

You are working in the DNA sequencing facility at a large research institution that is studying resistance of bacteria to antibiotics and your group is collaborating with other bacteriologists from around the world. Your collaborators in Africa have isolated a strain of *Neisseria meningitidis* from a Sudanese patient suffering from bacterial meningitis; they found that this bacterium (Case A) is sensitive to sulfonamide drugs (one of the first types of antibiotic to be developed for human use)¹. Your collaborators in Scandinavia have isolated a strain of *N. meningitidis* from a Norwegian patient suffering from bacterial meningitis; they found that this bacterium (Case B) is resistant to these drugs. Your collaborators in North Carolina have isolated a strain of *Escherichia coli* (Case C) that is sensitive to sulfonamide drugs and another strain of *E. coli* (Case D) that is resistant to these drugs.²

You sequence part of the dihydropteroate synthase gene in each strain and find the following results (the *non-template* strand is shown, 5' to 3'):

A: 5'-ACGCCCGATTCTTTTTCCGACGGCGGGCGCG-3'

B: 5'-ACGCCCGATTCTTTGTCCGACGGCGGGCGCG-3'

C: 5'-ACGCCTGATTCTTTTTCGGATGGTGGCACG-3'

D: 5'-ACGCCTGATTCTTTGTCGGATGGTGGCACG-3'

1.* Assuming a nucleotide difference(s) within this region are responsible for sulfonamide resistance of these strains, which nucleotide difference(s) among these strains do you think is responsible for drug resistance? Why?

2. Why would the dihydropteroate enzyme be a good drug target? (Think about how you would explain your answer to Bio067 students)**

3. Have bacteria been discovered with mechanisms of sulfonamide resistance other than mutations in this enzyme? (Think about how you would explain one such mechanism to Bio067 students)**

* Each group of Bio067 students will work to predict protein sequence from one of these cases, then we will compare the sequences among four cases to determine whether we can develop a hypothesis about what part of the protein is important for sulfonamide drugs to be effective.

** You can consult *scientific* sources on the web to address these questions.

¹ This case is based on a study by Fermer, C., Kristiansen, B.-E., Skold, O. and Swedberg, G. (1995) "Sulfonamide resistance in *Neisseria meningitidis* as defined by site-directed mutagenesis could have its origin in other species" *J. Bact.* **177**: 4669-4675.

² This case is based on a study by Dallas, W.S., Gowen, J. E., Ray, P. H., Cox, M. J. and Dev, I. K. (1992) "Cloning, sequencing, and enhanced expression of the dihydropteroate synthase gene of *Escherichia coli* MC4100" *J. Bact.* **174**: 5961-5970.