Drug target for the treatment of MRSA (a superbug) infections

With the support by the National Natural Science Foundation of China and National Science and Technology Major Project, the research team led by Prof. Lan Lefu at the State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, and Prof. Li Jian (**李剑**) at the Shanghai Key Laboratory of New Drug Design, School of Pharmacy, East China University of Science and Technology, reported recently on inhibiting *Staphylococcus aureus* (*S. aureus*) virulence of naftifine and its new derivatives by targeting a diapophytoene desaturase (CrtN), which was published in *Nat Chem Biol* (2016, 12: 174—179).

With the emergence of resistance, new agents targeting multidrug resistant *S. aureus* (including MRSA) are urgently needed. In this study, the team screened a collection of commercially available drugs for their ability to inhibit biosynthesis of the golden pigment (staphyloxanthin), an important virulence factor that protects *S. aureus* from host oxidant killing. They found that the FDA-approved antifungal drug Naftifine Hydrochloride is a reversible competitive inhibitor of CrtN, an enzyme which is essential for staphyloxanthin biosynthesis. Naftifine could attenuate the virulence of MRSA in mouse infection models, revealing CrtN as an attractive and druggable target against *S. aureus* infections. Based on the chemical structure of naftifine, more potent CrtN inhibitors featuring new molecular scaffolds with enhanced oral bioavailability were created (*J Med Chem*, 2016, 59: 3215—3230). Meanwhile, the global rights to develop and commercialize new CrtN inhibitors, including naftifine, were acquired by the Humanwell Healthcare Group Co., a pharmaceutical company headquartered in Wuhan in Hubei Province of China. The pre-clinical investigation of CrtN inhibitors is currently under way by the research and development team at Humanwell Healthcare. The investigational new drug application for the further clinical development of those new agents in China will be submitted to the Chinese FDA in near future.

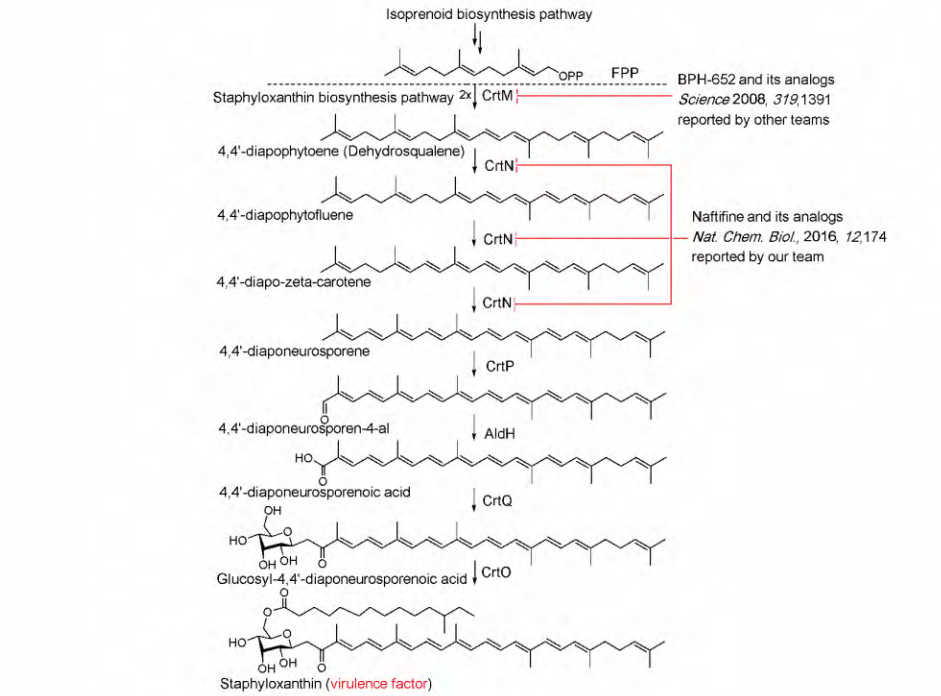

Figure A range of enzymes mediating the biosynthesis of staphyloxanthin (virulence factor) and enzymic inhibitors reported to date.