🔬 **Deciphering Antibiotic Resistance in DHFR Mutants**

In my first study in 2022, **"DHFR Mutants Modulate Their Synchronized Dynamics with the Substrate by Shifting Hydrogen Bond Occupancies,"** we explored how mutations in dihydrofolate reductase (DHFR) reshape enzyme dynamics and substrate interactions, contributing to antibiotic resistance.

Using **molecular dynamics simulations (sub-microsecond range)**, we classified nine trimethoprim-resistant DHFR mutants based on their mechanisms:

🧬 **Direct modifications** – Mutants like L28R and W30G alter the binding site structure.
⚙️ **Structural distortions** – W30R introduces a new salt bridge (E139-R30), disrupting binding affinity.
🤯 **Allosteric & dynamic shifts** – Our findings suggest a potential cryptic site arising from allosteric and dynamic effects, where mutations (D27E, F153S, I94L) modify a hydrogen-bonding motif, impacting site flexibility.
📎 **Epistatic mutations** – I5F, A26T, and R98P appear sequentially, suggesting interdependent evolution.

Our findings highlight **hydrogen bond dynamics** as a key factor in antibiotic resistance, offering valuable insights for developing more effective inhibitors.

📎 Read more: DOI Link

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