Bacterial resistance to dendritic nanomaterials

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Cationic nanoparticles, metal nanoparticles and dendritic polymers, such as. dendrimers, are considered among the most promising antibacterial agents, whose main mechanism of action involves the destabilization of the outer membrane of gram-negative bacteria. Despite the abundance of such agents as alternatives to antibiotic resistance, these antibacterial systems may lose their properties during prolonged application. Although bacterial resistance to metal nanoparticles has been widely discussed, the possible development of resistance to cationic polymers as dendrimers, has not been fully investigated. Here, we report that gram-negative bacteria Pseudomonas aeruginosa PAO1 can develop resistance to cationic carbosilane dendrimers after repeated exposure. Resistance results from changes occurring on the bacterial membrane surface, leading to alterations of membrane permeability. The use of initial low doses of dendrimers causes resistance not only to polymers themselves but also to antibiotic polymyxin B. On the other hand, the use of a high dose of dendrimer initially does not cause resistance at the same time increasingt sensitivity to chloramphenicol. Prolonged use of cationic dendrimers as antibacterial agents may therefore be associated with the risk of developing resistance to both dendrimers and antibiotics, although the immediate use of a high dose can eliminate this phenomenon. Therefore, the first contact with low or high concentration of cationic dendrimers will be decisive for the development of resistance or sensitivity to them and antibiotics simultaneously. The obtained results shed new light on the way of using bacterial outer membrane permeabilizers as antibacterial agents to avoid the development of resistance to this type of nanosystems.

References

[1] S.L. Mitchell, N. V Hudson-Smith, D. Sharan, C.L. Haynes, E.E. Carlson, Modern materials provoke ancient behavior: bacterial resistance to metal nanomaterials, Environ Sci Nano 11 (2024) 483–493. https://doi.org/10.1039/D3EN00420A.

[2] W. Zheng, Y. Jia, Y. Zhao, J. Zhang, Y. Xie, L. Wang, X. Zhao, X. Liu, R. Tang, W. Chen, X. Jiang, Reversing Bacterial Resistance to Gold Nanoparticles by Size Modulation, Nano Lett 21 (2021) 1992–2000. https://doi.org/10.1021/acs.nanolett.0c04451

[3] O. McNeilly, R. Mann, M. Hamidian, C. Gunawan, Emerging Concern for Silver Nanoparticle Resistance in Acinetobacter baumannii and Other Bacteria, Front Microbiol 12 (2021). https://doi.org/10.3389/fmicb.2021.652863.

[4] Y. Xu, H. Li, X. Li, W. Liu, What happens when nanoparticles encounter bacterial antibiotic resistance?, Science of the Total Environment 876 (2023). https://doi.org/10.1016/j.scitotenv.2023.162856.

[5] A. Panáček, L. Kvítek, M. Smékalová, R. Večeřová, M. Kolář, M. Röderová, F. Dyčka, M. Šebela, R. Prucek, O. Tomanec, R. Zbořil, Bacterial resistance to silver nanoparticles and how to overcome it, Nat Nanotechnol 13 (2018) 65–71. https://doi.org/10.1038/s41565-017-0013-y.

Figures

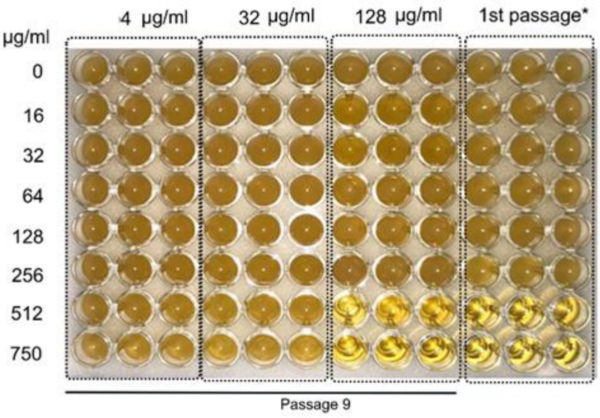

Figure 1. Plate presents the density of bacteria from passage 9 with a subinhibitor concentration of 128 µg/mL in comparision with bacteria from the first passage, i.e. bacteria treated with dendrimer BDTRP001 for the first time.

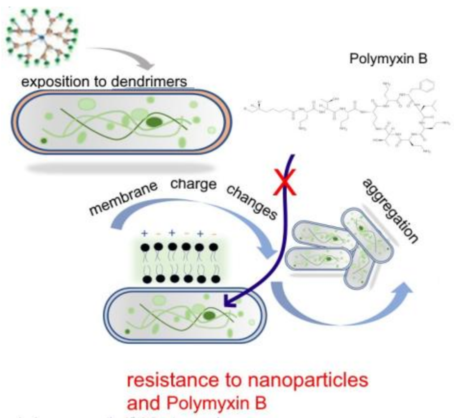

Figure 2. Long term exposition of small dose of dendrimers will develop the resistance to nanoparticles and polymyxin B.