

Toxicity of DNA Intercalating Agents in the Human Body



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INTRODUCTION:

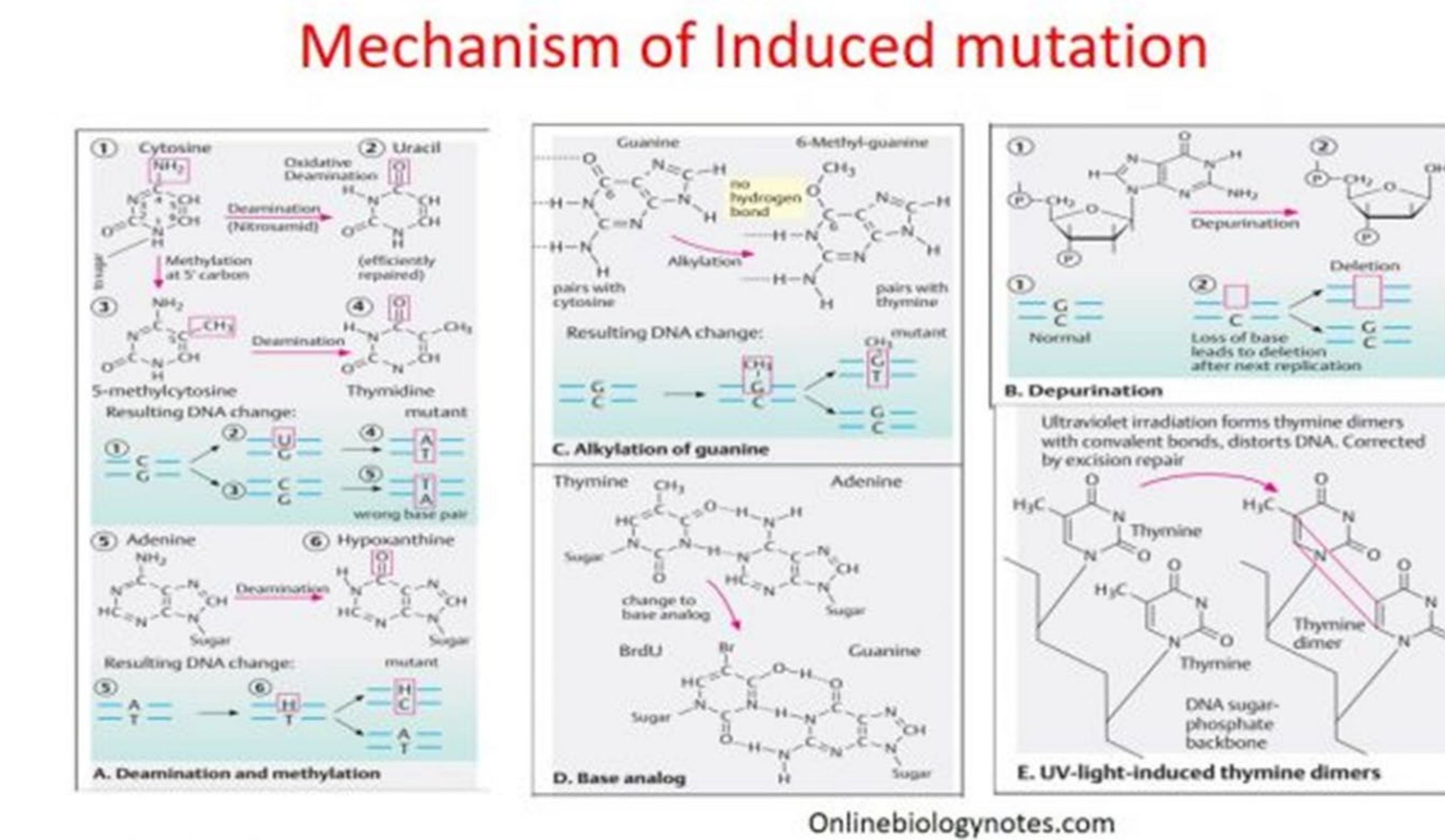
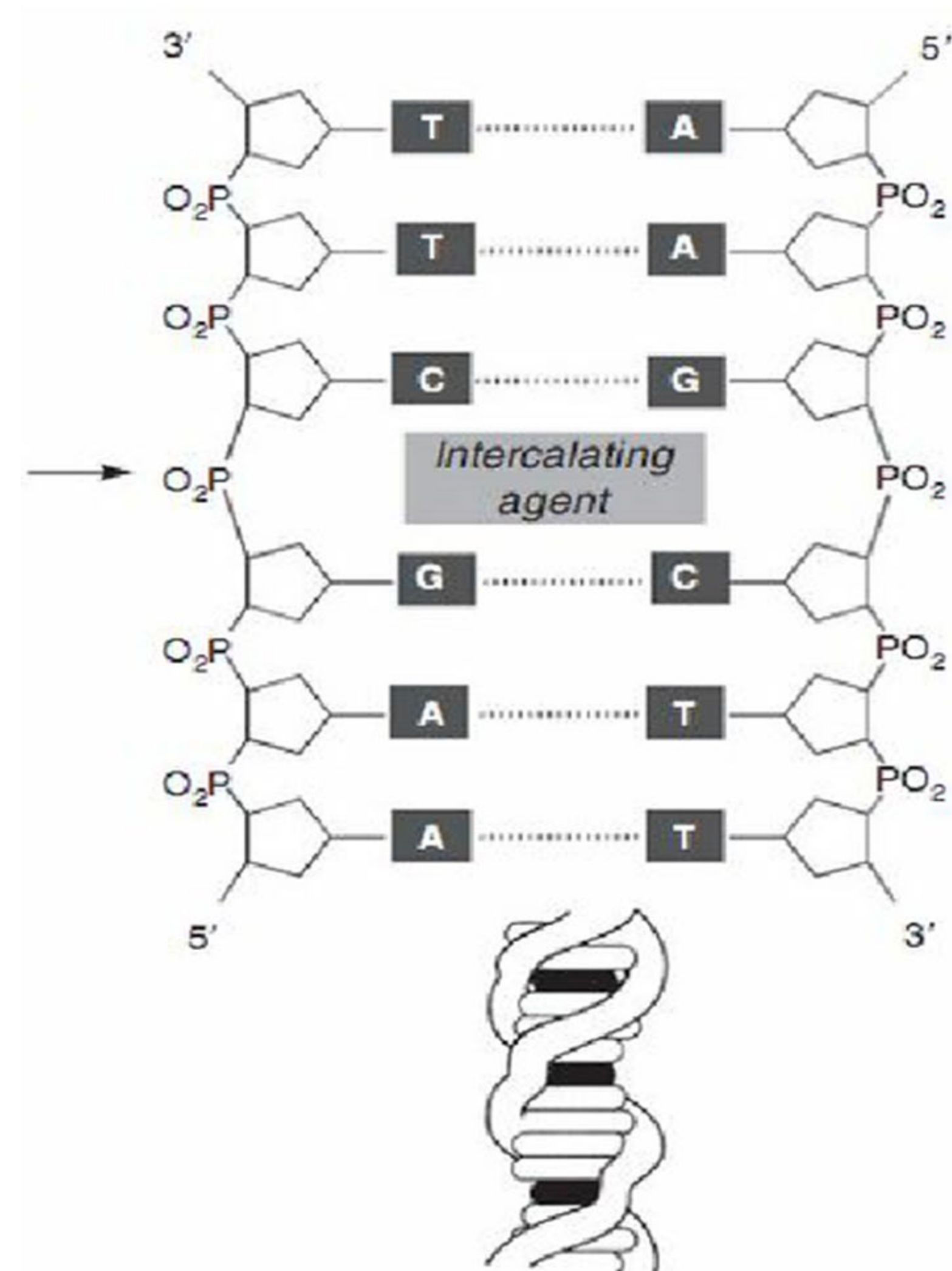
Throughout this Poster I will be showing the research and knowledge I have gathered not only on the importance of this topic but on how Intercalating agents could possibly be used in the future as a possible very successful cancer treatment. Discussed will be the mechanism and concepts of the process that these drugs perform inside the body.

