5  | 22.1  | [62] |
| 109      | 19.4 | 10.9     | >30     | 21.7  | >30   | [61, 64] |
| 110      | 24.8 | 25.7     | 23.3    | 23.7  | 25.9  | [61, 64] |
| 111      | 18.1 | 7.8      | 10.0    | 8.7   | 24.3  | [61, 64] |
| 112      | 24.1 | 15.2     | 7.6     | 10.5  | 20.1  | [61, 65] |
| 113      | 8.2  | 7.5      | 12.6    | 19.2  | 7.8   | [61, 65] |
| 114      | 3.7  | 9.0      | 6.6     | 6.9   | 5.4   | [61, 65] |
| 115      | 5.0  | 10.2     | 9.4     | 9.8   | 6.5   | [61, 65] |
| 116      | 3.8  | 5.9      | 5.9     | 4.7   | 3.7   | [61, 65] |
| 117      | 3.8  | 8.4      | 6.2     | 7.3   | 5.0   | [61, 65] |
| 118      | 29.7 | >30      | 22.1    | 27.2  | 24.8  | [61, 65] |
| 119      | 10.1 | 7.8      | 11.3    | 9.0   | 9.0   | [61, 65] |
| 120      | 16.89| 16.3     | 26.8    | 27.5  | 20.4  | [61, 65] |
| 121      | 15.1 | 4.1      | 5.3     | 5.0   | 5.5   | [61] |
| 122      | 4.3  | 3.4      | 4.0     | 3.8   | 3.9   | [61] |
| 123      | 6.3  | 4.3      | 6.7     | 4.9   | 5.2   | [61] |
| 124      | 16.8 | 4.8      | 13.1    | 5.4   | 10.5  | [61] |
| 125      | 19.0 | 3.8      | 6.9     | 5.3   | 5.4   | [61] |
| 126      | 27.1 | 15.9     | 26.8    | 22.3  | 25.2  | [61] |
| 127      | >30  | 13.2     | 25.9    | 21.6  | >30   | [61] |
| 128      | >30  | 10.9     | >30     | 33.0  | >30   | [64] |
| 129      | >30  | >30      | >30     | >30   | >30   | [64] |
| 130      | >30  | >30      | >30     | >30   | >30   | [64] |
| 131      | >30  | >30      | >30     | >30   | >30   | [64] |
| 9        | >30  | 7.5      | >30     | 20.5  | 28.1  | [60] |
| 10       | 7.5  | 12.3     | 4.8     | 11.7  | 10.5  | [60] |

Data expressed as ED$_{50}$ values (µg/mL).

*A549* human lung cancer cell line, *SK-MEL-2* human skin cancer cancer cell line, *SK-OV-3* human ovarian cancer cell line, *HCT15* human colon cancer cell line, *XF498* human CNS cancer cell line.
tumor cells [62]. These results indicate that the $\Delta^{8(10),11(12)}$ conjugated double bonds may increase cytotoxicity, whereas the $\Delta^{15(16),17(18)}$ double bonds possibly decrease activity. Taken together, the characteristics of double bonds including number, position and configuration show significant effects on the cytotoxicity of sesterterpenes.

**Challenges and future directions**

One challenge for cancer chemotherapy is the lack of effective antitumor drugs. The traditional chemotherapeutic medicines cannot selectively kill cancer cells, and consequently cause serious side effects including immuno-
logical, neurological, metabolic, and infectious diseases. Developing compounds from natural source as anticancer drugs is a new strategy to overcome or decrease these side effects. Interestingly, many sesterterpenoids from natural sources have been reported to exhibit strong cytotoxicities by inhibiting cancer cell proliferation and/or inducing cell death. These sesterterpenoids are attracting more interest and may represent new promising compounds in cancer therapy.

Although many sesterterpenoids have been reported to exhibit significant cytotoxicities in vitro, few studies have provided insights into their molecular targets and mechanisms. Thus, it is necessary to further explore studies on signal transduction involved in cancer pathways, the in vivo physiological roles and the systematic structure–activity relationships of these compounds. The detailed mechanistic understanding of sesterterpenoids may provide critical insights into future development and investigation of cancer therapeutics with higher specificity and selectivity. The commendable understanding of relationship between structures and activities can, in turn, help us to chemically modify and synthesize powerful compounds against tumor cells. Furthermore, we anticipate establishing a sesterterpenoid compound-bank to screen effective and specific compounds against various diseases, including but not limited to cancer. Sesterterpenoids may be used in combination with other chemotherapeutic drugs to increase effectiveness and decrease doses of individual compounds, therefore reducing side effects.

Acknowledgments This work was supported by the National Natural Science Foundation of China (31470395). We would like to express our gratitude to Dr. Li Qiu for critically reading the manuscript and for facilitating discussions. We apologize to our colleagues whose work is not cited due to space limits.

Conflict of interest There is no conflict of interest to be declared by the authors.

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