

Supporting Information for:

Cell-Selective Biological Activity of Rhodium Metalloinsertors Correlates with Subcellular Localization

Alexis C. Komor, Curtis J. Schneider, Alyson G. Weidmann, and Jacqueline K. Barton*

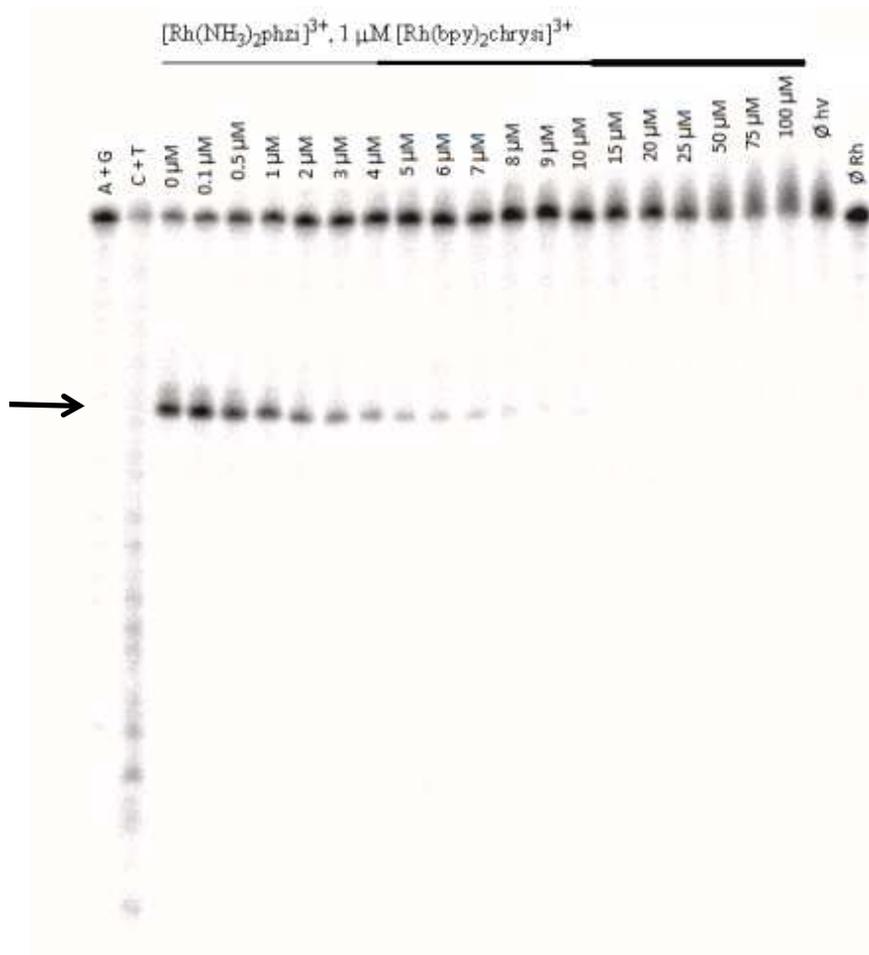


Figure S1 Binding affinities determined through DNA photocleavage. The DNA hairpin sequence is 5*'-GGCAGGCATGGCTTTTGGCCATCCTGCC-3' (underline denotes the mismatch, asterisk denotes the radiolabel). Samples were irradiated and electrophoresed through a 20% denaturing PAGE gel. A light control (ØRh, without rhodium) and dark control (Øhv, without irradiation) were included. A representative autoradiogram of a photocleavage competition titration between 1 μM *rac*-[Rh(bpy)₂(chrysi)]³⁺ and 0-100 μM [Rh(NH₃)₄(phzi)]³⁺ is shown. Arrow indicates the position of the mismatch.

