



# Inhibiting Holliday Junction Resolution: A Novel Antibacterial Target

## Controlling cellular proliferation by attacking an intracellular target

Holliday junctions (HJ) are central intermediates in many essential prokaryotic and eukaryotic cellular processes. Homologous recombination (HR) and site-specific recombination (SSR) performed by tyrosine recombinases are the canonical pathways for the formation of HJ. In eukaryotes, HR is mandatory for meiosis. In both prokaryotes and eukaryotes, recombination repair of DNA lesions and collapsed replication forks proceed through HJ intermediates. Therefore, inhibiting the resolution of HJ provides a novel target for reducing cellular

proliferation, critical in controlling bacterial infections and cancer.

Dr. Anca Segall of San Diego State University has designed a series of peptides that kill bacteria by interfering with the activity of intracellular targets involved in the resolution of HJ. The peptides cause accumulation of DNA breaks that leads to filamentation, faulty DNA partitioning and anucleate cells. The peptides bind to branched DNA repair intermediates, thereby blocking its completion and decreasing cell viability.

The HJ-trapping peptides inhibit the proliferation of both gram(-) and gram(+) bacteria and show a synergistic effect on cancer cells when used with DNA-nicking chemotherapies. Because the peptides inhibit a replication process most prevalent in rapidly dividing cells (e.g., cancer, bacteria), their collateral effect on normal cells is minimal.

Dr. Segall has also devised a means of screening for peptide inhibitors of HJ resolution that work with enzymes that can be used to block prokaryotic binary

fission. This is an excellent means of developing antibiotics that specifically attack bacteria without harming host eukaryotic cells.

This technology is a superb method of dealing with the growing list of antibiotic resistant strains of bacteria and of discovering new cancer therapy drugs.

### Benefits

- Minimal toxicity issues
- A new mechanism of action
- Addresses current medical needs
- Inhibits gram+ and gram- bacteria
- Synergistic activity with DNA-nicking compounds

### Advantages Over Existing Technology

- Enables discovery of a broader range of antibiotics
- Lower resistance rate
- Target to specific cell types
- Non-cytotoxic long-term expression



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