BIOPROSPECTING NOVEL NATURAL PRODUCTS FOR POTENTIAL ANTI-INFECTIVE DRUGS

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Key words: three key word in font Arial 10, cursive, centered

Natural products occupy tremendous chemical structural space unmatched by any other small molecule families. One of the major limiting factors in Natural products drug discovery industry is that pharmaceuticals have been traditionally designed to target individual factors in a disease system, but diseases are complex in nature and vulnerable at multiple attacks. Therefore, a systematic novel synergistic drug screening approach based on a multifactorial principle is urgently needed. Many drugs could be more effective at a reduced dosage if low dosages of other synergistic compounds are introduced simultaneously. To rapidly discover new antifungal agents especially for drug-resistant pathogens, we developed a high-throughput synergy screening (HTSS) strategy for novel microbial natural products. Here we also report an unexpected consequence of MDR1 upregulation: it confers enhanced sensitivity to the natural product berberine. We show that berberine is indeed highly efficacious in inhibiting the growth of azole-resistant clinical C. albicans isolates, with upregulated MDR1, from HIV infected patients. This effect is at least in part due to enhanced accumulation of berberine inside cells and a number of berberine structural analogues exhibited similar MDR1-dependent antifungal activity. Our study reveals a novel function of MDR1 in increasing sensitivity of drug-resistant fungal pathogens to selected natural products.

Conclusions. Write your conclusions precisely, based on your results.

Acknowledgements. The source of any financial support received for your work can be indicated in this section.

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