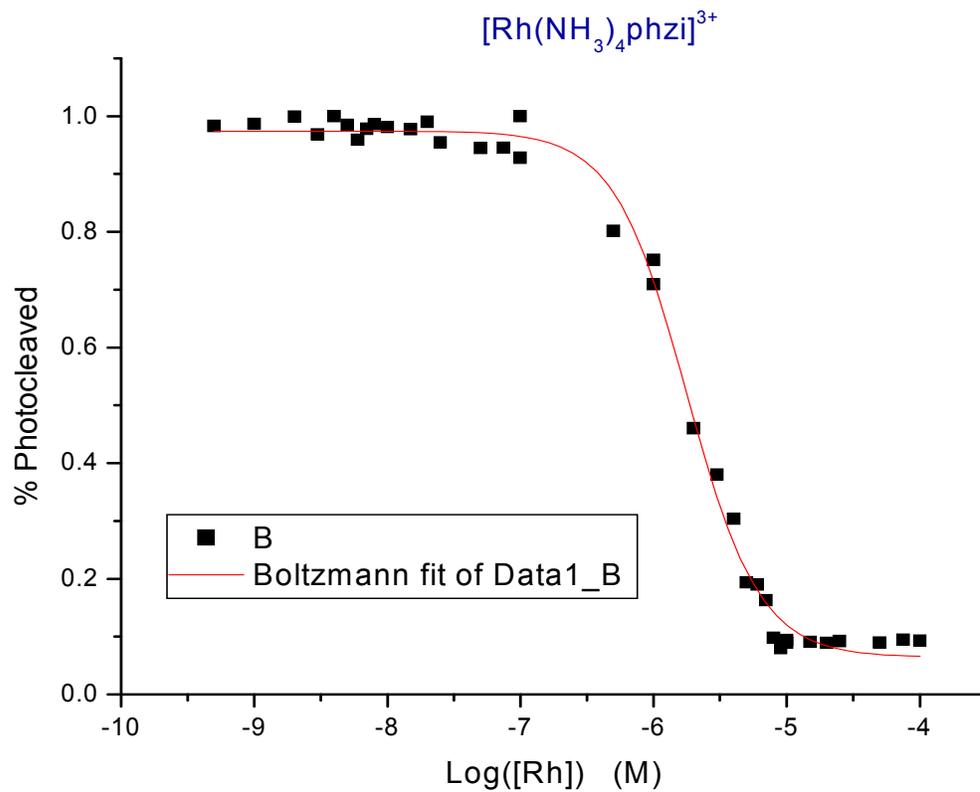


Figure S2 Representative sigmoidal curve fit of pooled data from photocleavage competition titrations between $1 \mu\text{M } \textit{rac}\text{-}[\text{Rh}(\text{bpy})_2(\text{chrysi})]^{3+}$ and $0\text{-}100 \mu\text{M } [\text{Rh}(\text{NH}_3)_4(\text{phzi})]^{3+}$ for binding constant determination is shown.

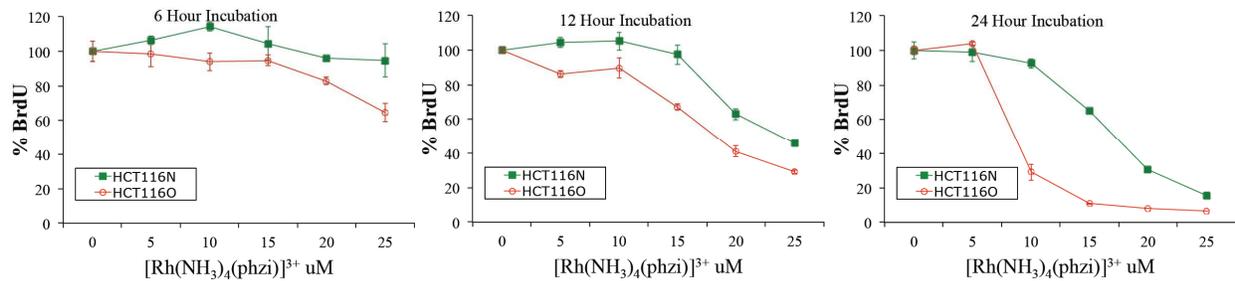


Figure S3 Inhibitory effects of $[\text{Rh}(\text{NH}_3)_4(\text{phzi})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as no activity was observed.

