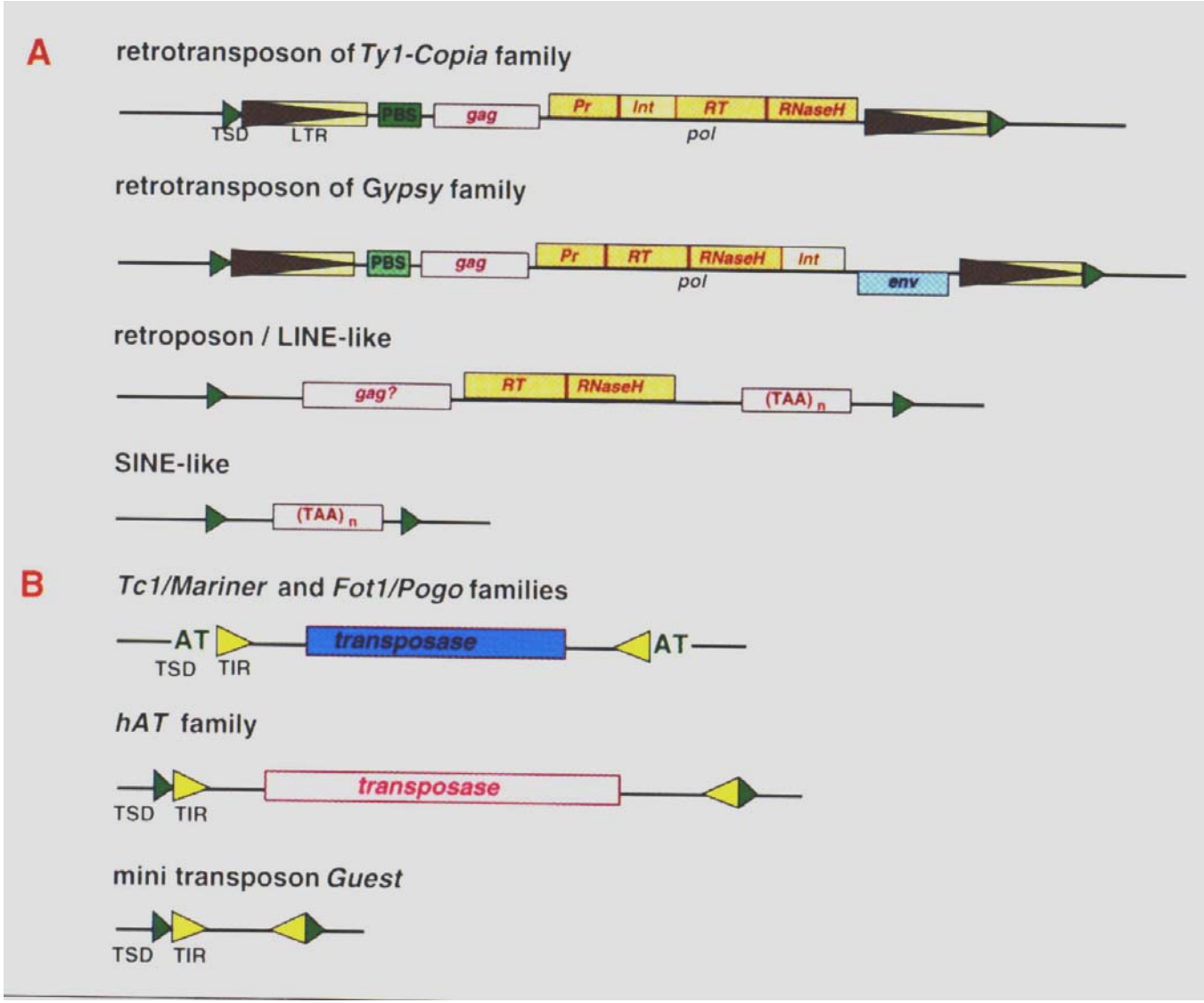
Interspergierte Repetitive Elemente

- SINEs = short interspersed nuclear elements
- LINES = long interspersed nuclear elements
- MIR = mammalian wide interspersed repeats (Säugerspezifisch?)
- DNA-Transposons
- Retroelemente
- Pro-/Retroviren

