

**Stony Brook University  
The Graduate School**

Doctoral Defense Announcement

**Abstract**

Live cell dynamics of PML nuclear bodies upon entry into and exit from mitosis

By

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Promyelocytic leukemia nuclear bodies (PML NBs) have gained much attention due to its role in leukemogenesis. In 98% of acute promyelocytic leukemia (APL) patients, a single chromosomal translocation t(15; 17) results in a PML-RAR $\alpha$  fusion protein causing the disruption of PML NBs. Interestingly, all-*trans*-retinoic acid (atRA) and arsenic trioxide (As<sub>2</sub>O<sub>3</sub>) treatment can induce complete remission and results in the reformation of PML NBs. In addition, extensive studies have implicated that PML NBs may act as active catalytic domains, nuclear storage sites, or nuclear sensors; however, the functions of PML NBs are still largely unknown. In order to reveal the function of these nuclear bodies, we are particularly interested in their dynamics and how they are segregated to daughter cells during the process of cell division. We developed a U2OS cell line stably expressing ECFP-PML and EYFP-Sp100, two fusion proteins localizing in PML NBs. Live cell imaging (4-D) revealed that prior to nuclear envelope breakdown, 40% of PML NBs exhibit rapid directed movement in prophase cells as compared to only 12% in interphase nuclei. The PML NBs move dynamically within the interchromatin space and fuse to form fewer mitotic PML NBs which contain low level of Sp100 protein. During metaphase, directed movements reduced and 90% of PML NBs move by diffusion. After cytokinesis, Sp100, Daxx, and HP1-alpha enter the daughter nuclei, prior to the entry of PML protein, however, the formation of PML NBs is initiated only after the multimerization of the PML protein. The newly assembled PML NBs appear only after a functional nuclear membrane has been reformed. These studies suggest that chromatin condensation, upon entry into prophase of mitosis, results in a loss of tethering between regions of chromatin and PML NBs thereby resulting in their increased dynamics. Upon chromatin decondensation at the end of mitosis, PML NB formation initiates by PML protein. Future studies will examine the molecular basis of PML NB dynamics upon entry into and exit from mitosis.

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**Dissertation Advisor:** Dr. David L. Spector

**Place:** James Library, CSHL, 1 Bungtown Rd, Cold Spring Harbor, NY 11724