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## Asia 3 Roundtable on Nucleic Acids 2024

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2001- Present Professor, Nankai University  
1994-2001 Postdoc and Research Associate, BCMP, Harvard Medical School, USA  
1994 PhD Uppsala University, Sweden  
1988 MS Nankai University  
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#### Research Interests:

- 1) Medicinal Chemistry of Nucleic Acid,
- 2) Molecular Basis of Pesticide Action,
- 3) QSAR on Biomolecular Selectivity and Drug Resistance.

#### Selected Publications:

1. Huangze Yang, Hongyun Liu, Sanghong Li, Dawei Wang, Zhen Xi. Understanding the Effects of Ligand Configuration on Protoporphyrinogen IX Oxidase with Rationally Designed 3-(N-Phenyluracil)but-2-enoates. *J. Agric. Food Chem.*, **2024**, *72(15)*, 8401-8414.
2. Liqing Lu, Dejun Ma, Zhen Xi. Coexpression of TP53, BIM, and PTEN Enhances the Therapeutic Efficacy of Non-Small-Cell Lung Cancer. *Biomacromolecules*, **2024**, *25(2)*, 792-808.
3. Yaqi An, Boshi Bi, Han Xu, Dejun Ma, Zhen Xi. Co-application of Brassinolide and Pyraclostrobin Improved Disease Control Efficacy by Eliciting Plant Innate Defense Responses in *Arabidopsis thaliana*. *J. Agric. Food Chem.*, **2024**, *72(1)*, 916-932.
4. Zhiqiang Xie, Yuchen Yang, Dejun Ma, Zhen Xi. Design, synthesis, and cell-based in vitro assay of deoxyinosine-mixed SATE-dCDN prodrugs that activate all common STING variants. *Org. Biomol. Chem.*, **2023**, *22(3)*, 606-620.
5. D. Wang, Z. Pang, H. Yu, B. Thiombiano, A. Walmsley, S. Yu, Y. Zhang, T. Wei, L. Liang, J. Wang, X. Wen, H. J. Bouwmeester, R. Yao, Z. Xi. Probing strigolactone perception mechanisms with rationally designed small-molecule agonists stimulating germination of root parasitic weeds. *Nature Communications*, **2022**, *13(1)*, 3987.
6. L. Lu, T. Fang, T. Pang, Z. Chen, L. Cheng, D. Ma, Z. Xi. The Potential Application of Branch-PCR Assembled PTEN Gene Nanovector in Lung Cancer Gene Therapy. *ChemBioChem*, **2022**, *23*, e202200387.
7. X. Kang, H. Huang, C. Jiang, L. Cheng, Y. Sang, X. Cai, Y. Dong, L. Sun, X. Wen, Z. Xi, L. Yi. Cysteine-Activated Small-Molecule H<sub>2</sub>Se Donors Inspired by Synthetic H<sub>2</sub>S Donors. *J. Am. Chem. Soc.*, **2022**, *144(9)*, 3957-3967.
8. D. Zhang, N. Zhou, L. Yang, Z. Yu, D. Ma, D. Wang, Y. Li, B. Liu, B. Wang, H. Xu, Z. Xi. Discovery of (5-(Benzylthio)-4-(3-(trifluoromethyl)phenyl)-4H-1,2,4-triazol-3-yl) Methanols as Potent Phytoene Desaturase Inhibitors through Virtual Screening and Structure Optimization. *J. Agric. Food Chem.*, **2022**, *70(33)*, 10144-10157
9. T. Wei, X. Wen, C. Niu, S. An, D. Wang, Z. Xi, N. N. Wang. Design of Acetohydroxyacid Synthase Herbicide-Resistant Germplasm through MB-QSAR and CRISPR/Cas9-Mediated Base-Editing Approaches. *J. Agric. Food Chem.*, **2022**, *70(9)*, 2817-2824.

# Genome Therapy: A New Approach for Tumor Growth Inhibition

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By central dogma, chromatin DNA was spatial-temporally regulated at multiple levels, including chromatin unfolding, DNA transcription, post-transcription, mRNA translation, post-translation. Accordingly, gene regulation tools at multiple levels were also discovered and artificially exploited for different biological studies and gene therapy applications. With the deep knowledge of the evolution and progression of complex diseases such as cancers, single target based gene therapy has met with great challenges in reducing side-effect and drug resistance. The fast development of novel gene delivery methods and gene regulation technologies moved gene therapy from single gene causing illnesses to multiple gene-associated disorders in a more personalized, precise, safe and efficient manner. To find an efficient therapy solution, the strategies of mimicking chromatin DNA to precisely regulate gene expression through combining various gene regulation tools at different levels as an integrative toolbox are promising to combat complex diseases in the near natural way. In this way, a number of gene regulation tools could be rationally integrated as a smart toolbox and loaded into chromatin-like payloads to mimic the chromosome-mediated gene decoding process for disease therapy. Therefore, we here termed this artificial chromosome-like gene network regulation at multiple levels with different tools simultaneously as genome therapy. In this talk, we will discuss our efforts towards multiple gene regulations for antitumor efficacy with branch-PCR assembled gene nanovector mimicking chromatin-like activity.

1. Liu, J.; Wang, R.; Ma, D.; Ouyang, D.; Xi, Z. Efficient construction of stable gene nanoparticles through polymerase chain reaction with flexible branched primers for gene delivery. *Chem Commun* **2015**, *51*, 9208-9211.
2. Liu, J.; Wang, R.; Ma, D.; Li, Y.; Wei, C.; Xi, Z. Branch-PCR constructed stable shRNA transcription nanoparticles have long-lasting RNAi effect. *ChemBioChem* **2016**, *17*, 1038-1042.
3. Cheng, L.; Deng, H.; Ma, D.; Zhai, B.; Zhang, Q.; Li, L.; Xi, Z. Branch-PCR constructed tp53 gene nanovector for potential cancer therapy. *Chem Commun* **2018**, *54*, 9687-9690.
4. Cheng, L.H.; Ma, D.J.; Lu, L.Q.; Ouyang, D.; Xi, Z. Building customizable multisite-targeting c-myc shRNA array into branch-PCR-constructed DNA nanovectors for enhanced tumor cell suppression. *Chemistryselect* **2020**, *5*, 10250-10255.
5. Lu, L.; Fang, T.; Pang, T.; Chen, Z.; Cheng, L.; Ma, D.; Xi, Z. The potential application of branch-PCR assembled PTEN gene nanovector in lung cancer gene therapy. *ChemBioChem* **2022**, *23*, e202200387.
6. Lu, L.; Rao, D.; Niu, C.; Cheng, L.; Ma, D.; Xi, Z. Dibenzocyclooctyne-branched primer assembled gene nanovector and its potential applications in genome editing. *ChemBioChem* **2022**, *23*, e202100544.
7. Cheng, L.H.; Lu, L.Q.; Chen, Z.; Ma, D.; Xi, Z. Multiple gene regulation for enhanced antitumor efficacy with branch-PCR assembled TP53 and MYC gene nanovector. *Molecules*. **2022**, *27*(20), 6943.
8. Ma, D., Xi, Z. (2022). Gene Nanovector for Genome Therapy. In: Sugimoto, N. (eds) Handbook of Chemical Biology of Nucleic Acids. Springer, Singapore. [https://doi.org/10.1007/978-981-16-1313-5\\_60-1](https://doi.org/10.1007/978-981-16-1313-5_60-1).