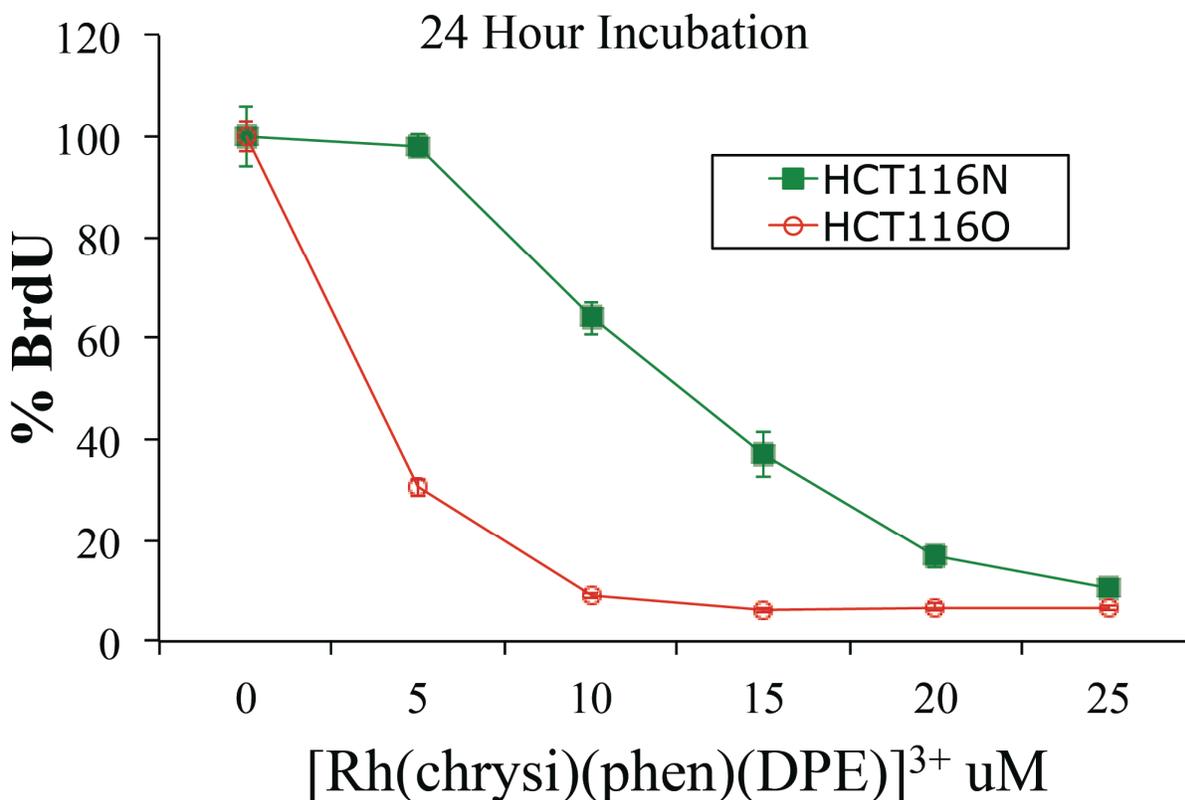


Figure S4 Inhibitory effects of $[\text{Rh}(\text{chrysi})(\text{phen})(\text{DPE})]^{3+}$. Shown is a plot of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 24 h. At the end of 24 h, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis.

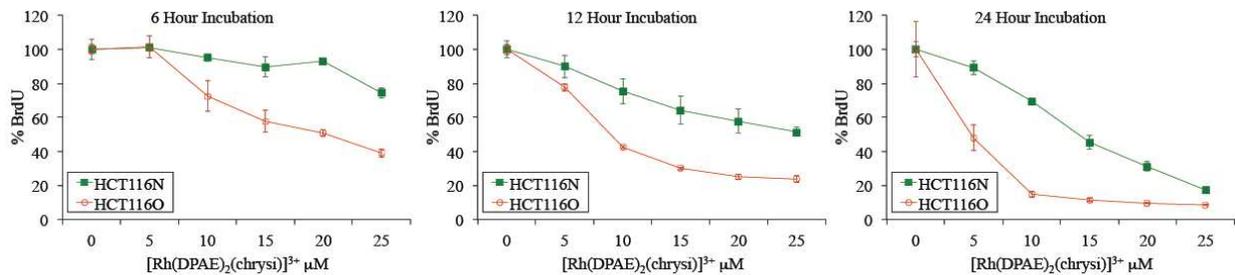


Figure S5 Inhibitory effects of $[\text{Rh}(\text{DPAE})_2(\text{chrysi})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as little to no activity was observed.

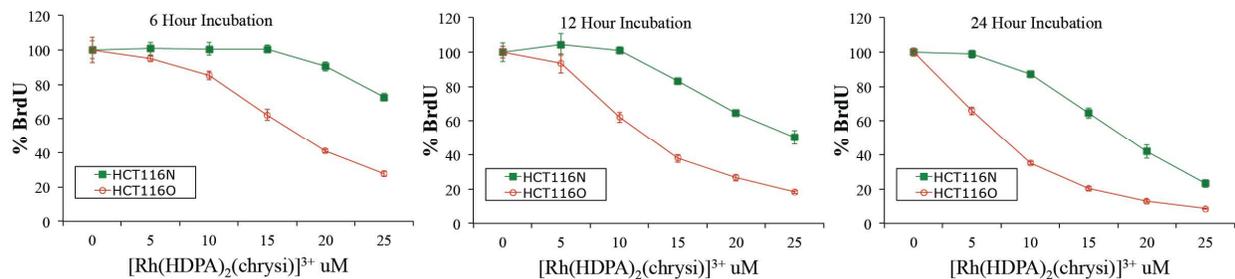


Figure S6 Inhibitory effects of $[\text{Rh}(\text{HDPA})_2(\text{chrysi})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as little to no activity was observed.