SINEs, LINEs, Retroelemente, DNA-Transposons

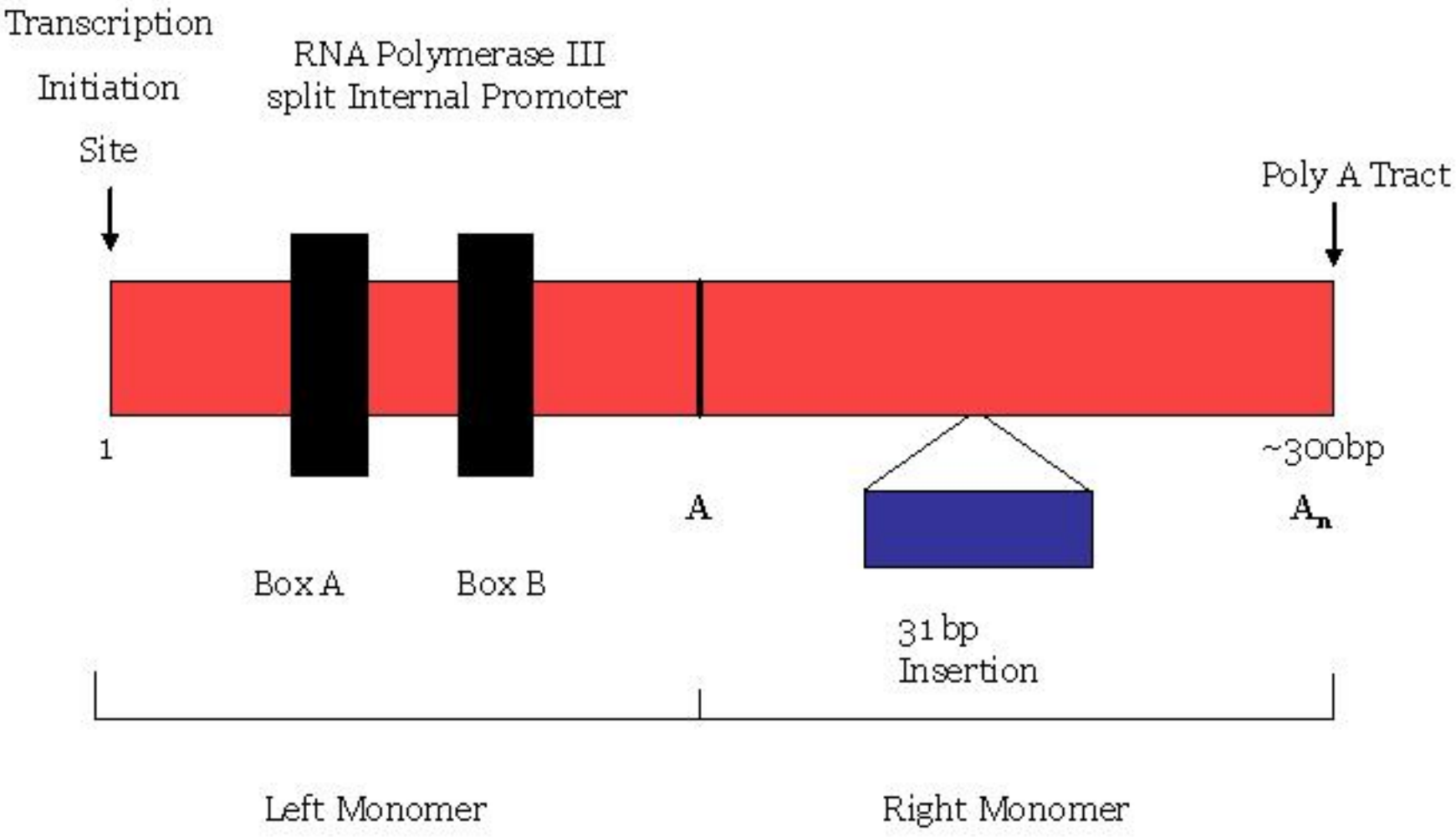


SINEs:
Alu-Elemente

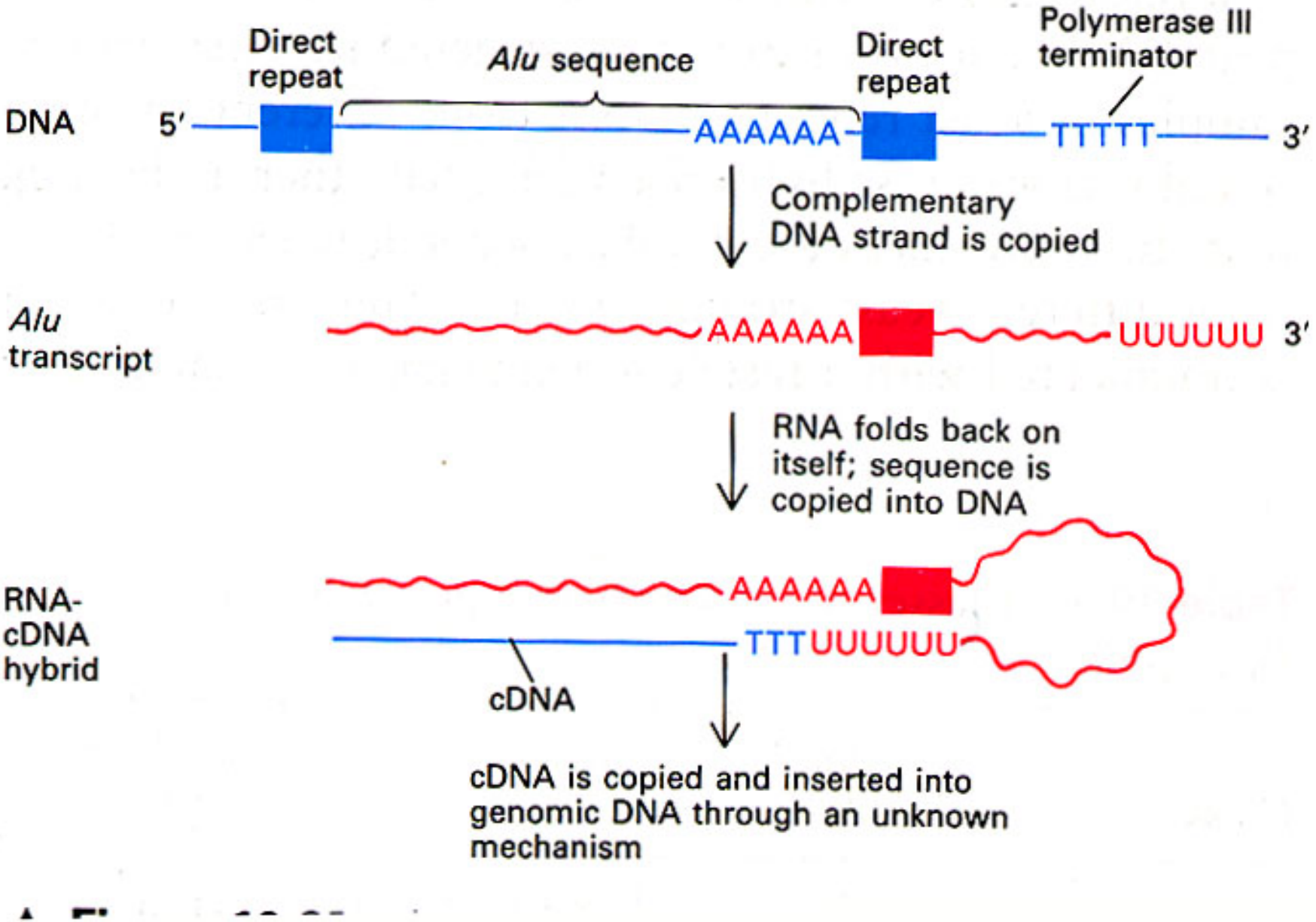
Table 11 Number of copies and fraction of genome for classes of interspersed repeat

