



# The Challenge and Opportunity of Gut Microbiota-Targeted Nanomedicine for Colorectal Cancer Therapy

Yaohua Wei<sup>1,2#</sup>, Feng Shen<sup>3#</sup>, Huidong Song<sup>4#</sup>, Ruifang Zhao<sup>1,2#</sup>, Weiyue Feng<sup>5</sup>, Yue Pan<sup>6</sup>, Xiaobo Li<sup>7</sup>, Huanling Yu<sup>8</sup>, Giuseppe Familiari<sup>9</sup>, Michela Relucenti<sup>9</sup>, Michael Aschner<sup>10</sup>, Hanping Shi<sup>11</sup>, Rui Chen<sup>12,13</sup>, Guangjun Nie<sup>1,2</sup>, Hanqing Chen<sup>8,\*</sup>

<sup>1</sup> CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, CAS Center of Excellence in Nanoscience, National Center for Nanoscience and Technology, Beijing 100190, China

<sup>8</sup>Department of Nutrition & Food Hygiene, School of Public Health, Capital Medical University, Beijing 100069, China



Yaohua Wei, Feng Shen, Huidong Song, Ruifang Zhao, Weiyue Feng, Yue Pan, Xiaobo Li, Huanling Yu, Giuseppe Familiari, Michela Relucenti, Michael Aschner, Hanping Shi, Rui Chen, Guangjun Nie, Hanqing Chen. The Challenge and Opportunity of Gut Microbiota-Targeted Nanomedicine for Colorectal Cancer Therapy. *iMeta* 3: e213. <https://doi.org/10.1002/imt2.213>



# Gut microbiota demonstrating intimate association with CRC development

- Colorectal cancer (CRC) is the third most prevalent malignancy and has become a clinically challenging disease along with the second leading cause of cancer-related deaths globally.
- Emerging evidence suggests that gut microbiota, especially pathogenic microbes, and their metabolites, constitute an integral component of the tumor microenvironment, demonstrating an intimate association with CRC initiation and progression
- Therefore, regulation of gut microbiota and its metabolites is a promising approach to inhibiting colorectal carcinogenesis and improving the therapeutic efficacy of CRC
- However, current approaches for gut microbiome modulation in treating CRC could not especially manipulate the intratumoral microbiome to enhance the antitumor efficacy. Meanwhile, the complexity of gut anatomical physiology and multiple physical barriers impede the precise editing of microbiota through conventional regimes.

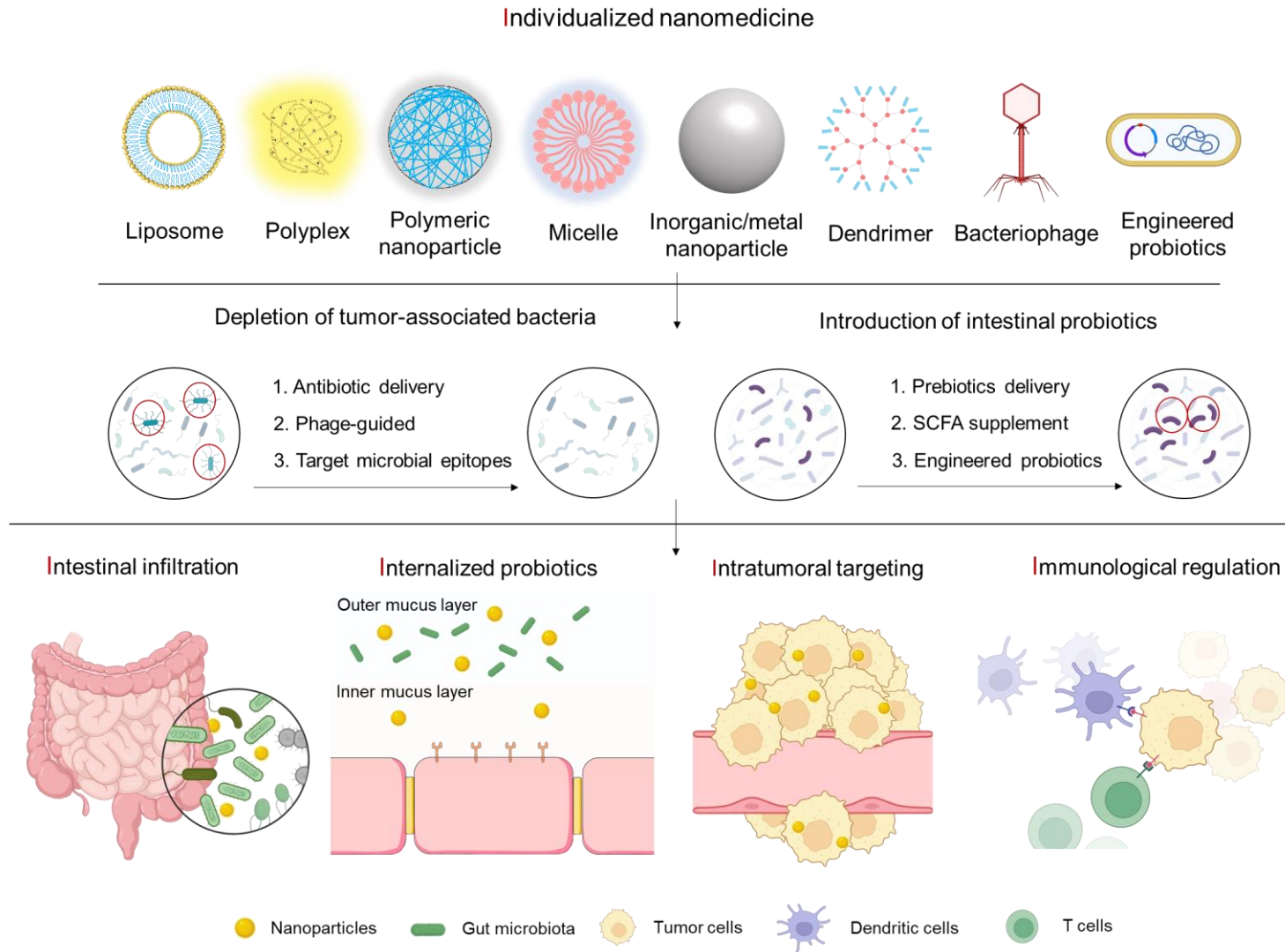
# Gut microbiota targeted nanomedicine for CRC therapy