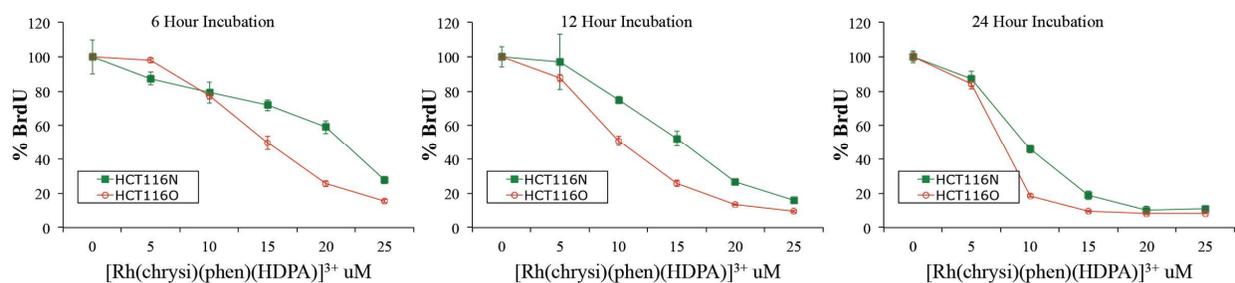


Figure S7 Inhibitory effects of $[\text{Rh}(\text{chrysi})(\text{phen})(\text{HDPA})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as little to no activity was observed.

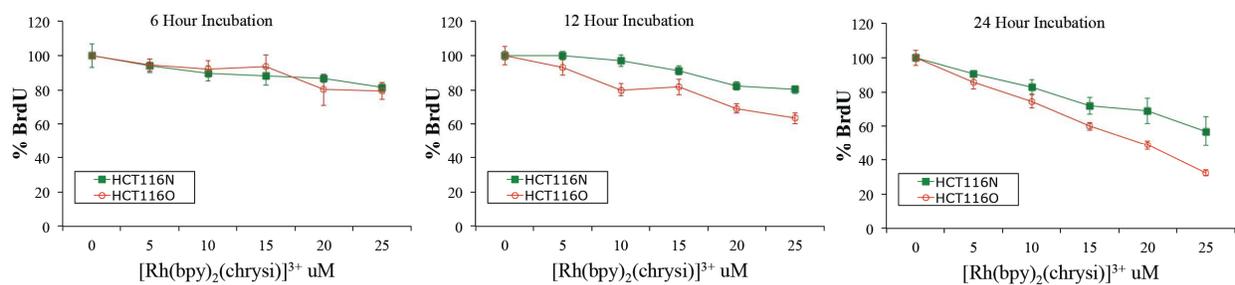


Figure S8 Inhibitory effects of $[\text{Rh}(\text{bpy})_2(\text{chrysi})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as no activity was observed.

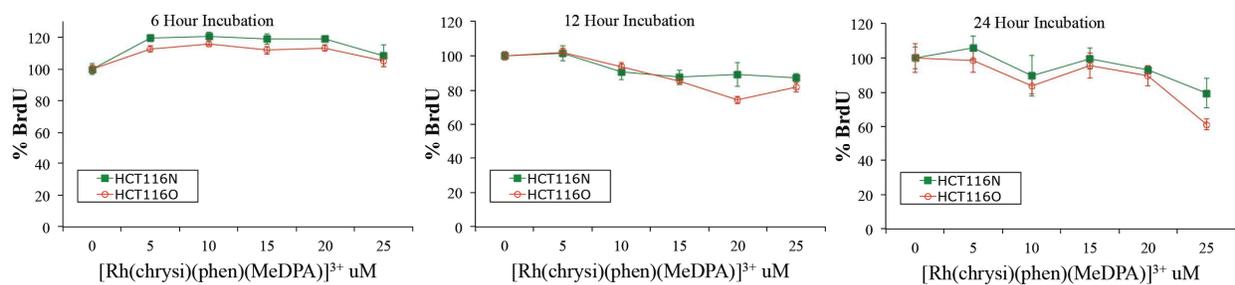


Figure S9 Inhibitory effects of $[\text{Rh}(\text{chrysi})(\text{phen})(\text{MeDPA})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as no activity was observed.

