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Structural studies to define the role that phosphorylation and acetylation play in regulating key SUMO-SIM interactions required for PML-nuclear body formation

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The interactions between SUMO-family proteins and SUMO-Interacting Motif (SIM) in nuclear bodies formed by the promyelocytic leukemia (PML) protein (PML-NBs) have been shown to be modulated by both phosphorylation SIM-containing proteins and acetylation of SUMO proteins. Given the potential role that these post-translational modifications play in regulating SUMO/SIM interactions in PML-NBs, we have characterized the interactions between the phosphorylated SIMs of key proteins found in PML-NBs and acetylated variants of SUMO1 using a combination of biophysical and X-ray crystallography studies. Our results demonstrate that SUMO-SIM interaction can be fine-tuned by discrete acetylation and/or phosphorylation events targeting either SUMO proteins or SIM-containing proteins to regulate protein transit in and out of PML-NBs.

In addition, the structures of the complexes suggest that there is considerable plasticity at the SUMO-SIM binding interface and this would provide for a robust mechanism to regulate proteins that transit in and out of PML-NB using various combinations of signaling mechanisms that function to regulate phosphorylation and acetylation of these factors.

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