	Number of copies (× 1,000)	Total number of bases in the draft genome sequence (Mb)	Fraction of the draft genome sequence (%)	Number of families (subfamilies)
SINEs	1,558	359.6	13.14	
Alu	1,090	290.1	10.60	1 (~20)
MIR	393	60.1	2.20	1 (1)
MIR3	75	9.3	0.34	1 (1)

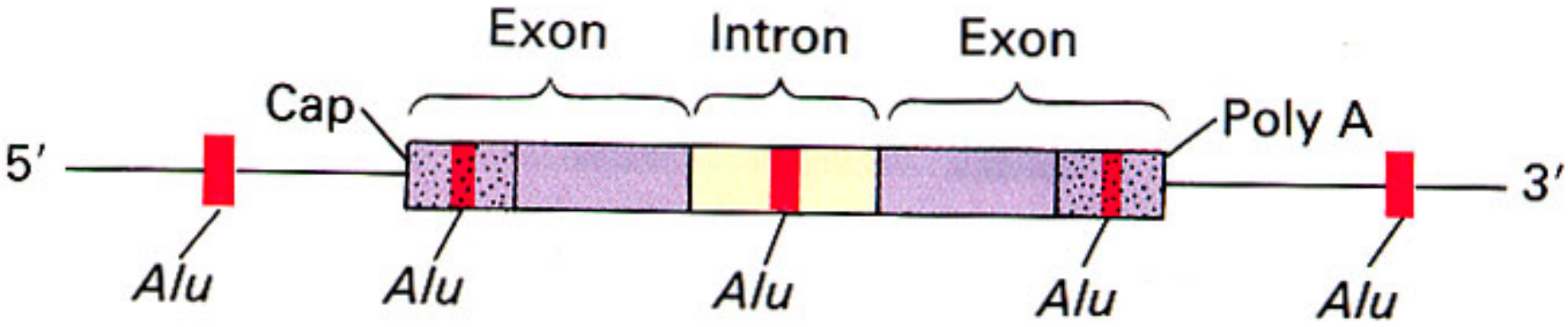
SINEs: Alu-Elemente



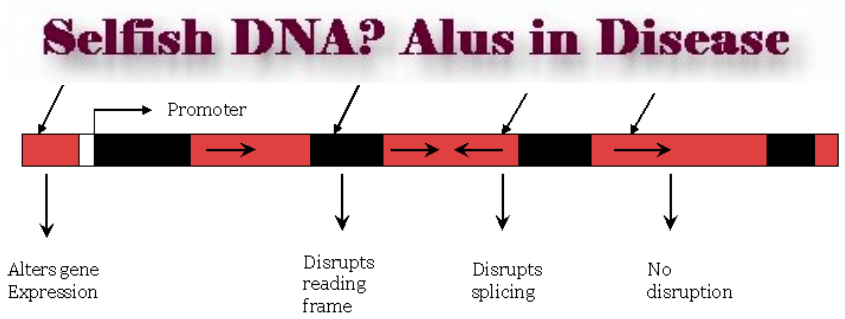
Alu-Elemente verbreiten sich durch Retroposition

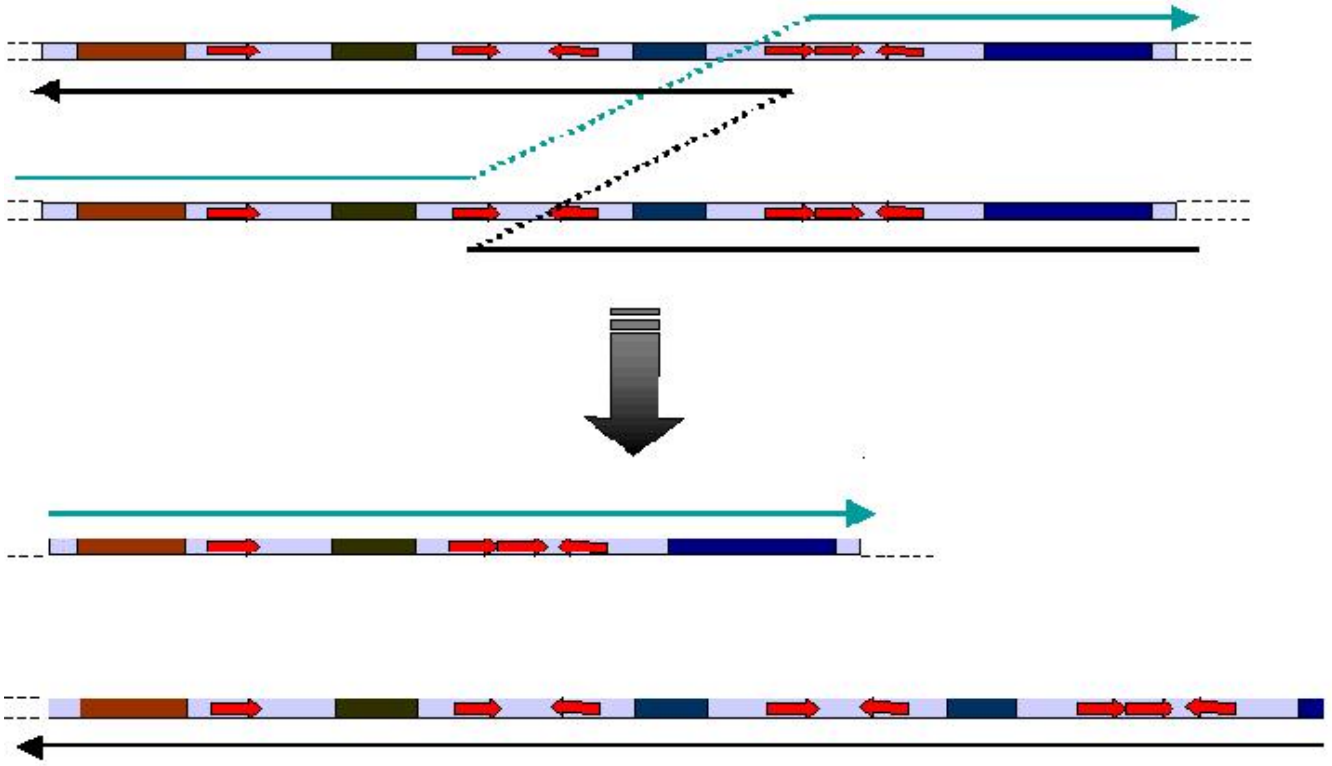


SINEs:
Alu-Elemente



SINEs.


