

REPLICATION

Ori binding protein binds to Ori
 ↓
 AT rich near ori unwinds

- Topoisomerase I
- Helicase
- DNA Primase
- DNA ligase
- DNA polymerase

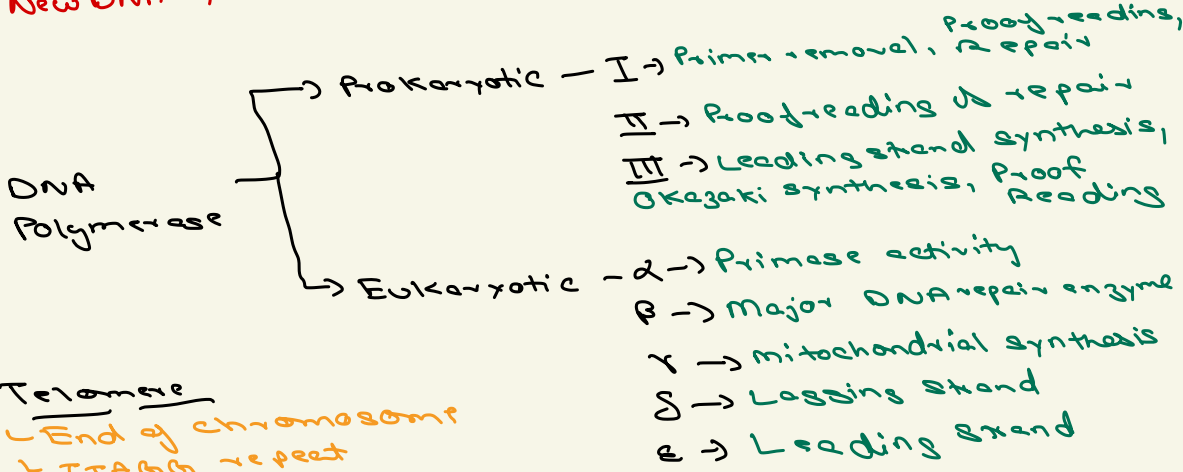
Single strand binding protein prevent re-linking

Leading strand

RNA primer - 5' to 3'
 ↓
 New DNA by DNA-Pol III

Lagging strand

RNA primer → Okazaki fragment
 → Removal of primer & filling of gap by DNA-Pol I → DNA ligase



Telomerase

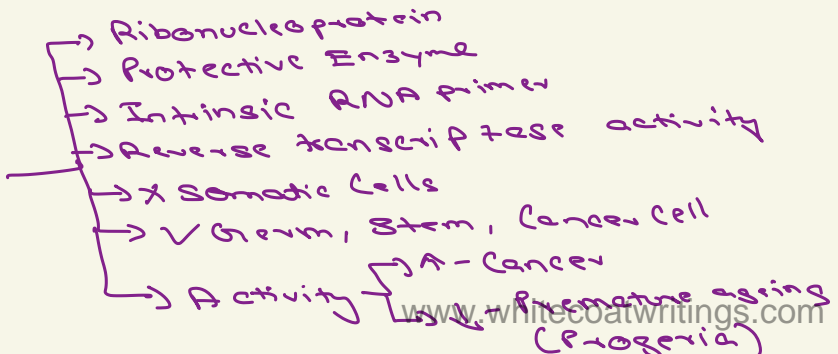
↳ End of chromosome
 ↳ TTAGG repeat

End Replication Error

↳ Leaves gap at 5'
 ↳ 3' not replicated
 ↳ If not corrected, shortening of DNA

↳ Consists by

Telomerase Enzyme



TRANSCRIPTION

No primer required ←

3' → 5' - Template, minus, Antisense
5' → 3' - Coding, plus, Sense

RNA Polymerase

- ↳ Prokaryotic: - One type = [Sigma Subunit + Core Enzyme = Holoenzyme]
 - ↳ β -unit → catalytic
 - ↳ sigma → binding of RNA P to Promoter
- ↳ Eukaryotic [Sensitivity to Amanitin]
 - ↳ I - rRNA - Least
 - ↳ II - mRNA, miRNA, snRNA, lncRNA - highest
 - ↳ III - tRNA, SSrRNA, certain snRNA - mid

