Abstract

Title: BT-benzo-29 inhibits bacterial cell proliferation by perturbing FtsZ assembly

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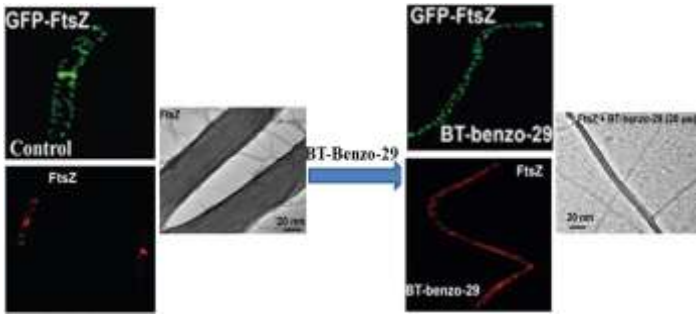
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I. Abstract Body

We have identified a potent antibacterial agent N-(4-sec-butylphenyl)-2-(thiophen-2-yl)-1H-benzo[d]imidazole-4-carboxamide (BT-benzo-29) from a library of benzimidazole derivatives that stalled bacterial division by inhibiting FtsZ assembly. A short (5 min) exposure of BT-benzo-29 disassembled the cytokinetic Z-ring in *Bacillus subtilis* cells without affecting the cell length and nucleoids. BT-benzo-29 also perturbed the localization of early and late division proteins such as FtsA, ZapA and SepF at the midcell. Further, BT-benzo-29 bound to FtsZ with a dissociation constant of 24± 3 µM and inhibited the assembly and GTPase activity of purified FtsZ. A docking analysis suggested that BT-benzo-29 may bind to FtsZ at the C-terminal domain near the T7 loop. BT-benzo-29 displayed significantly weaker inhibitory effects on the assembly and GTPase activity of two mutants (L272A and V275A) of FtsZ supporting the prediction of the docking analysis. Further, BT-benzo-29 did not appear to inhibit DNA duplication and nucleoid segregation and it did not perturb the membrane potential of B. subtilis cells. The results suggested that BT-benzo-29 exerts its potent antibacterial activity by inhibiting FtsZ assembly. Interestingly,BT-benzo-29 did not affect the membrane integrity of mammalian red blood cells. BT-benzo-29 bound to tubulin with a much weaker affinity than FtsZ and exerted significantly weaker effects on mammalian cells than on the bacterial cells indicating that the compound may have a strong antibacterial potential.

II. Image:



III. Reference:

1 Ray S, Jindal, B., Kunal, K., Surolia, A. and Panda, D, 2015. BT-benzo-29 inhibits bacterial cell proliferation by perturbing FtsZ assembly. The FEBS journal, 282: 4015-4033.

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IV. Biography:

Dr. Shashikant Ray has completed his Ph.D. from the Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay. After finishing his Ph.D. he has worked as a research scientist at Reliance Industries Limited which is considered as a world-leading company. Dr. Ray is highly interested in teaching and research and due to that, he has joined Assistant Professor Job at Mahatma Gandhi Central University Motihari. He has published more than 10 papers/book chapters in reputed journals and has been serving as reviewers and editorial board member of several reputed journals

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