Selfish DNA? Alus in Disease
Promoter
Alters gene Expression
Disrupts reading frame
Disrupts splicing
No disruption

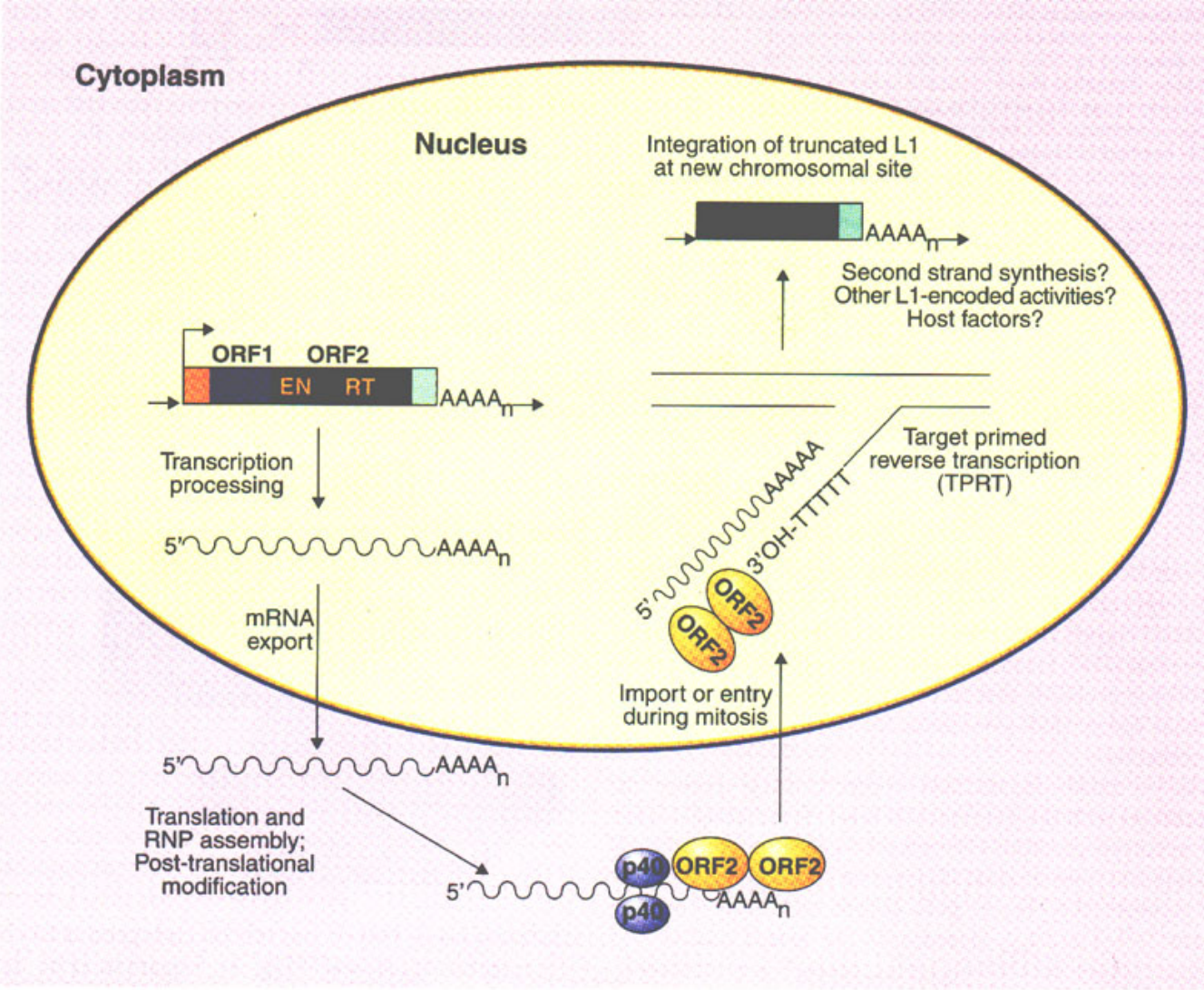


LINEs z. B. L1

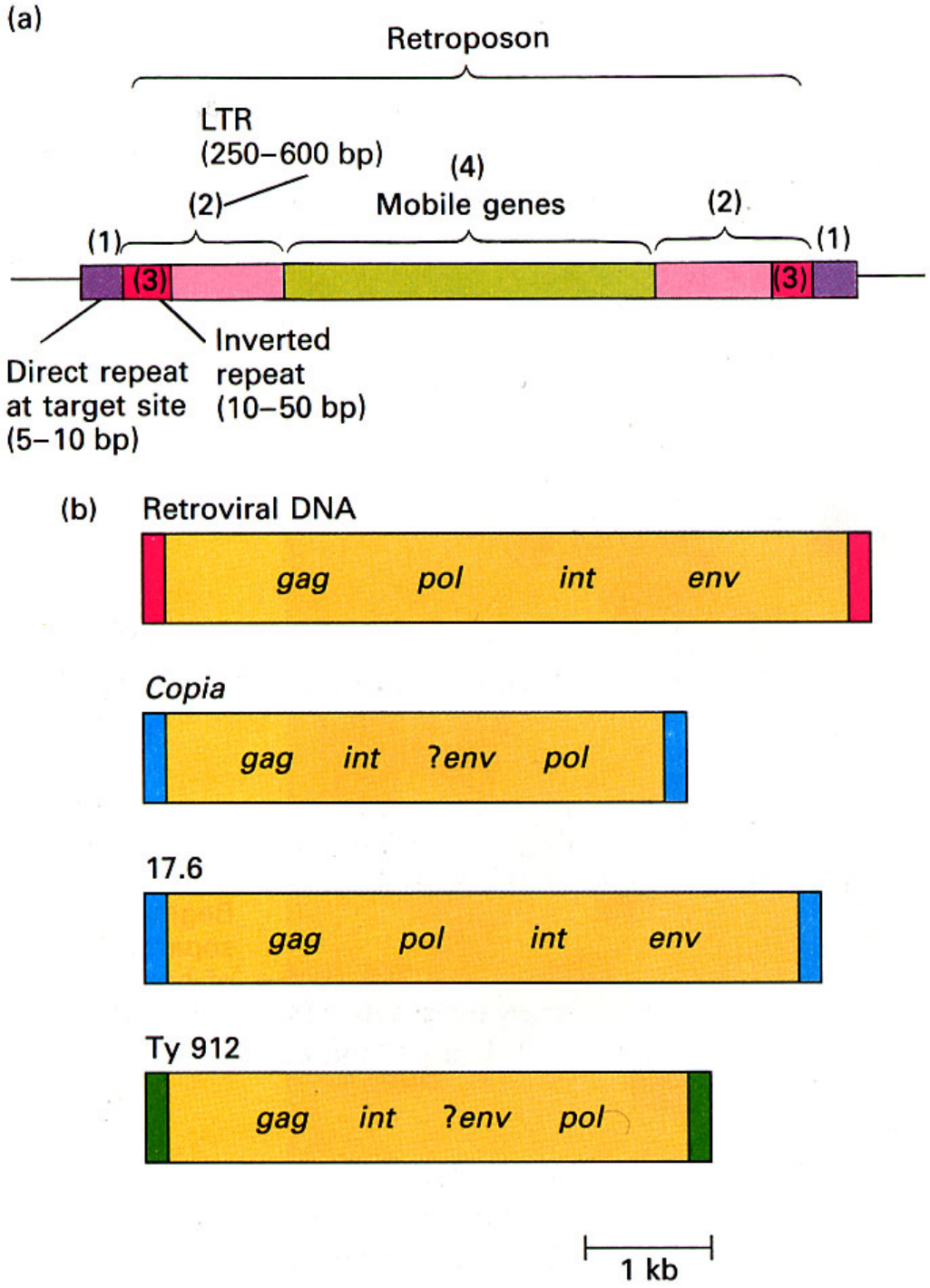
Table 11 Number of copies and fraction of genome for classes of interspersed repeat

	Number of copies (× 1,000)	Total number of bases in the draft genome	Fraction of the draft genome sequence (%)	Number of families (subfamilies)
LINEs	868	558.8	20.42	
LINE1	516	462.1	16.89	1 (~55)
LINE2	315	88.2	3.22	1 (2)
LINE3	37	8.4	0.31	1 (2)

LINEs z. B. L1


Cytoplasm
Nucleus
Integration of truncated L1
at new chromosomal site
AAAA$_n$
Second strand synthesis?
Other L1-encoded activities?
Host factors?
ORF1
ORF2
EN
RT
AAAA$_n$
Transcription
processing
5'
AAAA$_n$
mRNA
export
Target primed
reverse transcription
(TPRT)
AAAAA
3'OH-TTTTT
5'
ORF2
ORF2
Import or entry
during mitosis
5'
AAAA$_n$
Translation and
RNP assembly;
Post-translational
modification
p40
ORF2
ORF2
p40
5'
AAAA$_n$

