Supplemental Movie 1. Fluorescence recovery after photobleaching analysis of nuclear TIA-1 structures formed following HSV-2 infection. HeLa cells were transfected with a plasmid encoding GFP-tagged TIA-1. At 24 hours after transfection, cells were infected with HSV-2 strain HG52 at a MOI of 5 and cells were imaged at 10 hpi. The nuclear TIA-1 structure contained within the white circle was bleached and fluorescence recovery was allowed to proceed. Note that GFP-TIA-1 is rapidly recruited back into this structure. Arrowhead indicates a nuclear TIA-1 structure that was not bleached.

Supplemental Movie 2. Fluorescence recovery after photobleaching analysis of SGs formed following over expression of TIA-1. HeLa cells were transfected with a plasmid encoding GFP-tagged TIA-1. At 24 hours after transfection, cells were mock infected and cells were imaged at 24 hpi. The SG contained within the white circle was bleached and fluorescence recovery was allowed to proceed. Note that GFP-TIA-1 is rapidly recruited back into SGs. Arrowhead indicates a SG that was not bleached.

Supplemental Movie 3. Fluorescence recovery after photobleaching analysis of nuclear Sam68 structures formed following HSV-2 infection. HeLa cells were transfected with a plasmid encoding GFP-Sam68. At 24 hours after transfection, cells were infected with HSV-2 strain HG52 at a MOI of 5 and cells were imaged at 10 hpi. The region contained within the white circle was photobleached and fluorescence recovery was allowed to proceed. Note that GFP-Sam68 is rapidly recruited back into this structure. Arrowhead indicates a nuclear Sam68 structure that was not bleached.

Supplemental Figure 1. SG accumulation in HeLa cells treated with arsenite and/or phosphonoacetic acid. Mock infected HeLa cells were maintained in the presence or absence of 200 µg/ml phosphonoacetic acid (+PAA or -PAA, respectively). After 12 hours, cells were treated with 0.5 mM arsenite or mock treated (+ARS and -ARS, respectively) for 30 minutes. Cells were then fixed and stained with goat polyclonal antiserum specific for TIA-1 and mouse monoclonal antibody specific for HSV-2 ICP8 followed by staining with Alexa 488 conjugated donkey anti-goat IgG and Alexa 568 conjugated donkey anti-mouse IgG secondary antibodies. Nuclei were stained with Hoechst 33342. Stained cells were examined by fluorescence microscopy and representative images are shown. Numeric values in the merged image panels indicate the fraction of cells containing SGs from 30 independent fields of view for "-ARS+PAA" panel and 10 independent fields of view for "+ARS-PAA" and "+ARS+PAA" panels. Arrowheads indicate SGs in the cytoplasm. Note that PAA treatment alone does not induce SG formation and that the presence of PAA does not interfere with SG formation caused by arsenite treatment.

Supplemental Figure 2. Accumulation of SGs and nuclear TIA-1 structures in T12 cells. **A, B**. SG accumulation in T12 cells treated with arsenite or pateamine A. T12 cells were mock infected or infected with HSV-2 strain HG52 at a MOI of 5. At 4 hpi, cells were treated with 0.5 mM arsenite (+ARS), 300 nM pateamine A (+PATA) or untreated for 30 minutes. Cells were then fixed and stained with goat polyclonal antiserum specific for TIA-1 and mouse monoclonal antibody specific for HSV ICP27 (**A**) or G3BP (**B**) followed by staining with Alexa 488 conjugated donkey anti-goat IgG and

Alexa 568 conjugated donkey anti-mouse IgG secondary antibodies. Nuclei were stained with Hoechst 33342. Stained cells were examined by fluorescence microscopy and representative images are shown. Note that, in mock infected T12 cells, SGs accumulate following either arsenite or pateamine A treatment and that these SGs contain robust and roughly equivalent amounts of TIA-1 and G3BP. By contrast, in infected T12 cells, SG accumulation is inhibited following arsenite treatment and the SGs that accumulate following pateamine A treatment are largely devoid of TIA-1. **C.** Accumulation of nuclear TIA-1 structures in infected T12 cells. T12 cells were infected with HSV-2 strain HG52 at a MOI of 5 and at 10 hpi, cells were fixed and stained with goat polyclonal antiserum specific for TIA-1 and mouse monoclonal antibody specific for HSV ICP27 followed by staining with Alexa 488 conjugated donkey anti-goat IgG and Alexa 568 conjugated donkey anti-mouse IgG secondary antibodies. Nuclei were stained with Hoechst 33342. Stained cells were examined by confocal microscopy and representative images of sections through the midpoint of the nuclei are shown.

Supplemental Figure 3. Acyclovir inhibits the accumulation of nuclear TIA-1 structures. **A.** HeLa cells were infected with HSV-2 strain HG52 at a MOI of 5 in the presence or absence of 5 μM acyclovir. At 10 hpi cells were fixed and stained with goat polyclonal antiserum specific for TIA-1 and mouse monoclonal antibody specific for HSV ICP27 followed by staining with Alexa 488 conjugated donkey anti-goat IgG and Alexa 568 conjugated donkey anti-mouse IgG secondary antibodies. Nuclei were stained with Hoechst 33342. Stained cells were examined by fluorescence microscopy and representative images are shown. Note the reduced presence of nuclear TIA-1

structures in the presence of acyclovir. **B.** HeLa cells were mock infected or infected with HSV-2 strain HG52 at a MOI of 5 in the presence or absence of 5 μM acyclovir and whole cell extracts were prepared at 6 hpi. Equal volumes of whole cell extracts were electrophoresed through 10% polyacrylamide gels and transferred to PVDF membranes. Membranes were probed with antisera indicated on the right.

Supplemental Figure 4. Arsenite inhibits protein synthesis in HSV-2 infected cells. Mock infected and HSV-2 infected cells were metabolically labeled with L-homopropargylglycine from 4-5 hpi in the absence (-) or presence (+) of 0.5 mM arsenite. Control cells received no L-homopropargylglycine. Newly synthesized proteins that had incorporated L-homopropargylglycine were covalently coupled to biotin azide using click chemistry and were subsequently detected by Western blotting using horseradish peroxidase conjugated streptavidin. The migration positions of molecular mass markers (kDa) are indicated on the left.

Supplemental Figure 5. Analysis of total cellular levels of TIA-1 in HSV-2 infected cells. HeLa cells were mock infected or infected with HSV-2 strain HG52 at a MOI of 10. At 4 hpi, cells were treated with 0.5 mM arsenite or mock treated (+ and -, respectively) for 30 minutes and then whole cell extracts were prepared. Equal volumes of whole cell extracts were electrophoresed through 8% polyacrylamide gels and transferred to PVDF membranes. Membranes were probed with antisera indicated on the right.