When synthetic biology meets single-cell technology: developing Nannochloropsis into microalgal cell factory of "designer oils" from CO2 and seawater

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Marine microalgae capture a significant portion of atmospheric carbon dioxide and store the fixed carbon as energy-dense macromolecules such as oil or starch. However, for industrial oleaginous microalgae, understanding and rational engineering of such intracellular carbon capture and storage machineries have only just begun. Using *Nannochloropsis oceanica* as a model, we unveiled an intricate collaborative network of genes that underlies TAG synthesis, and showed that the fatty acid profiles on TAG can be rationally designed, for tailored benefits to nutrition and health. Along the process, we developed a series of targeted engineering tools to manipulate these networks. Moreover, we proposed a concept called Ramanome to rapidly phenotype and screen individual microalgal cells based on their metabolic state at single-cell resolution, and then developed Raman-activated Cell Sorter (RACS) to establish the phenotype-genotype link at single-cell resolution. In the end, I will present my thoughts for collaboratively crafting *Nannochloropsis oceanica* into a chassis for scalable production of biofuels, biomaterials and nutrients from carbon dioxide.

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Education:

PhD, 1997 – 2003 Biochemistry, Washington University in St Louis.

MSc, 2000 – 2003 Computer Science, Washington University in St Louis.

BSc, 1993 – 1997 Biotechnology, Peking University

Professional Career:

2003 – 2004 Postdoc, Center for Genome Sciences, Washington University

2004 – 2008 Research Instructor, Genome Institute, Washington University

2008- present Professor and Director, Single-Cell Center; then Assistant Director General, CAS-QIBEBT

Research Interests:

Microalgal synthetic biology and biofuels

Single-cell instrument development (ramanome and meta-ramanome, RACS-Seq, etc)

Microbiome and health

Selected publications

1. Li Wei, Chen Shen, Mohamed El Hajjami, Wuxin You, Qintao Wang, Peng Zhang, Yuetong Ji, Hanhua Hu, Qiang Hu, Ansgar Poetsch, Jian Xu, **Knockdown of carbonate anhydrase elevates Nannochloropsis productivity at high CO2 level**, *Metabolic Engineering*, 2019, https://doi.org/10.1016/j.ymben.2019.03.004

2. Yi Xin, Chen Shen, Yiting She, Hong Chen, Cong Wang, Li Wei, Kangsup Yoon, Danxiang Han, Qiang Hu, Jian Xu, **Biosynthesis of Triacylglycerol Molecules with Tailored PUFA Profile in Industrial Microalgae**, *Molecular Plant*, 2019. DOI: https://doi.org/10.1016/j.molp.2018.12.007. Commentary: Xiao Yang, Xiaofeng Cui, Editor's Highlights: **Designing Microalgal Oils** | Volume 12, ISSUE 4, P472-473, April 01, 2019, DOI:https://doi.org/10.1016/j.molp.2019.03.004

3. Yuehui He, Peng Zhang, Shi Huang, Tingting Wang, Yuetong Ji, Jian Xu, **Label-free, simultaneous quantification of starch, protein and triacylglycerol in single microalgal cells**, *Biotech Biofuels*, 2017, 10:275.

4. Yi Xin, Yandu Lu, Yi-Ying Lee, Li Wei, Qingtao Wang, Jing Jia, Dongmei Wang, Qiang Hu, Jin Liu, Yantao Li, Jian Xu, **Type-2 Diacylglycerol Acyltransferases from three distinct ancestors collaborate to produce triacylglycerols in the industrial microalga Nannochloropsis oceanica**, *Mol Plant*, 2017.

5. Li Wei, Yi Xin, Qintao Wang, Juan Yang, Hanhua Hu, Jian Xu, **RNAi-based targeted gene-knockdown in model oleaginous microalgae *Nannochloropsis* spp.** *The Plant Journal*, 2016, DOI: 10.1111/tpj.13411.

6. Qintao Wang, Yandu Lu, Yi Xin, Li Wei, Shi Huang, Jian Xu, **Genome editing of model oleaginous microalgae *Nannochloropsis* spp. by CRISPR/Cas9**, *The Plant Journal*, 2016. DOI: 10.1111/tpj.13307.

7. Xu Chenggang, Huang Ranran, Teng Lin, Jing Xiaoyan, Hu Jianqiang, Cui Guzheng, Wang

Yilin, Cui Qiu, Xu Jian: **Cellulosome stoichiometry in *Clostridium cellulolyticum* is regulated by selective RNA processing and stabilization.** *Nature Communications,*2015, 6:6900 doi: 10.1038/ncomms7900.

8. Li Jing, Han Danxiang, Wang Dongmei, Ning Kang, Jia Jing, Wei Li, Jing Xiaoyan, Huang Shi, Chen Jie, Li Yantao, Hu Qiang, Xu Jian: **Choreography of Transcriptomes and Lipidomes of *Nannochloropsis* Reveals the Mechanisms of Oleaginousness in Microalgae.** *Plant Cell* 2014. 10.1105/tpc.113.121418.

9. Wang Dongmei, Ning Kang, Li Jing, Hu Jianqiang, Han Danxiang, Wang Hui, Zeng Xiaowei, Jing Xiaoyan, Zhou Qian, Su Xiaoquan, Chang Xingzhi, Wang Anhui, Wang Wei, Jia Jing, Wei Li, Xin Yi, Qiao Yinghe, Huang Ranran, Chen Jie, Han Bo, Yoon Kangsup, Hill Russell T., Zohar Yonathan, Chen Feng, Hu Qiang, Xu Jian: ***Nannochloropsis* Genomes Reveal Evolution of Microalgal Oleaginous Traits**. *PLoS Genet* 2014, **10**(1):e1004094.