Retrotransposons

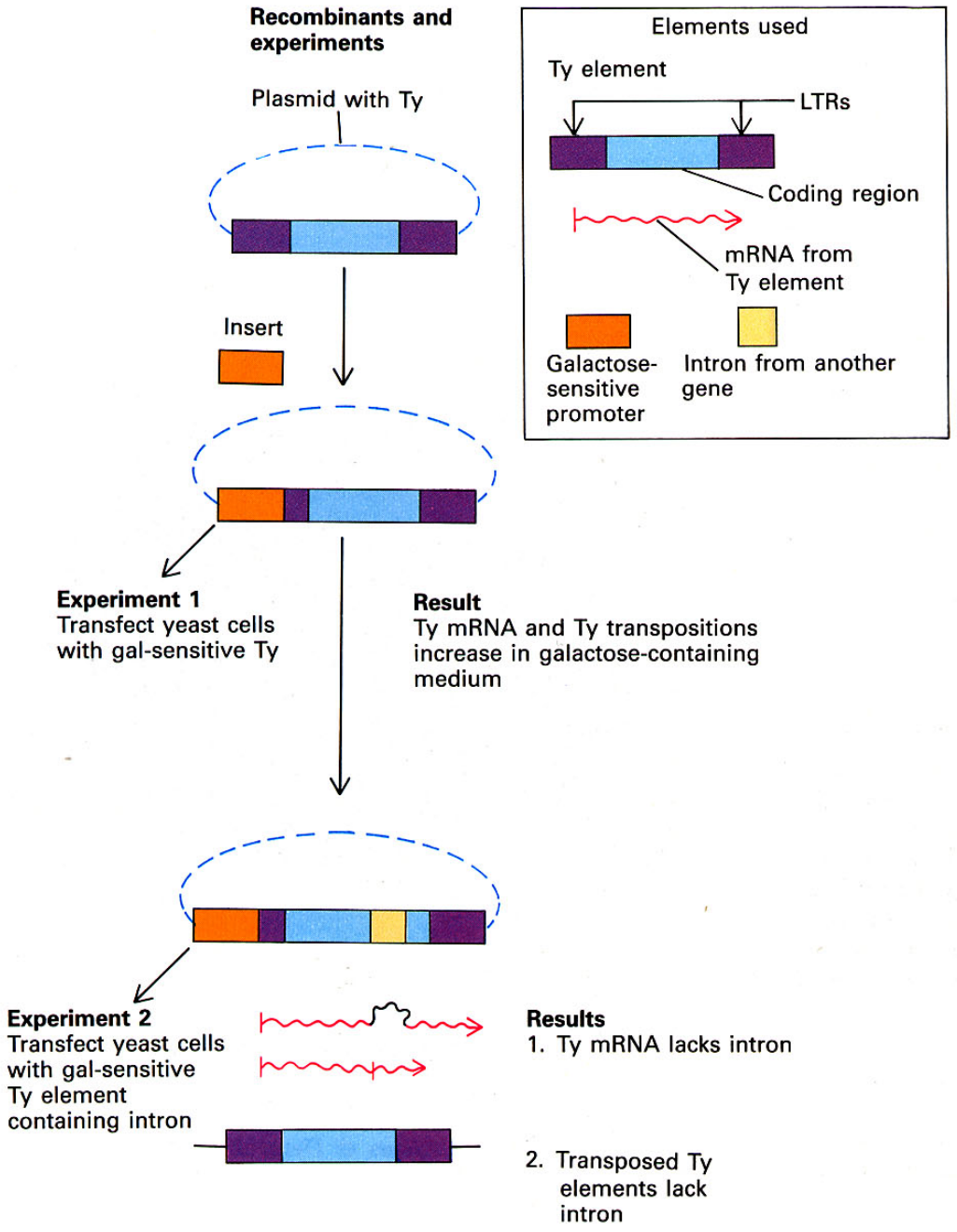


Retrotransposons

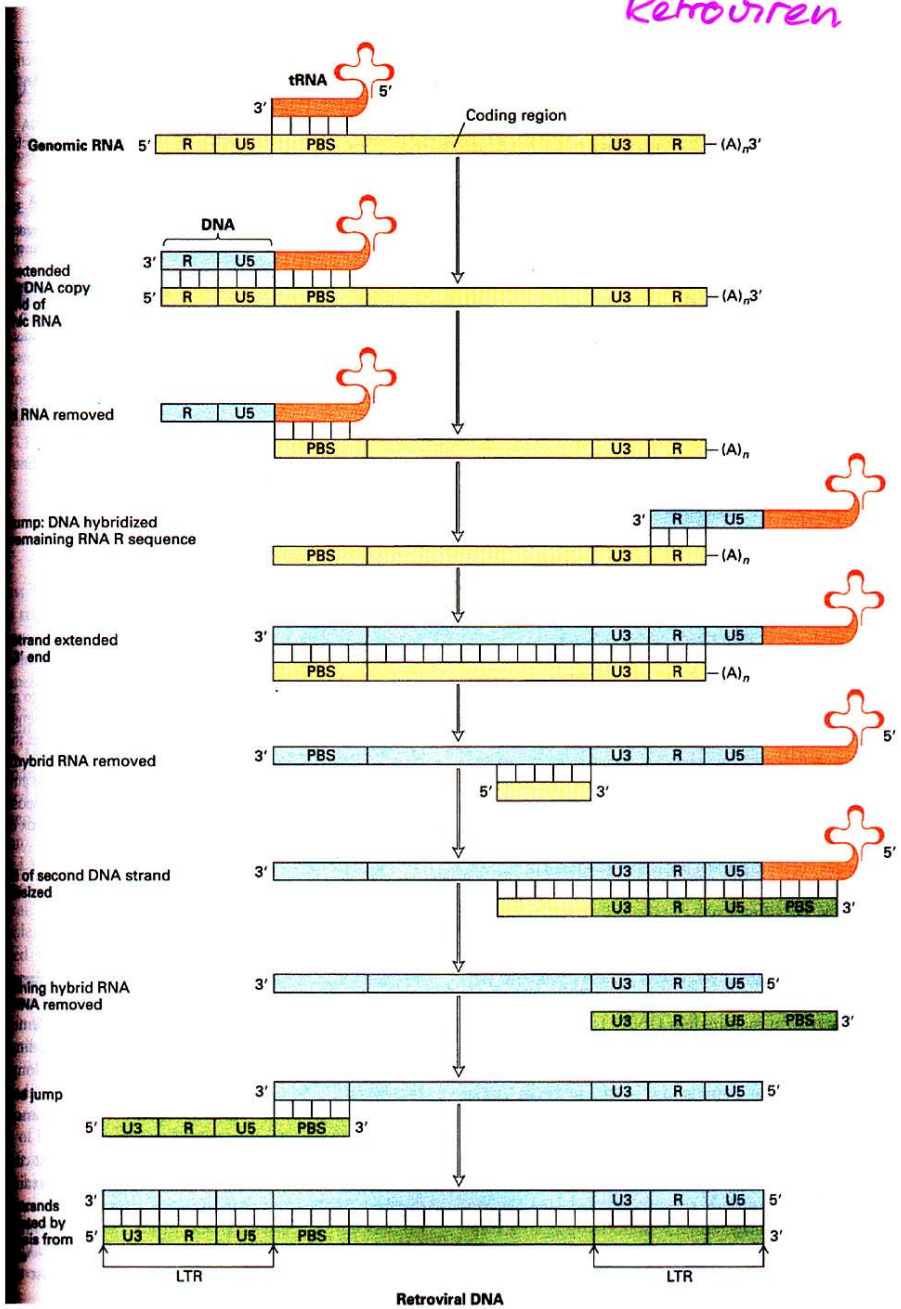
Table 19.1 Retroposons can be divided into the viral or nonviral superfamilies.

	Viral Superfamily	Nonviral Superfamily
Common types	*Ty (S. cerevisiae)* *copia (D. melanogaster)* LINES L1 (mammals)	SINES B1/Alu (mammals) Processed pseudogenes of pol III transcripts
Termini	Long terminal repeats	No repeats
Target repeats	4-6 bp	7-21 bp
Reading frames	Reverse transcriptase and/or integrase	None (or none coding for transposon products)
Organization	May contain introns (removed in subgenomic mRNA)	No introns

