

Ipatasertib, an oral AKT inhibitor, effectively inhibits cell proliferation and migration, and induces apoptosis in serous endometrial cancer cell lines *in vitro*: Endometrial Cancer Molecularly Targeted Therapy Consortium

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Introduction & Objectives

- Ipatasertib (IPAT) is an orally administered, selective protein kinase B (AKT) inhibitor.
- Data has been promising for IPAT's action against solid tumors in both pre-clinical studies and clinical trials.
- IPAT targets the PI3K/AKT/mTOR pathway, making endometrial cancer (EC) an apt candidate for investigation.
- Serous EC is more aggressive and less chemo-responsive in the recurrent setting than endometrioid EC.
- Our study evaluated the anti-proliferative efficacy of IPAT in human serous EC cell lines.

Materials & Methods

- Two human serous EC cell lines were chosen for this study: ARK-1 (PTEN wild type), and SPEC-2 (PTEN mutant).
- Cells were exposed to varying concentrations of IPAT (Genentech).
- Cell proliferation was assessed by MTT and colony assays.
- Cell cycle progression was measured by Cellometer.
- Apoptosis was assessed by cleaved caspase-3 assay.
- Cell adhesion and wound healing assays were used to evaluate impact on cell migration and invasion.
- Western immunoblotting determined effects on CDK4, CDK6, BCL-1, MCL-1, and snail and slug proteins.
- Pathway protein expression was analyzed by western immunoblotting.

