A thymidine triphosphate shape analog lacking Watson-Crick pairing ability is replicated with high sequence selectivity

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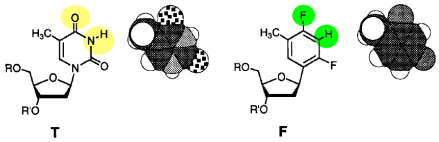
Main Thrust: Replication uses *shape* recognition



- F (Difluorotoluene nucleoside) is the same shape (space-filling) as T *but*
- F lacks Watson-Crick base pairing ability: cannot form hydrogen bonds for base pairing
- DNA polymerase tends to pair up F with A *during replication*

Binding without DNA polymerase experiment

- measure melting temperature of DNA strands
- F does not bind selectively with A,G,C,T

dFTP can be used in DNA polymerisation

- DNA polymerase inserts $F \rightarrow A$, $A \rightarrow F$, $F \rightarrow F$ (inserted base $\rightarrow$ template base)
- replication pauses only briefly (2 minutes) for $F \rightarrow A$ and continues normally afterwards
- F is only slightly less efficient than the T when pairing with A via DNA polymerase

Conclusions

- In the absence of polymerase, H-bonding is important since F-A is less stable then T-A
- H-bonding not as important to DNA polymerase since F works like T
- DNA polymerase is enforcing the pairing since A and F do not selectively pair naturally
- F is the same shape as T, but does not H-bond
- F is almost as good as T during replication
- Results support a model of replication that involves *shape* complementarity.