- Directly interfering with the tumor-colonized or intra-tumoral microbiome
- To improve drug delivery efficiency by modulation of the intestinal mucosal immune barrier and pathogenic physiological structures
- Bioengineered probiotics to colonize CRC tumors selectively enable novel strategies to augment the synergistic effect for CRC prevention and treatment.

Microbial targeting	Mechanism	Nanomedicine	Drug carriers
<b>Depletion of tumor-associated bacteria</b>			
<i>Fusobacterium nucleatum</i>	Interaction between Fap-2 and Gal-GalNAc	Liposomes	Colistin [8]
<i>Fusobacterium nucleatum</i>	Phage-guided targeting	Bioinorganic hybrid bacteriophage	Silver nanoparticles [9]
<i>Fusobacterium nucleatum</i>	Phage-guided targeting	Dextran nanoparticles	Irinotecan [10]
Tumor-associated bacteria	Electrostatic affinity	Inorganic nanoparticles	TPP [12]. <sup>a</sup>
Intracellular microbiome	In response to elevated glutathione	Self-assembled nanoparticles	MTZ <sup>b</sup> and 5-FU [14]. <sup>c</sup>
Intracellular microbiome	Expose microbial epitopes	Liposomes	Silver and tinidazole [15]
<b>Introduction of intestinal probiotics</b>			
Gut microbiota	Production of anti-cancer SCFAs <sup>d</sup>	Nanoparticles	Clostridium butyricum and Dextran [19]
Gut microbiota	Probiotic proliferation and SCFA production	Xylan-stearic acid conjugates	Capecitabine [20]
Engineering <i>E. coli</i> Nissle 1917	Tumor-colonizing probiotics	Orally-deliverable platform	Heparan sulphate proteoglycan [17]



# A future perspective on gut microbiota modulation in CRC treatment



**1. Individualized nanomedicine**

**2. Intestinal infiltration**

**3. Internalized probiotics**

**4. Intratumoral targeting**

**5. Immunological regulation**



# Summary

- ❑ The gut microbiota constitutes an integral component of the CRC microenvironment and is intimately associated with CRC initiation, progression, and therapeutic outcomes
- ❑ We reviewed recent advancements in utilizing nanotechnology for modulating gut microbiota, discussing strategies and the mechanisms underlying their design
- ❑ For future nanomedicine design, we propose a 5I principle to follow for individualized nanomedicine in CRC management

Yaohua Wei, Feng Shen, Huidong Song, Ruifang Zhao, Weiyue Feng, Yue Pan, Xiaobo Li, Huanling Yu, Giuseppe Familiari, Michela Relucenti, Michael Aschner, Hanping Shi, Rui Chen, Guangjun Nie, Hanqing Chen.

The Challenge and Opportunity of Gut Microbiota-Targeted Nanomedicine for Colorectal Cancer Therapy. *iMeta* 3: e213.

<https://doi.org/10.1002/imt2.213>



**iMeta:** Integrated meta-omics to change the understanding of the biology and environment

**WILEY**



“***iMeta***” is an open-access Wiley partner journal launched by iMeta Science Society consist of scientists in bioinformatics and metagenomics world-wide. iMeta aims to promote microbiome, and bioinformatics research by publishing research, methods/protocols, and reviews. The goal is to publish high-quality papers (top 10%, IF>20) targeting a broad audience. Unique features include video submission, reproducible analysis, figure polishing, bilingual, and promotion by social media with 500,000 followers. Since 2022 have been published 160 papers and cited > 2300 times. Index by [ESCI](#), [Google Scholar](#), [DOAJ](#) and [Scopus](#).



Society: <http://www.imeta.science>

Publisher: <https://wileyonlinelibrary.com/journal/imeta>

Submission: <https://wiley.atyponrex.com/journal/IMT2>



[office@imeta.science](mailto:office@imeta.science)



[Promotion Video](#)



[iMetaScience](#)



[iMetaScience](#)