Purpose:

The main purpose for research in this field mainly leads to the ideology of procuring a treatment to cancer that is less damaging to healthy cells than radiation therapy. With exceeding research in this field, the possibility of targeted cell destruction using these compounds could be very possible.

Intercalation?

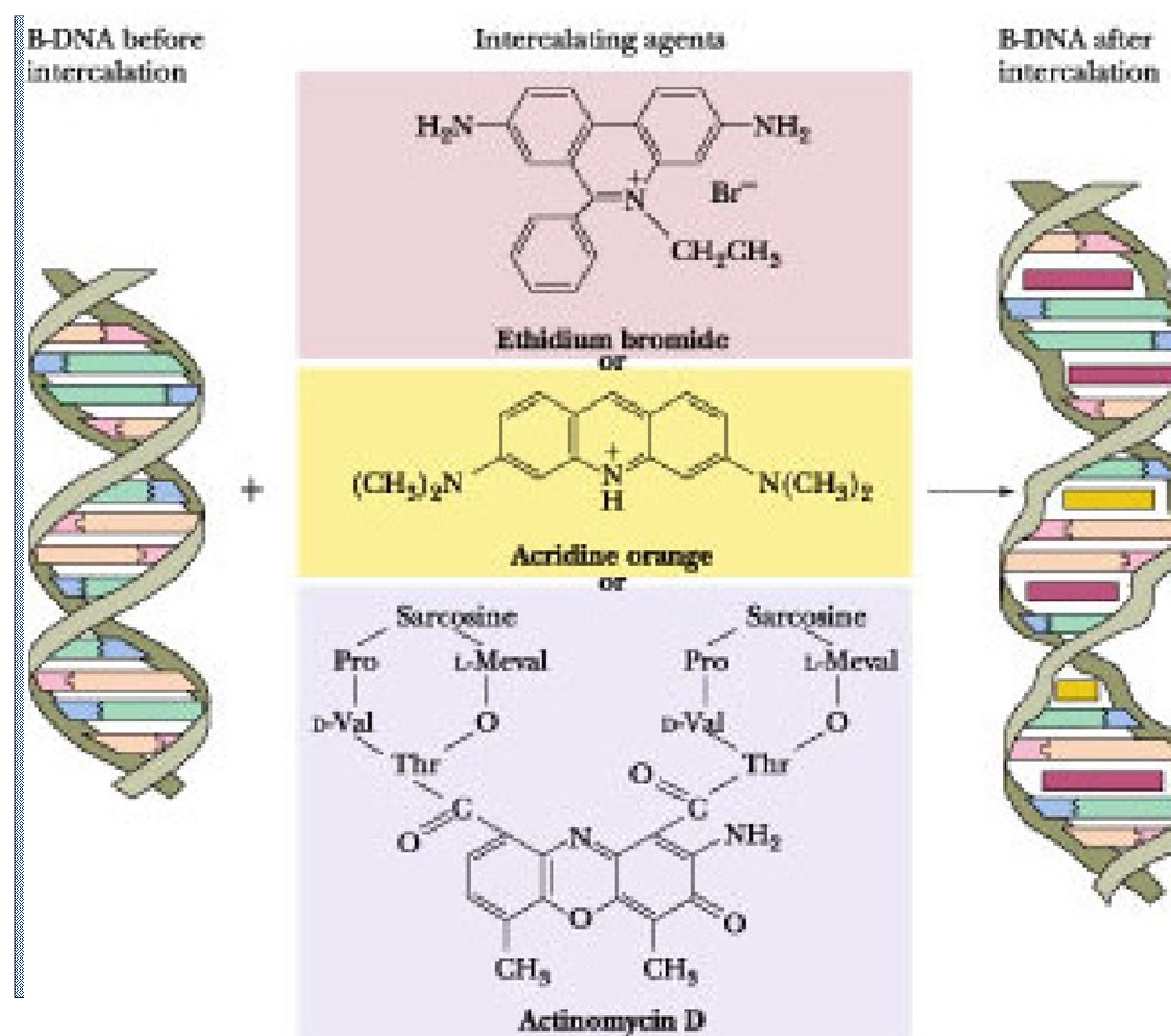
- It is the Insertion of molecules into nucleic acid structures to create space.
- The binding of these agents bind in planar fashion as to fit completely in the DNA molecule
- This interrupts the basic structure of the DNA molecule
- This insertion is very toxic to the cell and to the body, so this leads to cell death and the halting of cell replication



Chemical Mechanisms of Intercalation occurring

Agents, Mechanisms and Toxicity:

