

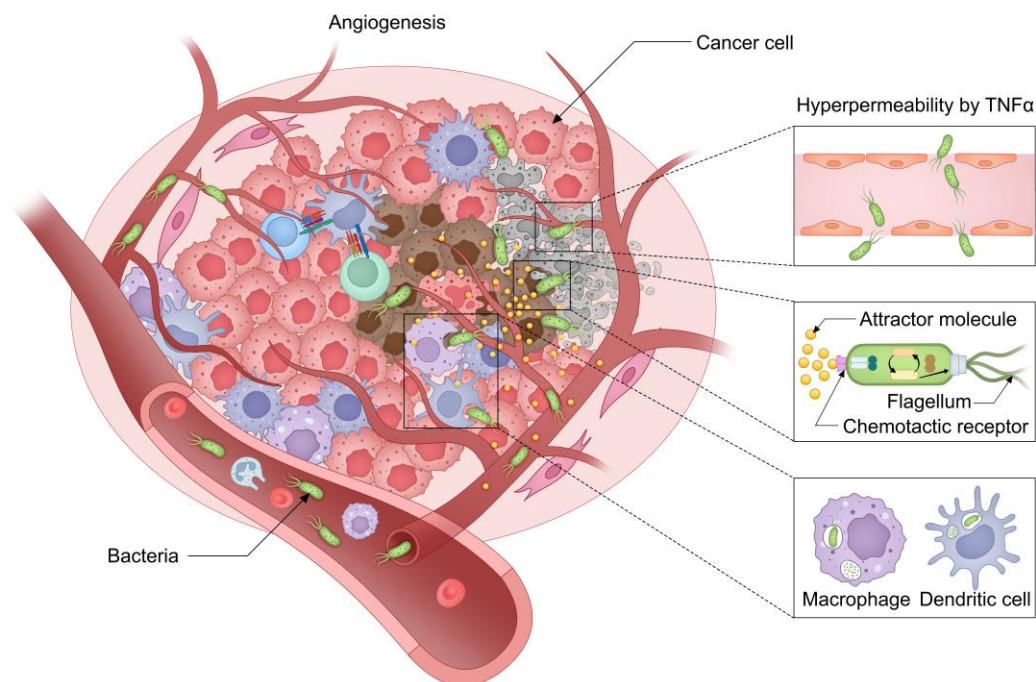
Exploiting bacteria for cancer-specific drug delivery

Jung-Joon (John) Min, MD, PhD

Institute for Molecular Imaging and Theranostics, Department of Nuclear Medicine, Chonnam National University Medical School, Hwasun, Jeonnam, Republic of Korea
jjminmd@gmail.com

Bacteria was first employed in the 19th century, when the antitumor effect of Coley's toxin in patients with inoperable cancer was reported. Coley's toxin enabled tumor regression through enhanced anti-cancer immunity. Several genera of facultative and obligate anaerobic bacteria, such as *Clostridium*, *Bifidobacterium*, *Listeria*, *Salmonella*, *Escherichia*, *Proteus* and *Lactobacillus*, all of which possess the ability to specifically target and inhibit tumor growth, have been studied extensively. Notably, these bacterial species have been further genetically engineered to increase not only tumor specificity but also safety and payload delivery. For example, we engineered attenuated *S. typhimurium* CNC018 strain, the level of which reached greater than 1×10^{10} CFU/g of tumor tissue after intravenous injection, with a tumor-to-normal organ bacterial ratio exceeding 10,000:1. As a tumor-targeting drug carrier, bacteria can be genetically engineered to produce potent therapeutic payloads such as cytotoxic agents, immunomodulators, cytokines, prodrug converting enzymes, small interfering RNAs and nanobodies. In this presentation, I outline the progress in the engineering of bacteria for cancer immunotherapy, focusing mainly on studies using *S. typhimurium* and *E. coli*, the most widely investigated strains in the context of genetic engineering and cancer immunotherapy.

Figure 1. Tumor targeting mechanisms used by live bacteria



References Times New Roman 10 pt Bold; references themselves Times New Roman 10 pt

1. Kang, S. R., Nguyen, D. H., Yoo, S. W. & Min, J. J. Bacteria and bacterial derivatives as delivery carriers for immunotherapy. *Adv Drug Deliv Rev* **181**, 114085 (2022).
2. Nguyen, D. H., Chong, A., Hong, Y. & Min, J. J. Bioengineering of bacteria for cancer immunotherapy. *Nat Commun* **14**, 3553 (2023).
3. Zhou, S., Gravekamp, C., Bermudes, D. & Liu, K. Tumour-targeting bacteria engineered to fight cancer. *Nat. Rev. Cancer* **18**, 727-743 (2018).
4. Forbes, N. S. Engineering the perfect (bacterial) cancer therapy. *Nat. Rev. Cancer* **10**, 785-794 (2010).