- Promoters
 - ↳ Bacterial - Pribnow box - -10bp [TATAAT]
 - ↳ TGG box - -35bp
 - ↳ Eukaryotic - Hogness box - -25bp [TATA]
 - ↳ CAA box - -75bp
 - ↳ GC box
- ↳ Lhr (Initiator seq.)
- ↳ DPE (Downward promoter element)

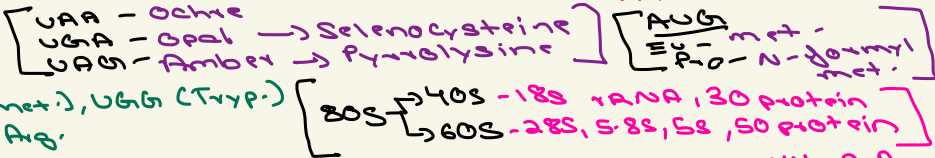
- ↳ Intragenic - Downstream - RNAP II
- Transcription Cycle
 - ↳ Template binding & closed promoter complex
 - ↳ Open promoter complex
 - ↳ Chain initiation & elongation

- Post-transcriptional modification
 - ↳ Termination
 - ↳ ρ dependent
 - ↳ ATP dependent
 - ↳ RNA-DNA helicase
 - ↳ ρ independent
 - ↳ Signal - GC rich & U rich
 - ↳ GC - hairpin, strong
 - ↳ UUA - weaker
 - ↳ Stabilize mRNA
 - ↳ cap binding complex
 - ↳ CAP-BINDING
 - ↳ helps in attachment of mRNA to 40S
 - ↳ Initiation of translation
 - ↳ Prevent attack of exo-nuclease

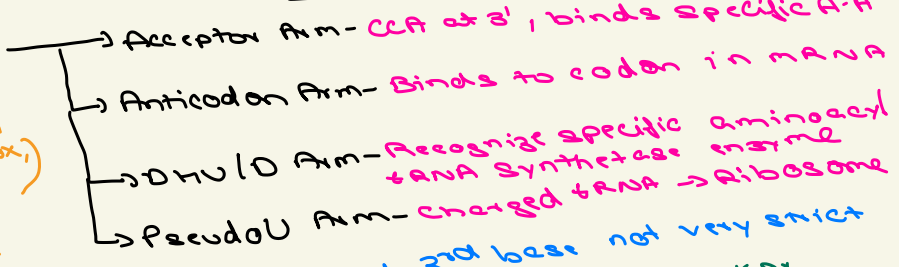
- ↳ Capping
 - ↳ 5' 7 methyl guanosine
 - ↳ Guanosine (N7) $\xrightarrow{\text{SAM}}$ 7-methyl guanosine
 - ↳ methyl transferase
- ↳ Tailins
 - ↳ 40-200 Adenosine residue
 - ↳ Polyadenylate polymerase
- Splicing
 - ↳ snRNP bind to exon-intron junction
 - ↳ Ligate 5' → 2' OH form bond & 5' PO₄ → 3'-5' exon-exon PE bond
 - ↳ Lariat structure [Spliceosome - snRNP + exon]
- Self-Splicing Intron [Thomas Cech]
 - ↳ Group I - No Lariat
 - ↳ Group II - Lariat
 - ↳ 100% translated
- Alternate mRNA processing
 - ↳ Exon spliced in diff. alternative ways

- RNA editing - Liver: - apoB gene → apoB mRNA → apoB100
 - ↳ Intestine: - apoB mRNA → C → U → CAA to UAA (STOP)
 - ↳ Use only translated apoB48 protein

Cistron smallest unit of gene expression
 ← **TRANSLATION** ← Marshall Nirenberg & P. Gobind Khurana



- Codon
 - ↳ Single - AUG (met.), UGG (Tryp.)
 - ↳ 6 - Ser., Leu., Arg.
- tRNA
 - ↳ Soluble RNA
 - ↳ 20 - clover leaf
 - ↳ 30 - L shape
 - ↳ Large no. unusual base (DihydroU, hypox., Pseudou)
 - ↳ Has thymine
 - ↳ 74-95 nucleotide



- wobbling → Anticodon interaction at 3rd base not very strict
- Charging
 - ↳ 1st AUG seq. after marker
 - ↳ seq. is start codon

