DNA Tautomerization
Tautomerism

- **Tautomerism** is the ability of a molecule to exist in more than one chemical form.

- Many **tautomers** are formed by migration of a hydrogen atom, accompanied by a switch of a single bond and neighboring double bond.

- In cyclic structures, H-atoms can move from one atom to another or from ring to another, so they cannot be assigned a fixed location. This movement is called tautomeric shift.
• In DNA, H- atoms usually prefer specific atomic location in purine and pyrimidin bases.
• The N- atoms attached to C, G and A are in the amino form ( - NH₂ )
• The O- atom in G and T are in Keto form ( = O )
• Keto (C=O) enol (C-OH)
• Amino- (NH₂) imino (=NH)
Some possible tautomeric conversions for bases

(a) Thymine (keto or lactam form) ↔ Thymine (enol or lactim form)

(b) Guanine (keto or lactam form) ↔ Guanine (enol or lactim form)
Base pairing of the rare forms

(base pairing rules are reversed)

\[\begin{align*}
A(\text{amino}) &= C^* (\text{imino}) \\
A^* (\text{imino}) &= C (\text{amino}) \\
G (\text{keto}) &\equiv T^* (\text{enol}) \\
G^* (\text{enol}) &\equiv T (\text{keto})
\end{align*}\]

AC base pairs

GT base pairs
Rare tautomers of DNA bases can cause mispairing

NORMAL: keto tautomer of T pairs with A

RARE: enol tautomer of T pairs with G

Tautomer: Isomers that differ in the position of atoms, and the bonds between them. Tautomeric forms are in equilibrium.

Enol: An organic compound containing a hydroxyl group bonded to a carbon atom, which in turn is doubly bonded to another carbon atom.
G:T mispairs

**NORMAL:**
ketone tautomer of G pairs with C

**RARE:**
enol tautomer of G pairs with T
**C:A mispairs**

**NORMAL:**
Amino tautomer C pairs with G

**RARE:**
Imino tautomer of C pairs with A

**Amino:** Relating to an amine or other chemical compound containing an NH$_2$ group...

**Imino:** A compound derived from ammonia and containing the bivalent NH group...
**A:C mispairs**

**NORMAL:**
amino tautomer A pairs with T

**RARE:**
imino tautomer of A pairs with C
• Normal base pairing in DNA is A-T and G-C. The tautomers forms are capable of unusual base pairing like T-G and C-A.

Tautomers can cause genetic mutations by pairing incorrectly with complementary bases. Mutations are the precursors to many molecular-based diseases, including cancer.
Deamination of Cytosine can lead to the formation of Uracil, which pairs with A.

Or, 5-methyl cytosine can be converted directly to T.
Function- Structure Relationship in DNA

* Why DNA strands are complementary?

- The complementary structure of DNA make it possible through replication to give exact copies of itself, So it fulfills its function as a genetic material and transmit genetic information exactly from generation to another.
Why DNA contain T rather than U?

- The product of C deamination is U which is recognized as foreign base in DNA and removed by repair system.
- If DNA is normally contained U in its structure; U resulting from C deamination could not be recognized and this will lead to a permanent change in the sequence as the new U will pair with A during replication which gradually leads to decrease in G-C base pair and increase in A-U base pair in DNA.
- This change will not be consistent with the function of DNA as a genetic material because genetic material should not be changed with time.
*Why A & C in amino form and G & T in keto form?*

- It's essential to the biological function of DNA that the H-atoms have fixed location. If not, A could pair with C & G with T.
- So, the sequence of the bases on two DNA strands will not be complementary, and on replication, DNA cannot give two identical molecules similar to the parent molecule.
* Why DNA has some unusual sequences?

- These sequences give different variations of DNA structure as hairpin, cruciform and H-DNA which are important in replication, transcription and recombination of DNA.