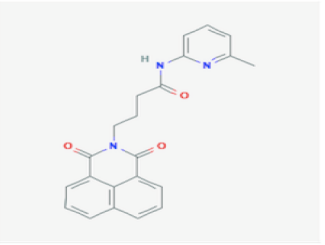
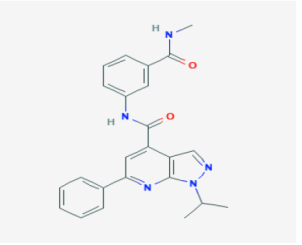
Antibacterial Compositions for Preventing Antibiotic Resistance in Bacteria by Inhibition of SOS Response

Applications

- MDRD1 and MDRD2 can act as adjuvants to ciprofloxacin in the treatment of a variety of infections.
- Use of ciprofloxacin was restricted to serious infections in order to prevent resistance, which makes an effective and inexpensive antibiotic is thus no longer an option. Tests with ciprofloxacin and MDRD1 and MDRD2, shows the reduction in mutation rates and inhibition of the SOS response, implying that using MDRD1 and MDRD2 as an adjuvant to ciprofloxacin can prevent resistance development to this antibiotic. Ciprofloxacin might then be utilized to treat a broader range of infections, keeping the use of a valuable antibiotic from becoming outdated.



MDRD 1 Compound
4(1,3dioxobenzo[de]isoquinolin-2-yl)-N-(6-methylpyridin-2-yl)butanamide



MDRD 2 Compound
N-[3-(methylcarbamoyl)phenyl]-6-phenyl-1-propan-2-ylpyrazolo[3,4-b]pyridine-4-carboxamide]

Inventors

Dr. Shyamali Dutta
Applicant: Telscie Genetics (OPC) Pvt Ltd

Categories of this invention

- Pharmaceutical research

Intellectual Property

Antibacterial compositions for preventing resistance in bacteria by inhibition of SOS response.

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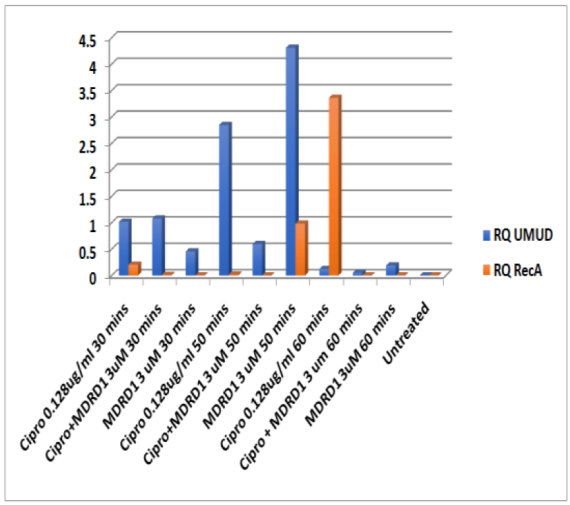
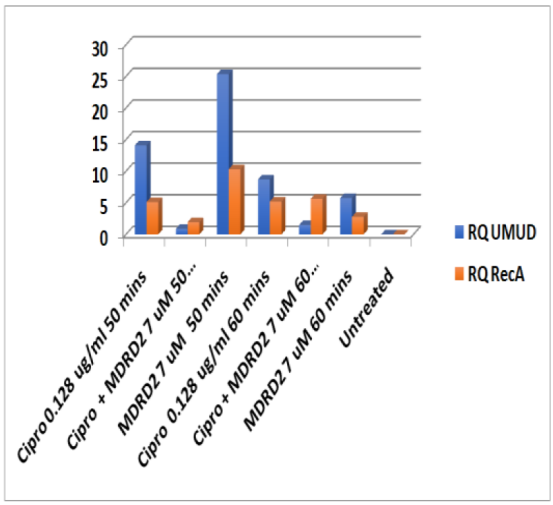
Problem Addressed

The number of effective antibiotics that may be used to safely and efficiently treat community-acquired and hospital infections is continuously decreasing due to the development of bacterial resistance.. Measures to reduce the ability of bacteria to adapt the antibiotics and exchange resistance genes by horizontal transfer are required. One of the key regulators of bacterial adaptive mechanisms is the SOS response. Inhibition of the SOS response should contribute to the reduction in the incidence of resistance to some commonly used antibiotics like ciprofloxacin.

Technology

Antibiotic resistance in bacteria can be prevented by inhibiting the SOS response. The combination of the antibiotic ciprofloxacin with any of the two small organic compounds named MDRD1 & MDRD2 which have the lowest binding energy, inhibited the SOS response in bacteria induced by the ciprofloxacin treatment. The protein Lex A, a conserved serine protease in bacteria, is a critical regulator of the SOS response. Auto-cleavage of LexA by DNA damage and activation of Rec A promotes antibiotic resistance evolution through mutations and horizontal transfer of resistance genes among bacteria. MDRD1 and MDRD2 inhibits the LexA autocleavage.





The E.Coli cultures were exposed to 4xMIC ciprofloxacin for 50-60mins, where MDRD1 & MDRD2 reduced the gene expression of UMUD and RecA, with MDRD1 having the lowest effective dose of 0.5 uM & MDRD2 having the lowest dose of 3 uM.

Advantages

- The antibiotics and the adjuvants (MDRD2 &MDRD2) can treat common infections without developing resistance.
- Existing antibiotics can regain efficacy.
- Suitable for oral use
- Prevents multiple resistance pathwaysi in bacteria

Reach Us

Dr. Amaresh Panda
Lead, Technology Transfer Office, KIIT-TBI
amaresh@kiitincubator.in, tto@kiitincubator.in | +91-98190-53408 |

Dr. Samuel Rout
Manager, Technology Transfer Office, KIIT-TBI
samuel@kiitincubator.in, tto@kiitincubator.in | +91-77353-89456 |