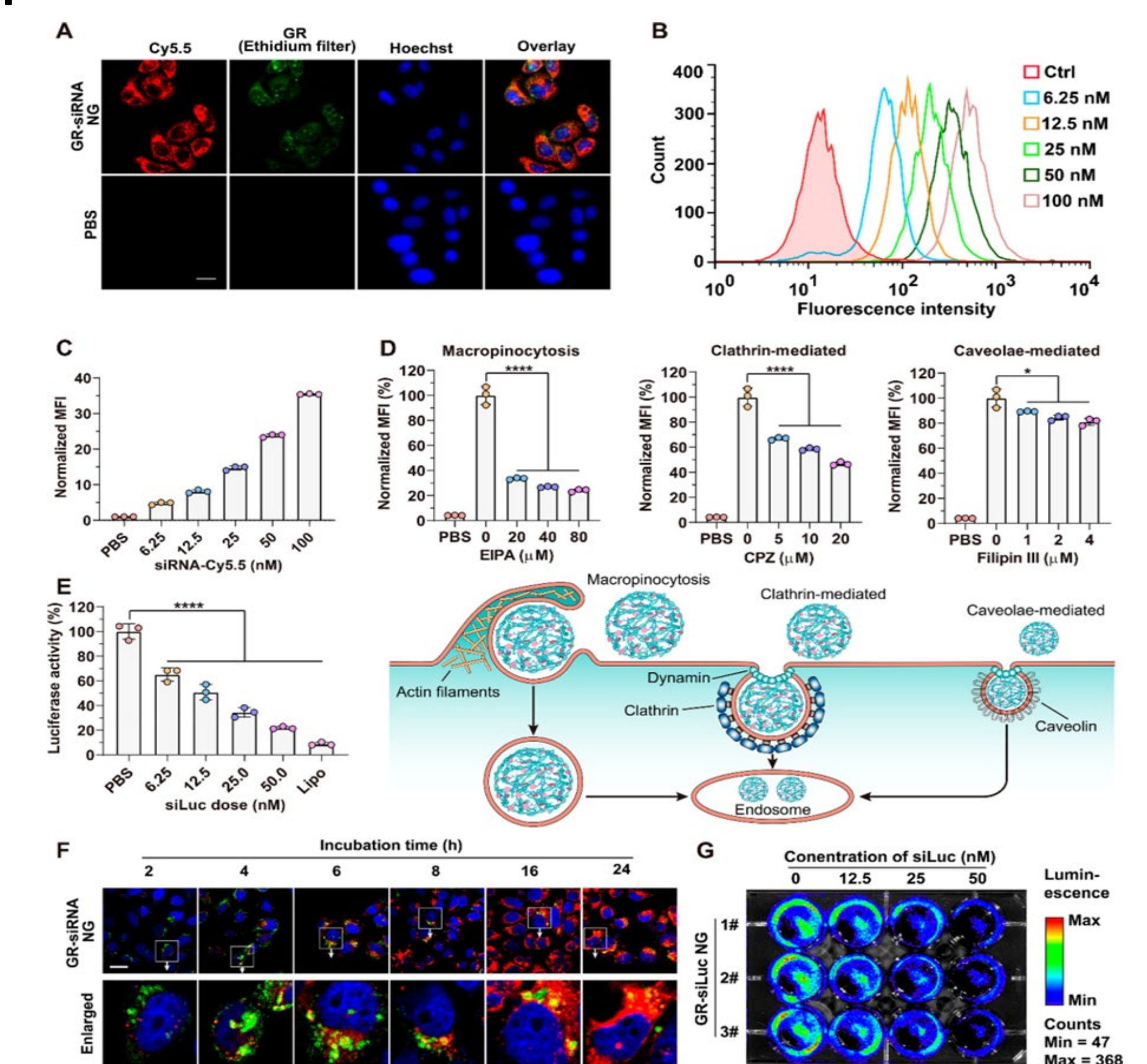
- There are multiple intercalating agents under research, the three main ones being, Acridine, Actinomycin, Ethidium Bromide.
- These agents bind to DNA which in turn inhibits a key replication enzyme called TOPO Isomerase II
- Due to this inhibition and space between base pairing, mutations can arise in DNA replication
- Not only is replication inhibited but all DNA repair and translation becomes effected leading to cell death



Pictured above are the three main agents being studied

Acridine and Measurement of Binding Affinity:

- Due to the property of fluorescence Acridine has it makes it very easy to measure and study in the body
- Acridine has a very high binding affinity leading to high success rates in DNA binding
- The permanent inhibition this agent has on DNA replication makes it very useful to study intercellular complex mechanisms with.



Statistical Measurements of successful binding affinity to DNA

Possibilities for the Future:

With cancer being uncontrollable cell replication this research and technology with extreme studies performed could lead to a breakthrough in successful cancer research. If a way to attach a signal ligand to tumor cells and avoid healthy cells was discovered, this would lead to an extreme increase in cell selectivity and binding affinity. It is impossible for treatments such as radiation therapy to avoid healthy cells while trying to eliminate the tumorous ones.

References:

Ferguson LR, Denny WA. Genotoxicity of non-covalent interactions: DNA intercalators. *Mutat Res.* 2007 Oct 1;623(1-2):14-23. doi: 10.1016/j.mrfmmm.2007.03.014. Epub 2007 Apr 6. PMID: 17498749.

Baguley BC, Wakelin LP, Jacintho JD, Kovacic P. Mechanisms of action of DNA intercalating acridine-based drugs: how important are contributions from electron transfer and oxidative stress? *Curr Med Chem.* 2003 Dec;10(24):2643-9. doi: 10.2174/0929867033456332. PMID: 14529454.

Mukherjee A, Sasikala WD. Drug-DNA intercalation: from discovery to the molecular mechanism. *Adv Protein Chem Struct Biol.* 2013;92:1-62. doi: 10.1016/B978-0-12-411636-8.00001-8. PMID: 23954098.

Acknowledgments:

The entire Choose Ohio First Staff that has made this possible

Diagram Representation of an Intercalating agent