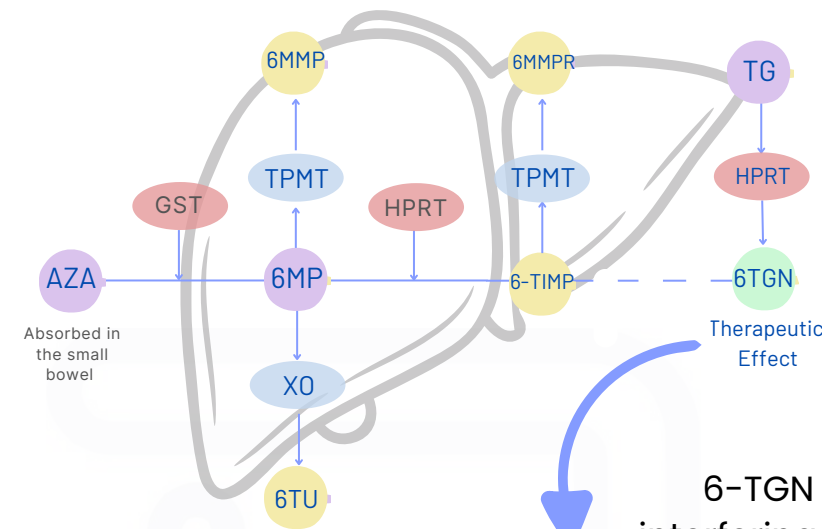


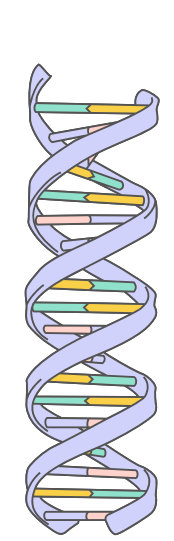
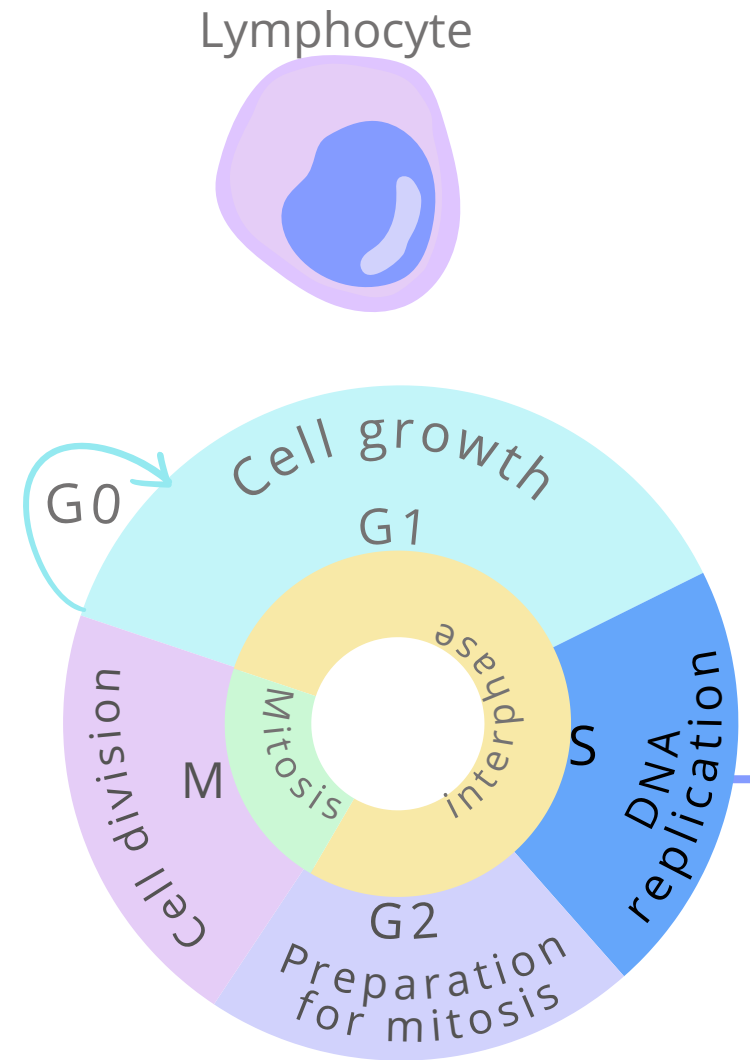
PROPOSED IMMUNOSUPPRESSANT FUNCTION- THIOPURINES

1

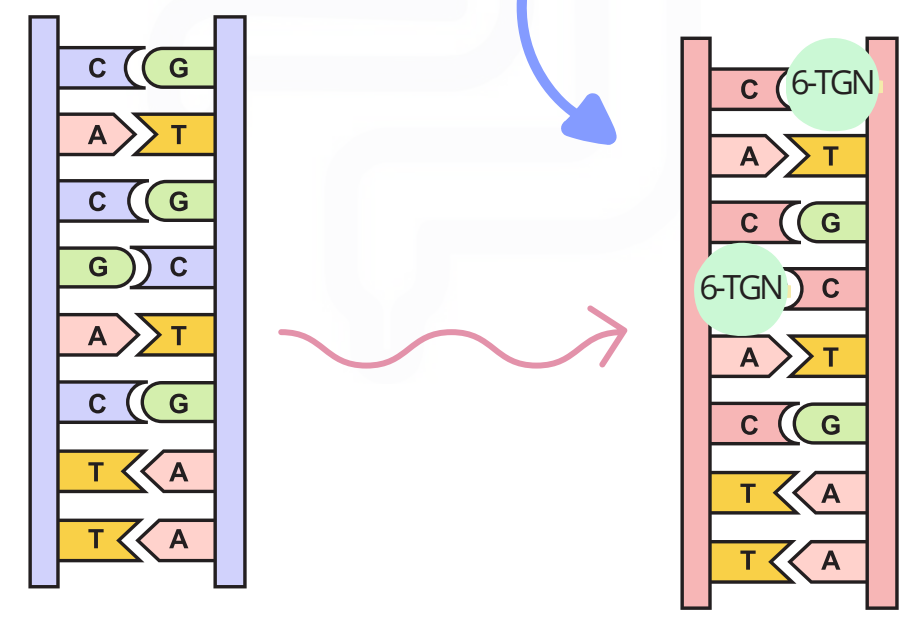
Hepatic activation of azathioprine, mercaptopurine and tioguanin



6-TGN is incorporated into DNA in place of guanine, interfering with normal DNA replication, inducing apoptosis.

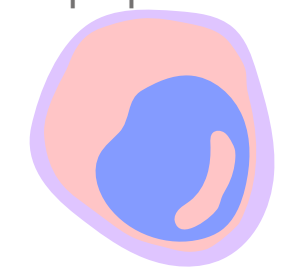


Normal DNA



Damaged DNA

lymphocyte apoptosis



6-TGN incorporates into the DNA during the S phase of all rapidly dividing cells, not just lymphocytes, which can lead to myelosuppression and gastrointestinal toxicity due to its effects on bone marrow & intestinal epithelial cells.

2

OTHER proposed mechanisms: Thiopurines have shown antibacterial activities in in vitro studies.

- 6-Mercaptopurine exhibits activity against Mycobacterium avium subspecies paratuberculosis & Corynebacterium species. 6-Thioguanosine 5'-triphosphate inhibits spore germination of Bacillus anthracis in infected macrophage cell lines & thioguanine inhibits growth of Mycoplasma pneumoniae.

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