# Noradrenaline decreases G0/G1 and increases S and G2/M phases of cell cycle while Ruthenium-Noradrenaline reverses these effects. Targeting tumour cellular growth

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**Introduction**. Neoplasia is defined as disorderly proliferation of cells with independent growth and loss of cellular differentiation. These cells can develop regardless of normal mechanisms that control cellular proliferation[1]. New compounds that regulate the cell cycle could be interesting targets to cancer therapy. Catecholamines, such as Noradrenaline (NA) and Adrenaline (A), are involved in the control of vascular tone and blood flow which are important determinants to tumour growth[2,3]. In the present work, we developed a ruthenium-catecholamine complex, i.e., ruthenium-noradrenaline (Ru-NA), with the following formula "$[Ru(NH_3)_4(NA)]Cl$", that has a steric hindrance on catechol site to evaluate the effect of this compound on cell cycle and cellular proliferation. **Methods**. The complex was characterized by UV-vis, FTIR, Raman, NMR spectroscopies, mass spectrometry, HPCL and electrochemical analyses. Cell cycle was evaluated on human umbilical vein endothelial cells (HUVEC) using Propidium Iodide (PI; 100 mg/mL) by flow cytometry. The cells were incubated 24h or 48h with vehicle, Noradrenaline (NA; 300 µM) or Ru-NA (300 µM). Intracellular calcium mobilization was measured on HUVEC with the selective dye for intracellular calcium Fluo-3AM (3 µM, 30 min) in the absence (basal condition) or presence of NA (1 µM) or Ru-NA (300 µM) after 10 minutes of stimulation. The wound-healing assay was performed on GAMG cells (human glioblastoma) in the absence or presence of NA or Ru-NA (200 µM) after 24h. One-way ANOVA, followed by Newman-Keuls pos-hoc were used as statistical analyses ($P<0.05$). **Results**. NA reduced G0/G1 phase and increased on S and G2/M phases compared to vehicle. Ru-NA reverted NA effect on G0/G1 and S phases after 24h. Ru-NA tended to increase G0/G1 phase and significantly reduced S phase compared to vehicle after 48h. Calcium mobilization was not changed by NA or Ru-NA. In the wound-healing assay, NA had no effect on cell growth and proliferation compared to control but Ru-NA decreased this parameters. **Conclusion**. Together, the results suggest that NA regulate cell cycle leading to cell growth and proliferation and Ru-NA reverses these effects in vascular and cancer cells, which could be interesting on control of tumour growth.

**References**

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