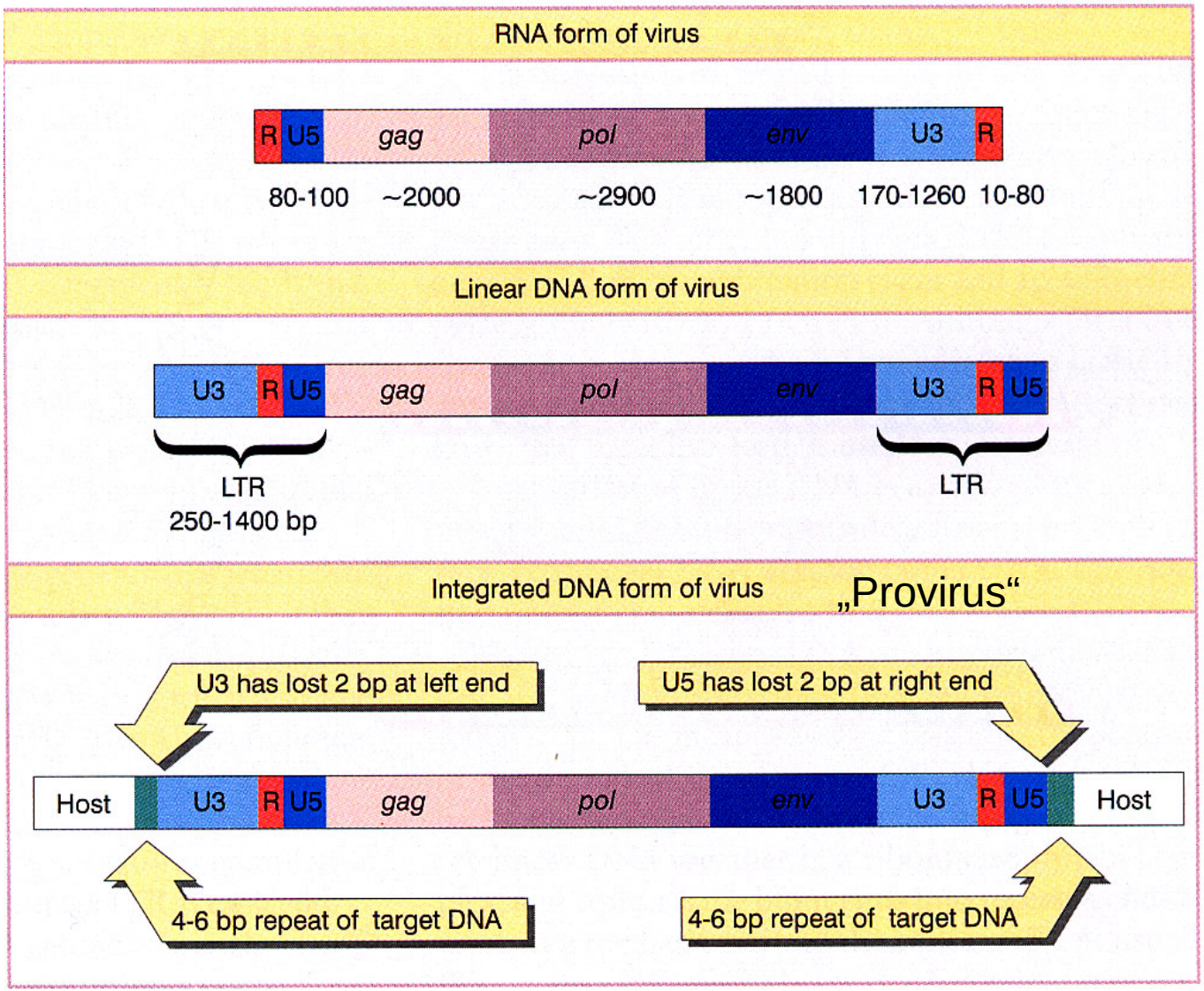
Beweis für Retro-transposition



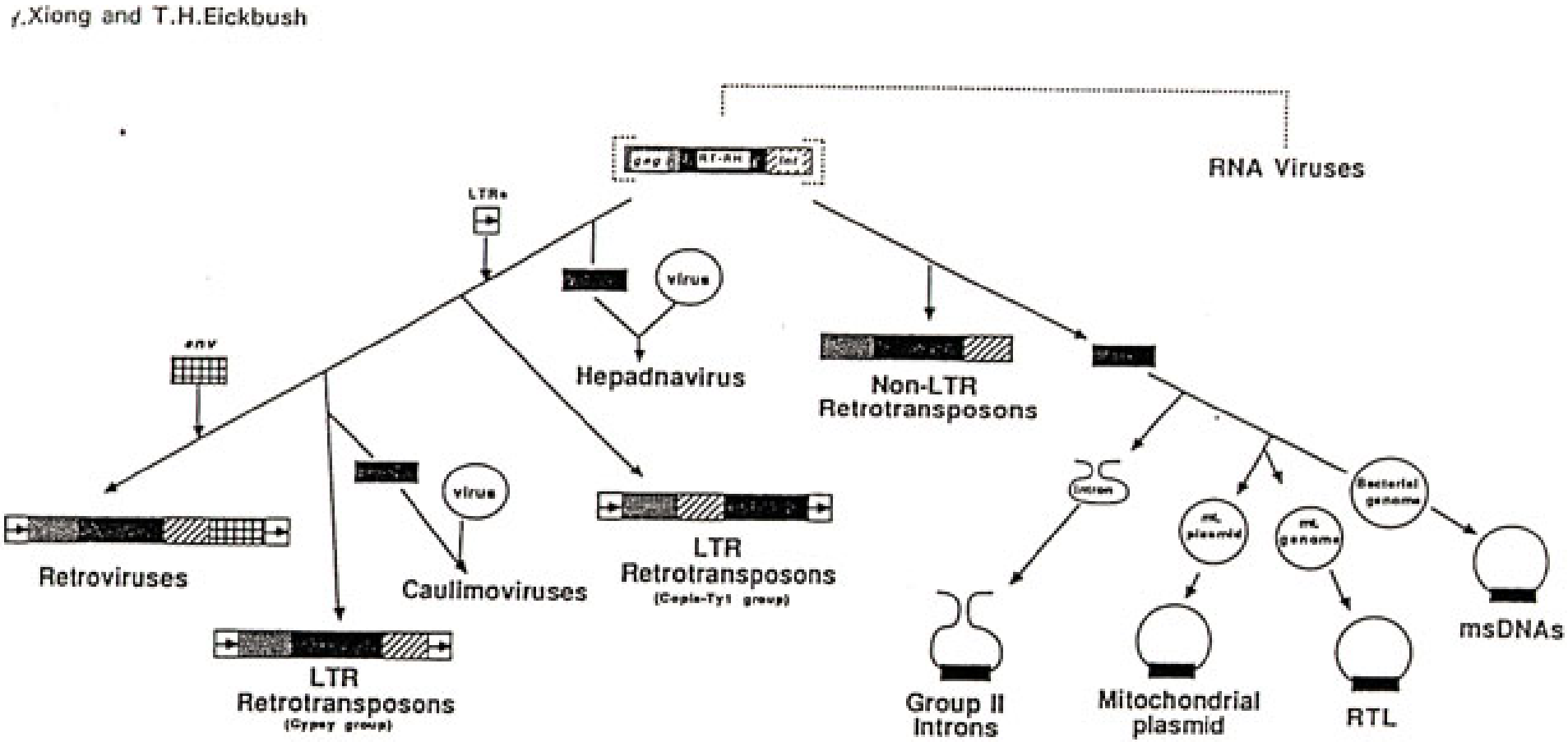
Replikation und LTR-Entstehung bei Retroviren



