Liquid-liquid phase separation of *Arabidopsis* transcriptional repressor VRN1

With the support by the National Natural Science Foundation of China and the Ministry of Science and Technology and China, the research team led by Prof. Lai LuHua (来鲁华) at BNLMS, College of Chemistry and Molecular Engineering, Peking-Tsinghua Center for Life Sciences, and Center for Quantitative Biology, Peking University recently reported that *Arabidopsis* transcriptional repressor VRN1 undergoes liquid-liquid phase separation with DNA in *Angew Chem Int Ed* (2019, 58: 4858—4862). This research uncovers the mechanism of DNA induced VRN1 phase separation and provides novel insight of phase separation mediated transcriptional repression. Zhou HuaBin, a graduate student from Lai's group, is the first author of this paper.

Genomic information encoded in DNA is tightly packed in the nucleus, which forms distinct chromatin domains. These chromatin structures control gene transcription and regulate many physiological processes, including vernalization. Vernalization is the requirement of exposure to a prolonged cold treatment before acquiring the ability of flowering. Vernalization 1 (VRN1) is an important transcriptional factor that promotes vernalization by stably repressing the transcription of *FLC*, the major repressor of flowering. However, the detailed mechanism of VRN1 induced gene silencing is still elusive.

Lai's group, in collaboration with Prof. Qu LiJia (College of Life Sciences, Peking University), and Prof. Qi Zhi (Center for Quantitative Biology, Peking University), found VRN1 undergoes phase separation with DNA both *in vitro* and *in vivo*. VRN1 contains two B3 DNA binding domains flanked by a long intrinsic disorder region (IDR). They found multivalent VRN1-DNA interactions are important for phase separation. Using single molecule DNA Curtains, they found VRN1 nucleates and compacts DNA to form puncta. Furthermore, the charge patterns of IDR in VRN1 modulate its phase behavior, both acidic patch and basic patch are important for liquid-liquid phase separation. More excitingly, VRN1 forms liquid-like puncta in the nucleus of plant cells, indicating phase separation may be important for down-stream gene repression. More follow-up studies are needed to elucidate how VRN1 regulates gene expression and vernalization in *Arabidopsis* through phase separation.

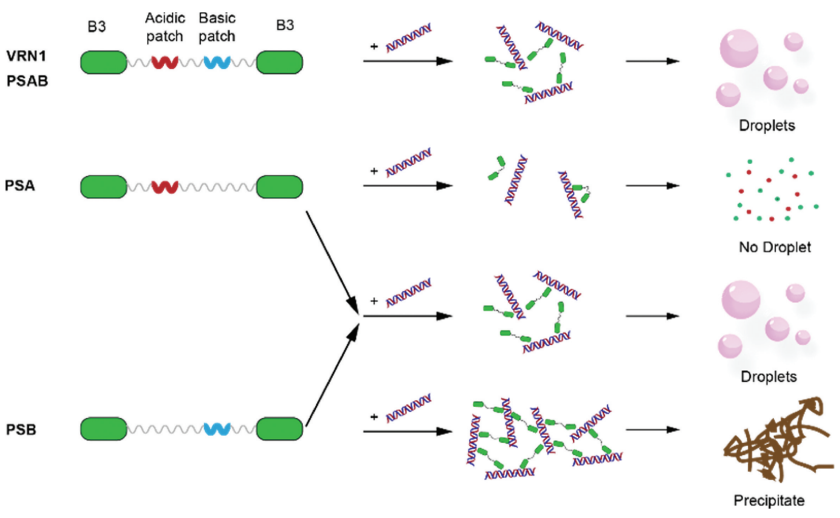

Figure Charge patterns in the VRN1 IDR determine its phase behavior with DNA. The negative-charge-abundant mutant does not demix with DNA, while positive-charge-rich mutant forms precipitation with DNA. Incorporation of both acidic and basic patches generates liquid-liquid phase separation with DNA in *cis* or in *trans*.