# BIOLOGICAL ACTIVITY

**FGTI-2734** is a RAS C-terminal mimetic dual **farnesyl transferase (FT)** and **geranylgeranyl transferase-1 (GGT)** inhibitor with IC₅₀ values of 250 nM and 520 nM for FT and GGT, respectively. FGTI-2734 can prevent membrane localization of KRAS, hence solving KRAS resistance problem and thwarting mutant KRAS patient-derived pancreatic tumors[^1].

**IC₅₀ & Target**

**IC₅₀**: 250 nM (for FT) and 520 nM (for GGT)[^1]

**In Vitro**

FGTI-2734 (1-30 μM; 72 hours) induces CASPASE-3 and PARP cleavage in MiaPaCa2, L3.6pl and Calu6 cells[^1]. FGTI-2734 (3-30 μM; 72 hours) inhibits both protein prenylation of HDJ2, RAP1A, KRAS and NRAS. FGTI-2734 inhibits KRAS membrane localization in RAS-transformed murine NIH3T3 cells and in mutant KRAS human cancer cells[^1].

**Apoptosis Analysis[^1]**

- **Cell Line:** MiaPaCa2, L3.6pl and Calu6 cells
- **Concentration:** 1, 3, 10, 30 μM
- **Incubation Time:** 72 hours
- **Result:** Induced CASPASE-3 and PARP cleavage in MiaPaCa2, L3.6pl and Calu6 cells.

**Western Blot Analysis[^1]**

- **Cell Line:** KRAS, HRAS, and NRAS-transformed NIH3T3 cells
- **Concentration:** 3, 10, 30 μM
- **Incubation Time:** 72 hours
- **Result:** Inhibited both protein prenylation of HDJ2, RAP1A, KRAS and NRAS.

**In Vivo**

FGTI-2734 (intraperitoneally; 100 mg/kg/daily for 18 to 25 days) only inhibits tumor growth in mutant KRAS-dependent tumors but not in mutant KRAS-independent tumors[^1].
**Animal Model:** Male SCID-bg mice following injection of MiaPaCa2, L3.6pl, Calu6, A549, H460 and DLD1 cancer cells[^1]

**Dosage:** 100 mg/kg

**Administration:** Intraperitoneally; daily; for 18 to 25 days

**Result:** Inhibited tumor growth in mutant KRAS-dependent tumors.

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**REFERENCES**