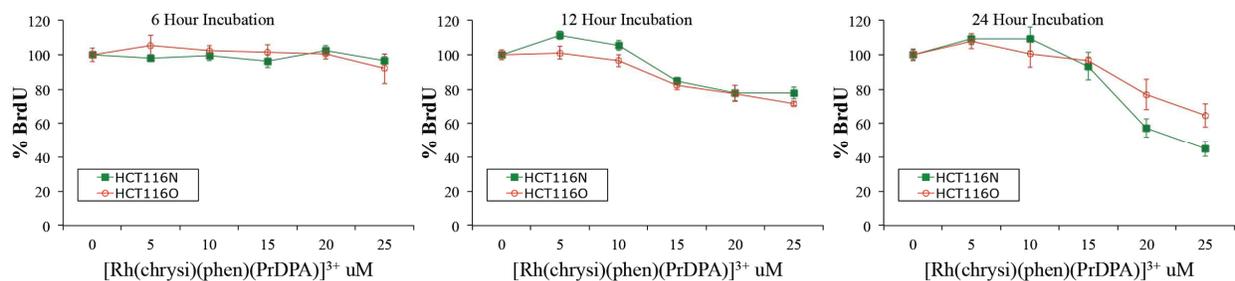


Figure S10 Inhibitory effects of $[\text{Rh}(\text{chrysi})(\text{phen})(\text{PrDPA})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as no activity was observed.

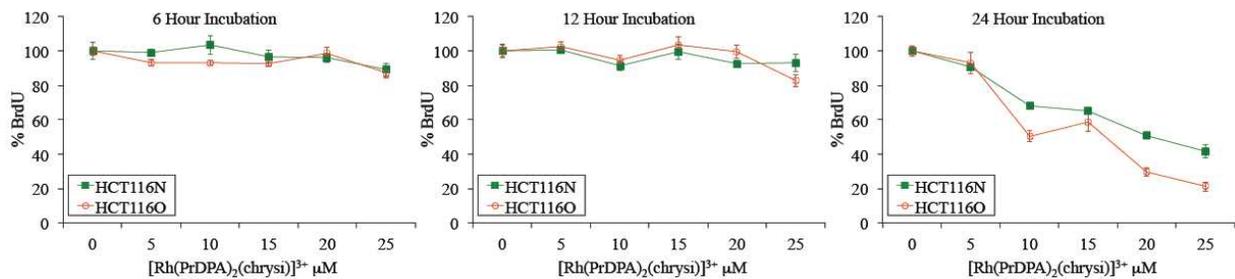


Figure S11 Inhibitory effects of $[\text{Rh}(\text{PrDPA})_2(\text{chrysi})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-25 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as no activity was observed.

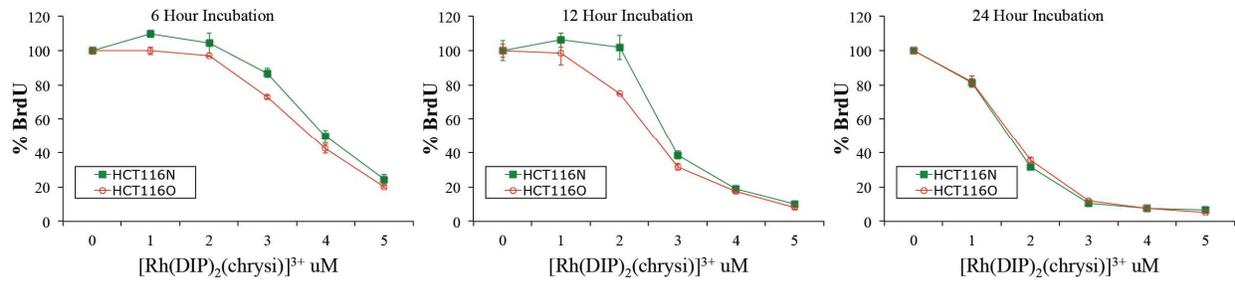


Figure S12 Inhibitory effects of $[\text{Rh}(\text{DIP})_2(\text{chrysi})]^{3+}$ as a function of incubation time on cellular proliferation. Shown are plots of BrdU incorporation (a measure of DNA synthesis and therefore cellular proliferation) normalized to the BrdU incorporation of untreated cells as a function of rhodium concentration. Standard error bars for five trials are shown. MMR-proficient HCT116N cells (green) and MMR-deficient HCT116O cells (red) were plated and allowed 24 h to adhere before incubation with 0-5 μM for 1, 3, 6, 12, or 24 h. At the end of the incubations, the medium containing rhodium was replaced with fresh medium for the remainder of the 72 h period, followed by ELISA analysis. BrdU was added to the medium 24 h prior to analysis. 1 and 3 h plots are not shown, as little to no activity was observed.