Investigating the Mechanism of Action Behind Novel Anti-Cancer Drugs

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Contributions to medicine – why does this research matter?

• Minimize side effects and toxicity in cancer patients receiving chemotherapy
• Advance current knowledge in the area of microtubule-targeted drugs
Research goals

- **Long-term**: determine a mechanism of action for Ind-V and AS6-H (microtubule-targeting drugs)

- **Short-term**: develop new assays to measure drug activity
  1. Immunofluorescence assay – qualitative info on microtubule structure
  2. Viacount assay – measure cell proliferation on a large scale
  3. Light scattering assay – measure amount of *in vitro* polymerized tubulin
  4. *In vivo* microinjection assay

*In vivo methods*: immunofluorescence (1) and microinjection for future experiments

- Primary antibody bound to tubulin protein
- Secondary antibody with fluorescent dye

Immunofluorescence schematic by Thermo-Fisher Scientific

Rhodamine-tubulin injected MCF7 breast cancer cell recorded by Kathy Kamath
**In vitro methods: light scattering assay (3)**

- **In vitro** = “test-tube experiment”
- Measures the amount of protein that polymerizes in the presence of different drug concentrations
- Less polymerized protein suggests that the drug inhibits microtubule polymerization, freezing the cells in mitosis

1. Immunofluorescence data shows the proportion of cells arrested in mitosis

**Mitotic index** = \( \frac{\text{Mitotic cells}}{\text{Total # of cells}} \)
2. Viacount assay data shows that higher drug concentrations lead to an increase in cell death

![Viacount assay data](image)

**Summer 2018 in review**

**Summer goals:**
1. Immunofluorescence assay
2. Viacount assay
3. Light scattering assay

**Results:**
1. Mitotic index from **immunofluorescence experiments** increases with drug concentration, suggesting that Ind-V induces cell cycle arrest in a concentration-dependent manner
2. Data from **Viacount assays** support the idea that the effects of Ind-V are concentration-dependent
3. Past data from **light scattering assays** shows that AS6-H decreases the amount of polymerized protein formed
Future goals and acknowledgements

• **In the future:**
  • Experiments:
    • Microinjection experiment with Ind-V and AS6-H
    • Additional flow cytometry experiments
  • Long-term goals:
    • Determine a mechanism of action for Ind-V & AS6-H
    • Eventually introduce the drug to human clinical trials

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