Elucidation of construction of epigenetic networks by proteomic approach

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Heterochromatin protein 1 (HP1) is thought to play a role in constitutive heterochromatin formation on specialized chromatin such as centromeres, telomeres and replication origins, by binding to methylated H3K9 and its interacting proteins. By semiquantitative proteomic analysis, we identified 82 HP1α binding proteins (HPBPs). In addition to known HP1 binding proteins such as CAF1, TIF1b, Sgo1, and Mis12, several uncharacterized and/or unexpected proteins were identified. Among them, POGZ bound to HP1α through a zinc finger-like motif (designated as HPZ; HP1-binding zinc finger motif), and its HPZ-mediated HP1 binding competed with a PxVxL protein INCENP (a component of chromosome passenger complex, CPC). Knockdown and complementation experiments revealed that POGZ is essential for Aurora B activation and the CPC translocation. Taken together with the dynamic relocation of HP1 and its binding with kinetochore proteins during mitosis, these data suggest a critical role of dynamic HP1 interaction network in mitotic progression. During the interphase, HP1 also bound to protein complexes involved in the establishment and maintenance of heterochromatin formation. Indeed, G9a-GLP histone H3K9 methyltransferase complex was found to be a unique class of HPBPs. Interestingly, Suz12, a component of PRC2 (polycomb repressive complex 2), was also identified as a HPBP. PRC2 complex is known to be a component of facultative heterochromatin enriched in H3K27 trimethylation, like Hox gene cluster, imprinted regions and inactive X chromosomes. HP1 may be a key molecule to mediate the crosstalk between constitutive and facultative heterochromatin.

Keywords: epigenetics, heterochromatin, HP1, polycomb, X chromosome