Results

Figure 1: IPAT inhibits cell proliferation

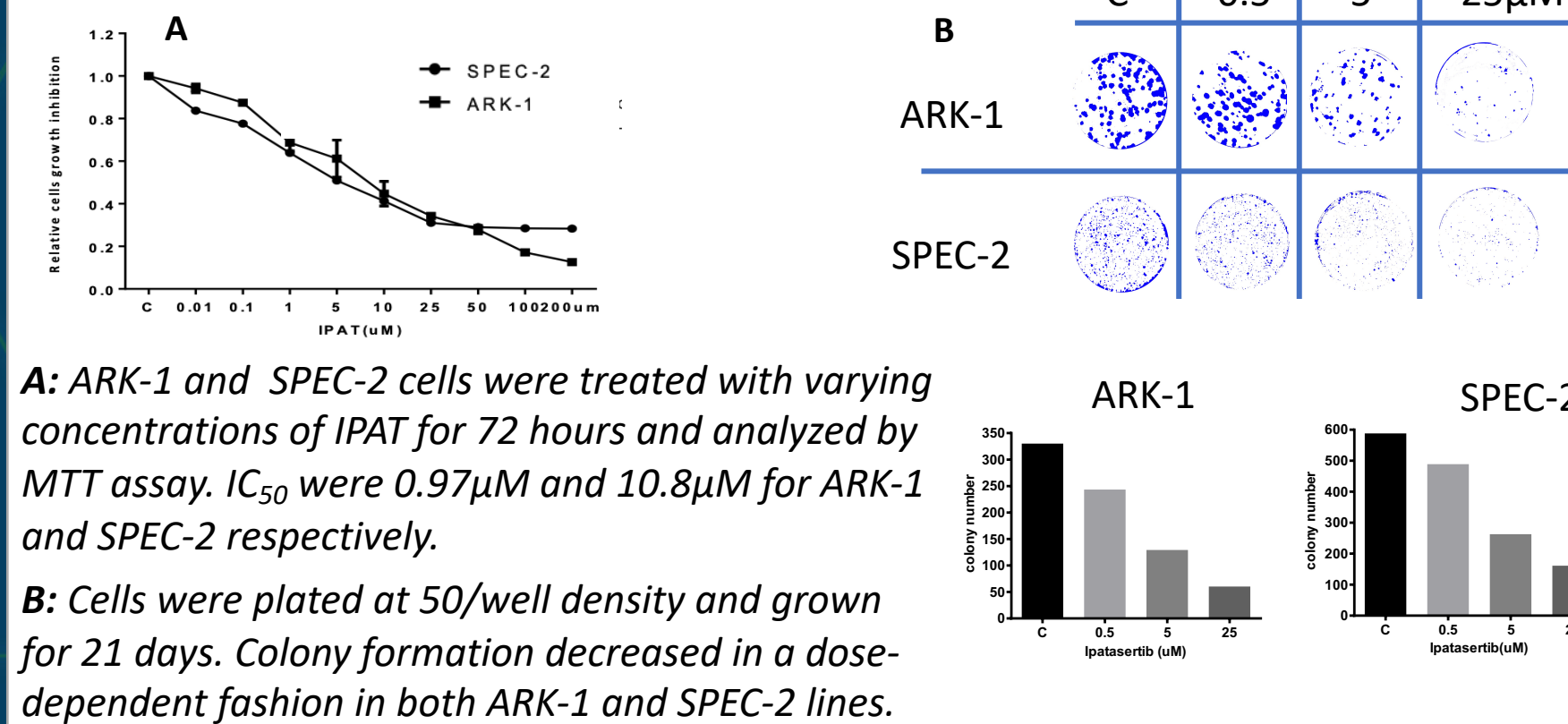


Figure 3: IPAT induces apoptosis via cleaved caspase 3

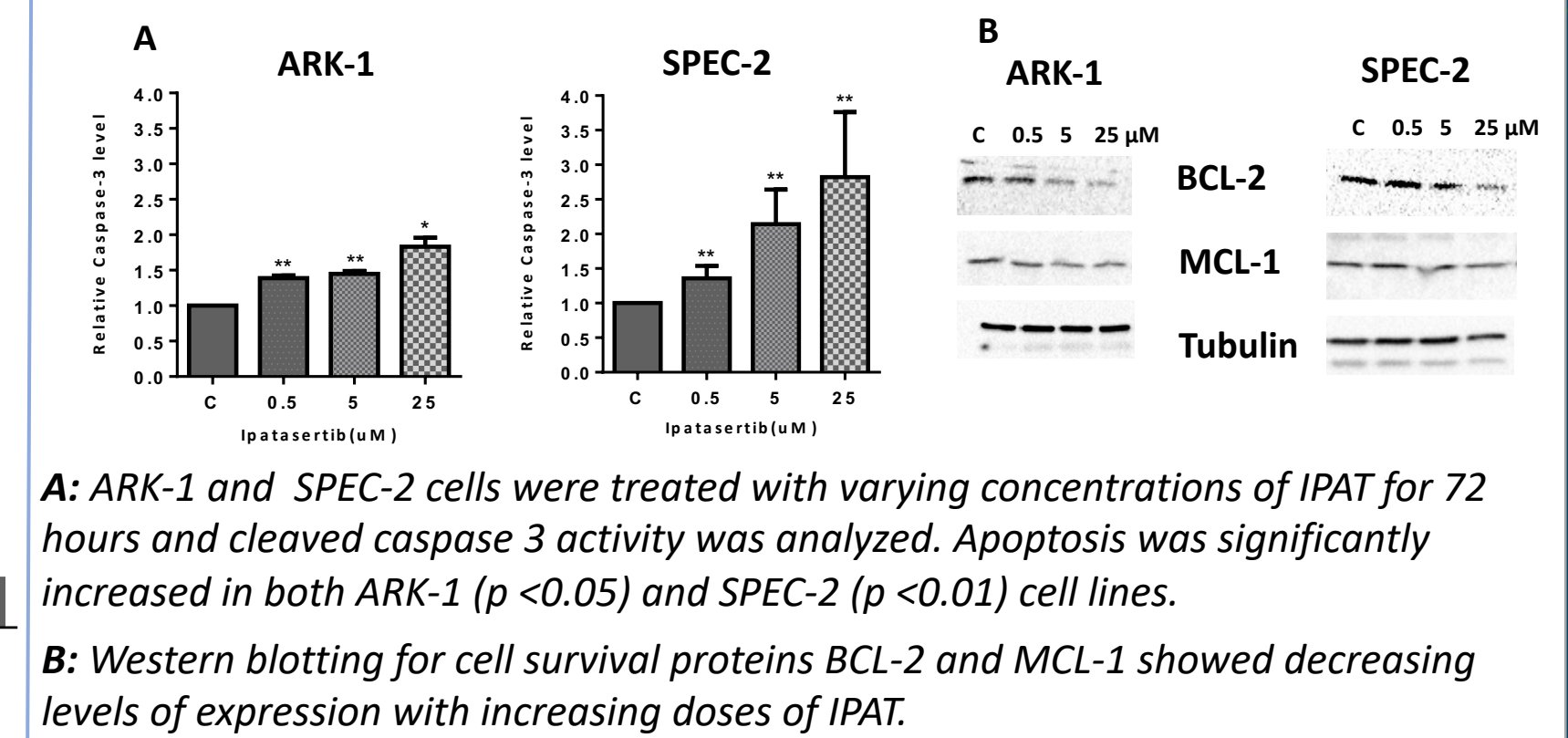


Figure 2: IPAT induces cell cycle arrest

