Fighting antibiotic resistance: Synthetic antibodies target and inhibit efflux pump membrane transporter of ESKAPE bacteria

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Antimicrobial resistance is a major current health challenge. Gram-negative bacteria from the ESKAPE group (*E. faecium, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, Enterobacter sp.*) thereby have the highest resistance indices [1]. One of the main mechanisms of resistance is overexpression of efflux pumps, which expel antibiotics from bacteria cells [2]. We report molecularly imprinted polymer (MIP) [3] nanogels obtained by solid-phase synthesis on an immobilized epitope peptide [4] able to target and inhibit an *E. coli* efflux pump. MIPs were characterized for their specificity and affinity through batch binding assays, and using flow cytometry and confocal microscopy on *E. coli* cells. They were able to inhibit the efflux pump resulting in increased antibiotic efficiency.

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References

- [1] J. Denissen et al. (2022) Prevalence of ESKAPE pathogens in the environment: Antibiotic resistance status, community-acquired infection and risk to human health. *Int. J. Hyg. Environ. Health* 244, 114006.
- [2] X. Wen, A. M. Langevin, M. J. Dunlop. Antibiotic export by efflux pumps affects growth of neighboring bacteria. *Sci. Rep.* 8, 1–9, 2018.
- [3] B. Tse Sum Bui, T. Auroy, K. Haupt (2022) Fighting Antibiotic-Resistant Bacteria: Promising Strategies Orchestrated by Molecularly Imprinted Polymers. *Angew. Chem. Int. Ed.* 61, e202106493.
- [4] B. Tse Sum Bui, A. Mier, K. Haupt (2023) Molecularly imprinted polymers as synthetic antibodies for protein recognition: The next generation. *Small* 19, 2206453.