STEPS

- Anticodon Arm UAC → DHU recognize tRNA → methionine → A.A attach to acceptor arm.
 - ↳ Pro. → Shine Dalgarno seq.
 - ↳ Eu. → Kozak consensus seq.
- Initiation → 80S $\xrightarrow{eIF3}$ 60S+40S
 - ↳ GTP + eIF2 + met-tRNA $\xrightarrow{40S}$ 43S
 - ↳ mRNA = 43S initiation complex
 - ↳ GTP, eIF \downarrow ← 60S
 - ↳ eIF2 80S initiation complex
- Elongation - elongation factor
 - ↳ aminoacyl tRNA → A site (EF-1, GTP hydrolysis)
 - ↳ Peptide bond [Ribosome, 23S]
 - ↳ Peptidyl transferase
 - ↳ ATP req.
 - ↳ Translocation of ribosome on mRNA (EF-2, GTP hydrolysis)
- Termination
 - ↳ UAF-2, Peptidyl transferase, hydrolysis

- ★ 4 Phosphate for 1 peptide bond form
- Charging x2, EFl-tRNA to A(C), Translocation (C)
- miRNA - 21 to 22nt [post-transcr. regulation]
 - ↳ Craig Mellow & Andrew Fire
 - ↳ Pre miRNA
 - ↳ Cappinst Tailins
 - ↳ Drosha Dicer
 - ↳ Trimmed miRNA
 - ↳ Exportin 5
 - ↳ Trimmed miRNA
 - ↳ TRBP direct nucleas
 - ↳ dsRNA
 - ↳ Loaded into RISC induced silencing complex
 - ↳ miRNA
- RNA interference
 - ↳ Binds with seed seq. in 3' UTR on mRNA
 - ↳ Perfect pairings - mRNA degraded
 - ↳ Mismatch - Translation arrest
 - ↳ Molecular patho - genesis of neoplasia
 - One arm - **Oncogenic miRNA**
- Non-protein coding RNA
 - ↳ Large: 23S, 18S
 - ↳ lncRNA, circRNA
 - ↳ siRNA - 21 to 22nt
 - ↳ Action mech. same as miRNA
 - ↳ Exogenous origin
 - ↳ small: 5.8S, 5S, tRNA, snRNA, miRNA, siRNA
 - ↳ lncRNA - Product of RNA Pol II
 - ↳ Regulation of gene expression
 - ↳ Gene Activation Factor Bindings
 - ↳ Prevent gene transcription
 - ↳ lncRNA + TF inhibit binding TF to promoter site - decoy mRNA
 - ↳ Epi genetic modification (DNA methylase & acetylase to histone & DNA)

Heme Synthesis

Succinyl CoA + Glycine

↓ ALA Synthase

δ -amino levulinate

$\times 2$ ↓ ALA dehydratase

Porphobilinogen

$\times 3$ \leftarrow \downarrow $\times 4$, PBG deaminase / α -MB Synthase /
Uroporphyrinogen III Synthase

Hydroxymethyl bilane

↓
Uroporphyrinogen I

↓

Coproporphyrin I

(no further step of
type I isomer
absent in body)

↓ U III Synthase

Uroporphyrinogen III

$4CO_2$ \leftarrow \downarrow U- Decarboxylase

Coproporphyrin III

↓ CPG oxidase

Protoporphyrin III

↓ PPG oxidase

Protoporphyrin

Fe \rightarrow ↓ Ferro chelatease

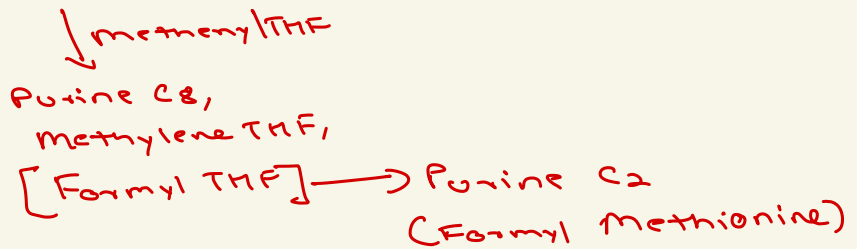
Heme

One Carbon Metabolite Reactions

• Glycine $\xrightarrow{\text{methylene THF}}$ Serine

• Methylene THF \longrightarrow Thymidylate Synthesis

• Histidine catabolism



• Homocysteine $\xrightarrow[\text{THF}]{\text{Methyl THF}}$ Methionine