Soft genome editing based on CRISPR nickases: it takes one break to tango

Wang, Q.

List of Publications

1. **Wang Q**, Capelletti S, Liu J, Janssen J and Gonçalves M. Selection-free precise gene repair using high-capacity adenovector delivery of advanced prime editing systems rescues dystrophin synthesis in DMD muscle cells. Nucleic Acids Res. (2024) Online ahead of print. DOI: 10.1093/nar/gkae057.

2. Fan C, **Wang Q**, Kuipers T, Cats D, Iyengar P, Hagenaars S, Mesker W, Devilee P, Tollenaar R, Mei H, Ten Dijke P. LncRNA LITATS1 suppresses TGF-β-induced EMT and cancer cell plasticity by potentiating TβRI degradation. EMBO J. 42:e112806 (2023).

3. **Wang Q**, Liu J, Janssen J and Gonçalves M. Precise homology-directed installation of large genomic edits in human cells with cleaving and nicking high-specificity Cas9 variants. Nucleic Acids Res. 51:3465-3484 (2023).

4. Tasca F, Brescia M, **Wang Q**, Liu J, Janssen J, Szuhai K and Gonçalves M. Large-scale genome editing based on high-capacity adenovectors and CRISPR-Cas9 nucleases rescues full-length dystrophin synthesis in DMD muscle cells. Nucleic Acids Res. 50:7761-7782 (2022).

5. Fan C, **Wang Q**, van der Zon G, Ren J, Agaser C, Slieker R, Iyengar P, Mei H and Ten Dijke P. OVOL1 inhibits breast cancer cell invasion by enhancing the degradation of TGF-β type I receptor. Signal Transduct Target Ther. 7:126 (2022).

6. **Wang Q**, Liu J, Janssen J, Tasca F, Mei H and Gonçalves M. Broadening the reach and investigating the potential of prime editors through fully viral gene-deleted adenoviral vector delivery. Nucleic Acids Res. 49:11986-12001 (2021).

7. **Wang Q**, Liu J, Janssen J, Le Bouteiller M, Frock R and Gonçalves M. Precise and broad scope genome editing based on high-specificity Cas9 nickases. Nucleic Acids Res. 49:1173-1198 (2021).

8. Maggio I, Zittersteijn H, **Wang Q**, Liu J, Janssen J, Ojeda I, van der Maarel SM Lankester A, Hoeben R and Gonçalves M. Integrating gene delivery and gene-editing technologies by adenoviral vector transfer of optimized CRISPR-Cas9 components. Gene Ther. 27:209-225 (2020).

9. Tasca F*, **Wang Q*** and Gonçalves M. Adenoviral vectors meet gene editing: a rising partnership for the genomic engineering of human stem cells and their progeny. Cells 9:953 (2020). * Shared first co-authorship.

10. Chen X*, Tasca F*, **Wang Q**, Liu J, Janssen J, Brescia M, Bellin M, Szuhai K, Kenrick J, Frock R and Gonçalves M. Expanding the editable genome and CRISPR-Cas9 versatility using DNA cutting-free gene targeting based on in trans paired nicking. Nucleic Acids Res. 48:974-995 (2020).

11. Xu H, Luo D, Gao X, Liu X, **Wang Q**, Sun A, Shen J, He R, Lu G, Li K, Zhang J and Xiao L. ZeoR: A Candidate for Assays Testing Enzymatic Activities and Off-Target Effects of Gene-Editing Enzymes. J. Biomed Nanotechnol. 15:662-673 (2019).

12. Yin Y*, **Wang Q***, Xiao L*, Wang F, Song Z, Zhou C, Liu X, Xing C, He N, Li K, Feng Y and Zhang J. Advances in the Engineering of the Gene Editing Enzymes and the Genomes: Understanding and Handling the Off-Target Effects of CRISPR/Cas9. J. Biomed. Nanotechnol. 14:456-476 (2018). * Shared first co-authorship.

13. **Wang Q***, Xiao L*, Zhou L, Sun W, Xing C, Li K and He N. Comparison of the Off-Target Effects Among One-Base to Three-Base Mismatched Targets of gRNA Using a Blue to White Assay. J. Nanosci Nanotechnol. 18:1594-1598 (2018). * Shared first co-authorship.

14. Xi B, Wang X, Xiao L, **Wang Q**, Ji J, Zhang L, Xue M, Liu W, Zhu R, Li K and Sun W. Gene editing effects of CRISPR/Cas on breakpoint cluster region gene targets using white-to-blue colony formation assay. Nanosci. Nanotechnol. Lett. 9:1998-2004 (2017). * Shared first co-authorship.

15. Zhou L*, **Wang Q*** and Li K. Construction of a vector with two repeats flanking CRISPR/Cas9 target for the evaluation of enzymatic activity in E.Coli. J. Nanosci. Nanotechnol. 16:12332-12336 (2016). * Shared first co-authorship.

16. Liu B, Zhou L, **Wang Q** and Li K. A mutation-sensitive switch assay to detect five clinically significant epidermal growth factor receptor mutations. Genet. Test Mol. Biomarkers 19:316-23 (2015).

Curriculum Vitae

Qian Wang was born on the 14th of March 1992 in Lianyungang, Jiangsu Province, China. From 2010 to 2014, she pursued her bachelor's degree in Pharmaceutical Engineering at Jiangsu Ocean University, China. She then started her master's study in Pharmacology at Soochow University, China, from 2014 to 2017. During her master's internship, she investigated the application of a Blue-White Colony Assay for the off-target evaluation of CRISPR-Cas9 activity under the supervision of Prof. Dr. Kai Li in the Molecular Medicine Laboratory.

In September 2017, Qian was awarded a China Scholarship Council (CSC)-Leiden University Scholarship and started her Ph.D. study in the group of Prof. Dr. Rob C. Hoeben under the supervision of Dr. Manuel A.F.V. Gonçalves in the Department of Cell and Chemical Biology at the Leiden University Medical Center (LUMC), Leiden, the Netherlands. Throughout her Ph.D. research, she worked on; (i) investigating new strategies to improve the efficiency, specificity and fidelity of double strand break-free genome editing based on testing different donor DNA structures and engineered programmable nickases; (ii) exploring the feasibility of rescuing dystrophin synthesis in DMD muscle cells via high-capacity adenovectors encoding prime editors; and (iii) studying the impact of the chromatin context on the performance of base editors and prime editors. The work of her Ph.D. research is presented in this thesis.

From March 2022 to March 2023, Qian continued her research in Gonçalves' lab as a postdoctoral researcher, focusing on a project on gene therapy for inherited cardiomyopathies. Since March 2023 until now, she has joined the group of Prof. Dr. Peter ten Dijke in the Department of Cell and Chemical Biology at the LUMC. Her current work focuses on deciphering the functions and mechanisms of long non-coding RNAs and circular RNAs in TGF-β signaling and breast cancer progression.

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