**SUPPLEMENTAL MATERIALS AND METHODS**

**Cell lines.** All cell lines were purchased from American Type Culture Collection (ATCC) and were cytogenetically tested and authenticated before being frozen. Each vial of frozen cells was thawed and maintained in culture for a maximum of 8 weeks. Enough frozen vials of each cell line were available to ensure that all cell-based experiments were conducted on cells that had been tested and in culture for 8 weeks or less. HCT116 and HT29 human colon cancer cells were cultured in McCoy’s 5A medium supplemented with 10% fetal bovine serum (FBS; Atlanta Biologicals, Lawrenceville, GA) and 1% antibiotic-antimycotic. DLD1 human colon cancer cells were cultured in RPMI1640 medium supplemented with 10% FBS (Atlanta Biologicals, Lawrenceville, GA) and 1% antibiotic-antimycotic.

**Reagents and antibodies.** Herbacetin (purity: > 90% by HPLC) was purchased from Indofine Chemical Company (Hillsborough, NJ). CNBr-Sepharose 4B beads were purchased from GE Healthcare (Piscataway, NJ). The recombinant human ODC protein was obtained from Abnova (Walnut, CA). The screening to determine the effect of herbacetin on the activity of 13 kinases was performed by Millipore (Temecula, CA). The antibody to detect Xpress was from Invitrogen (Grand Island, NY). Antibodies to detect total ERKs, phosphorylated ERKs (T202/Y204), total RSK and phosphorylated RSK (T356/S360) were from Cell Signaling Technology (Beverly, MA). Antibodies against ODC and -actin were purchased from Santa Cruz Biotechnology (Santa Cruz, CA).

**Lentiviral infection.** The lentiviral expression vector, *pLKO.1-shODC,* and packaging vectors, *pMD2.0G* and *psPAX*, were purchased from Addgene Inc. (Cambridge, MA). To prepare ODC viral particles, the viral vector and packaging vectors were transfected using JetPEI into HEK293T cells following the manufacturer’s suggested protocols. The transfection medium was changed at 4 h after transfection and then cells were cultured for 36 h. The viral particles were harvested by filtration using a 0.45 mm sodium acetate syringe filter and then combined with 8 g/ml of polybrane (Millipore, Billerica, MA) and infected overnight into 60% confluent HCT116 cells. The cell culture medium was replaced with fresh complete growth medium and after 24 h, cells were selected with 1.5 g/ml of puromycine for 36 h. The selected cells were used for experiments.

**Anchorage-independent cell growth.** Cells (8 × 103 per well) suspended in complete growth medium (McCoy’s 5A or RPMI1640 supplemented with 10% FBS and 1% antibiotics) were added to 0.3% agar with different doses of each compound in a top layer over a base layer of 0.6% agar with the same doses of each compound as in the top layer. The cultures were maintained at 37°C in a 5% CO2 incubator for 3 weeks and then colonies were counted under a microscope using the Image-Pro Plus software (v.4) program (Media Cybernetics).

**Luciferase assay for reporter activity.** Transient transfection was conducted using jetPEI (Qbiogene, Carlsbad CA) and assays for the activity of firefly *luciferase* and *Renilla* activity were performed according to the manufacturer’s instructions (Promega, Madison, WI). Cells (1 x 104 per well) were seeded the day before transfection into 12-well culture plates. Cells were co-transfected with reporter plasmid (250 ng) and internal control (*CMV-Renilla*, 50 ng) in 12-well plates and incubated for 24 h. Colon cancer cells were treated with herbacetin for 48 h and harvested in Promega Lysis Buffer. The *Luciferase* and *Renilla* activities were measured using substrates in the reporter assay system (Promega). The *luciferase* activity was normalized to *Renilla* activity.

**Cell proliferation assay.** Cells were seeded (1 × 103 cells per well) in 96-well plates and incubated for 24 h and then treated with different doses of each compound. After incubation for 1, 2 or 3 days, 20 μl of CellTiter96 Aqueous One Solution (Promega) were added and then cells were incubated for 1 h at 37°C in a 5% CO2 incubator. Absorbance was measured at 492 nm.