探討化合物下調外排幫浦之表現以恢復革蘭氏陰性菌株對於抗生素的敏感性

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摘要

細菌多重耐藥性的傳播，嚴重影響了抗生素的治療，其主要機制為藉由外排幫浦的作用將藥物轉運出菌體，降低菌體對於抗生素的敏感性。外排幫浦抑制劑以競爭/非競爭方式，增加抗生素在菌體內的作用，增加菌體對抗生素的敏感性。因此本篇報告主要探討化合物下調外排幫浦之表現，以恢復菌株對於抗生素的敏感性。 由 Benzochrome 純化的衍生物被證明具成為外排幫浦的潛力，且在有效濃度下不具細胞毒性，螢光累積試驗中顯示 Benzochrome 1(BC1) 具有抑制外排浦進而增加螢光在菌體中的累積，其累積螢光的能力較已知的外排幫浦抑制劑來的好，其中 BCI 與 MarR 抑制劑水楊酸鹽協同抗生素可以降低耐碳青黴烯抗藥性之腸桿菌科細菌的多重耐藥性。從 *Embelia tsjeriam-cottam* 分離出的 embelin 與幾丁聚醣金奈米粒子 (Chi-Au NPs) 的結合降低銅綠假單孢桿菌對ciprofloxacin 的 MIC 16倍；於大腸桿菌中 4 倍的 MIC。由 FIC 值得知待測物與抗生素之間具協同性作用，以增加菌株對於抗生素的敏感性。抗菌肽之藥物 Polymyxin b nonapeptide 具增加細胞膜通透性的能力，與外排幫浦抑制劑作用降低菌株對 Azithromycin 的 MIC 2133 倍，在有效濃度下能抑制耐藥性菌株生物膜的生長，與抗生素之間具協同作用。綜合上述三篇文獻所測試的待測物對革蘭氏陰性菌中外排幫浦具抑制作用，進而降低菌株之抗藥能力，以克服細菌的多重耐藥性具有開發成新藥的潛力。

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