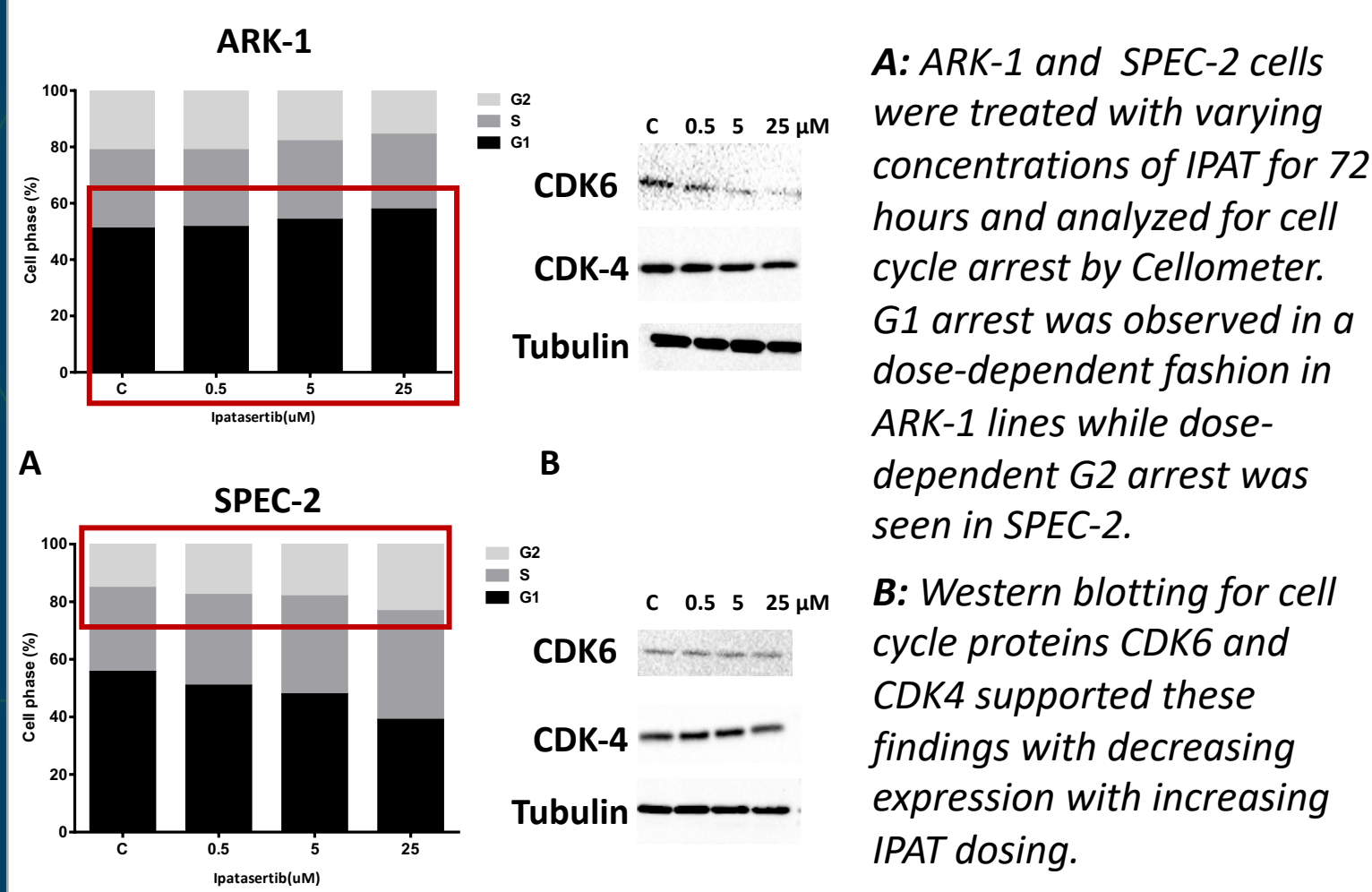
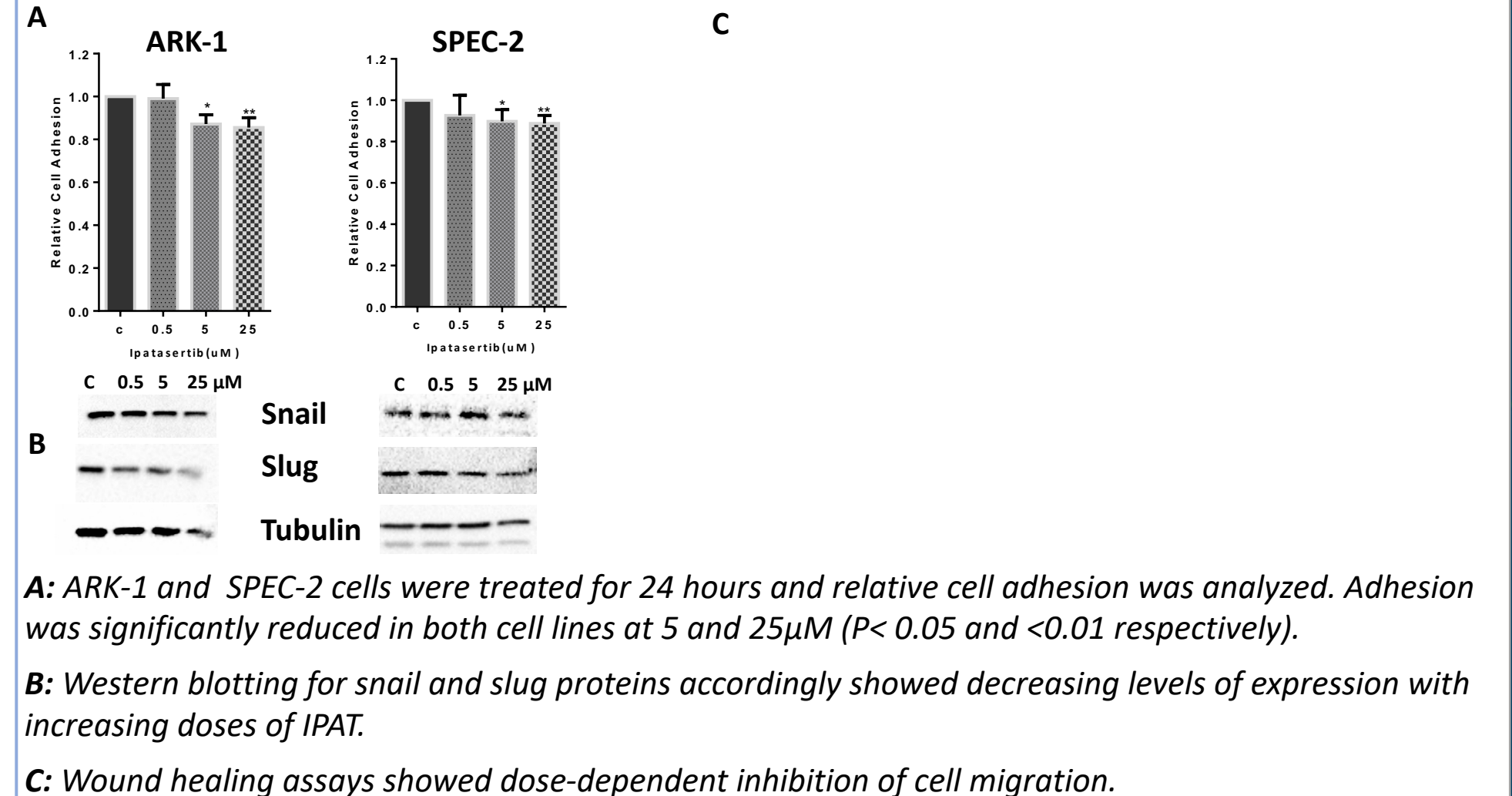
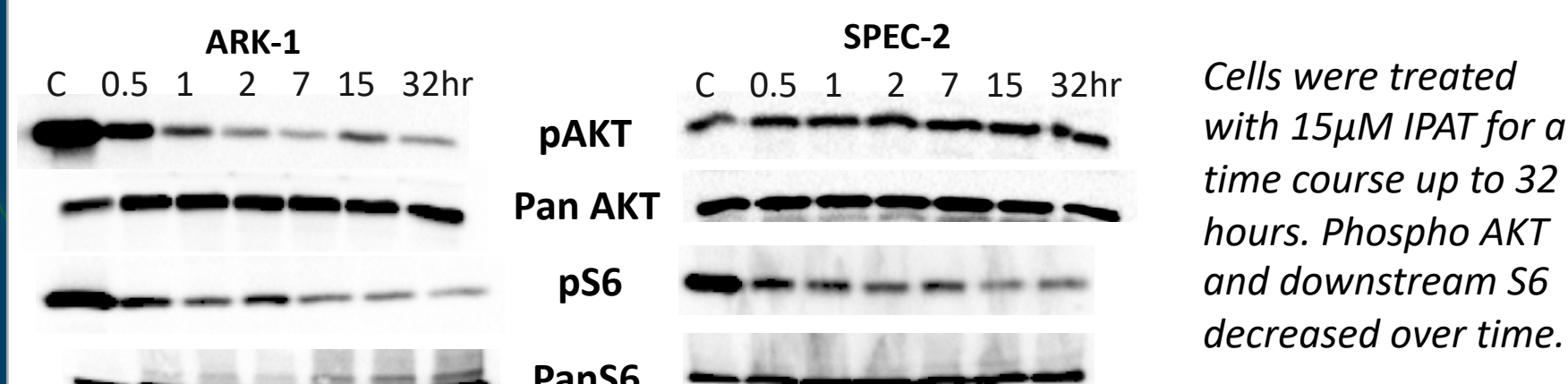


Figure 4: IPAT inhibits cell adhesion and migration



Results

Figure 5: IPAT alters expression of AKT pathway proteins



Conclusions

- IPAT significantly suppressed cell proliferation through inducing cell cycle arrest and apoptosis as well as inhibiting adhesion and migration in human serous EC cell lines.
- IPAT may be a promising targeted agent in the treatment of serous EC.
- Studies in transgenic and patient-derived xenograft EC mouse models are underway to assess the *in vivo* efficacy of IPAT.