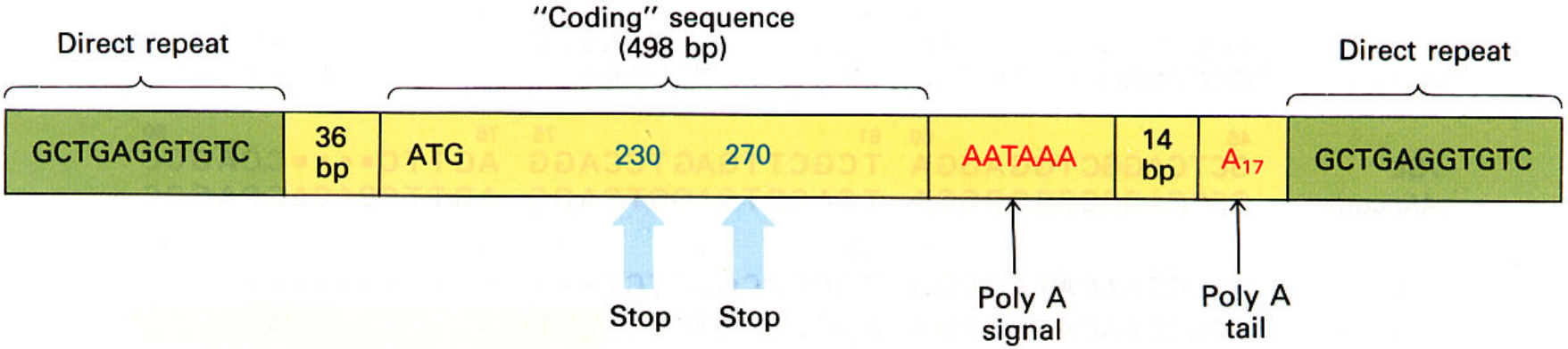
Retroviren unterscheiden sich in der DNA- und RNA-Form



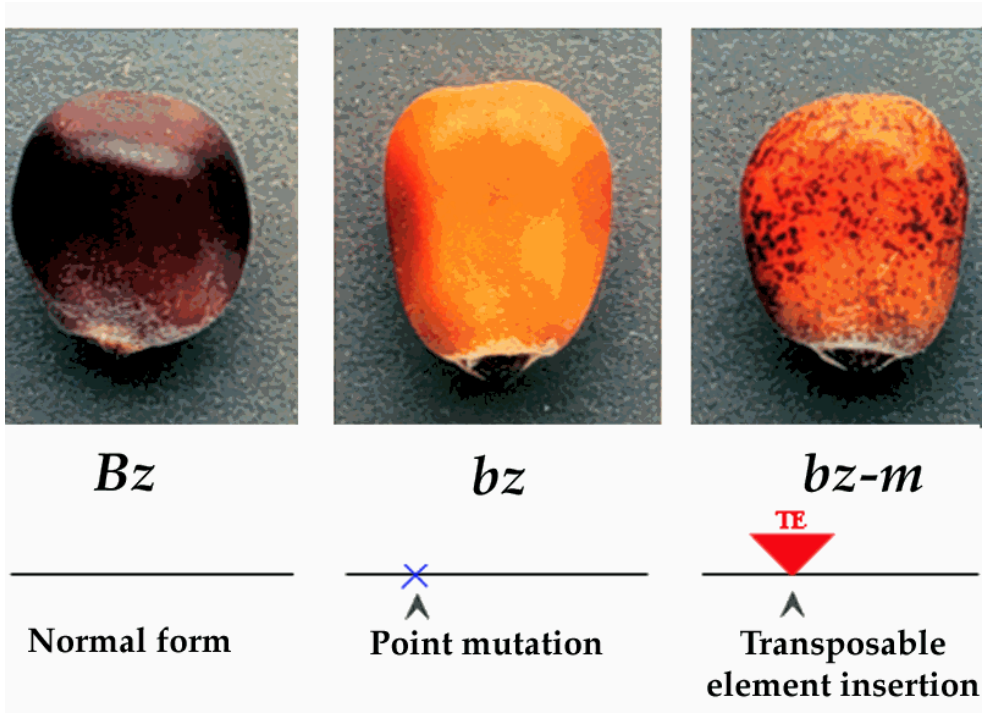
Evolution von Retroelementen: sind alle Retroelemente phylogenetisch verwandt?



Prozessierte Pseudogene



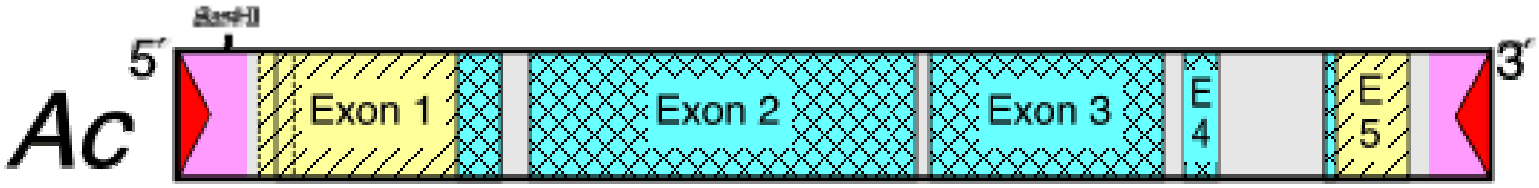
DNA-Transposons



Nobel-Preis 1983

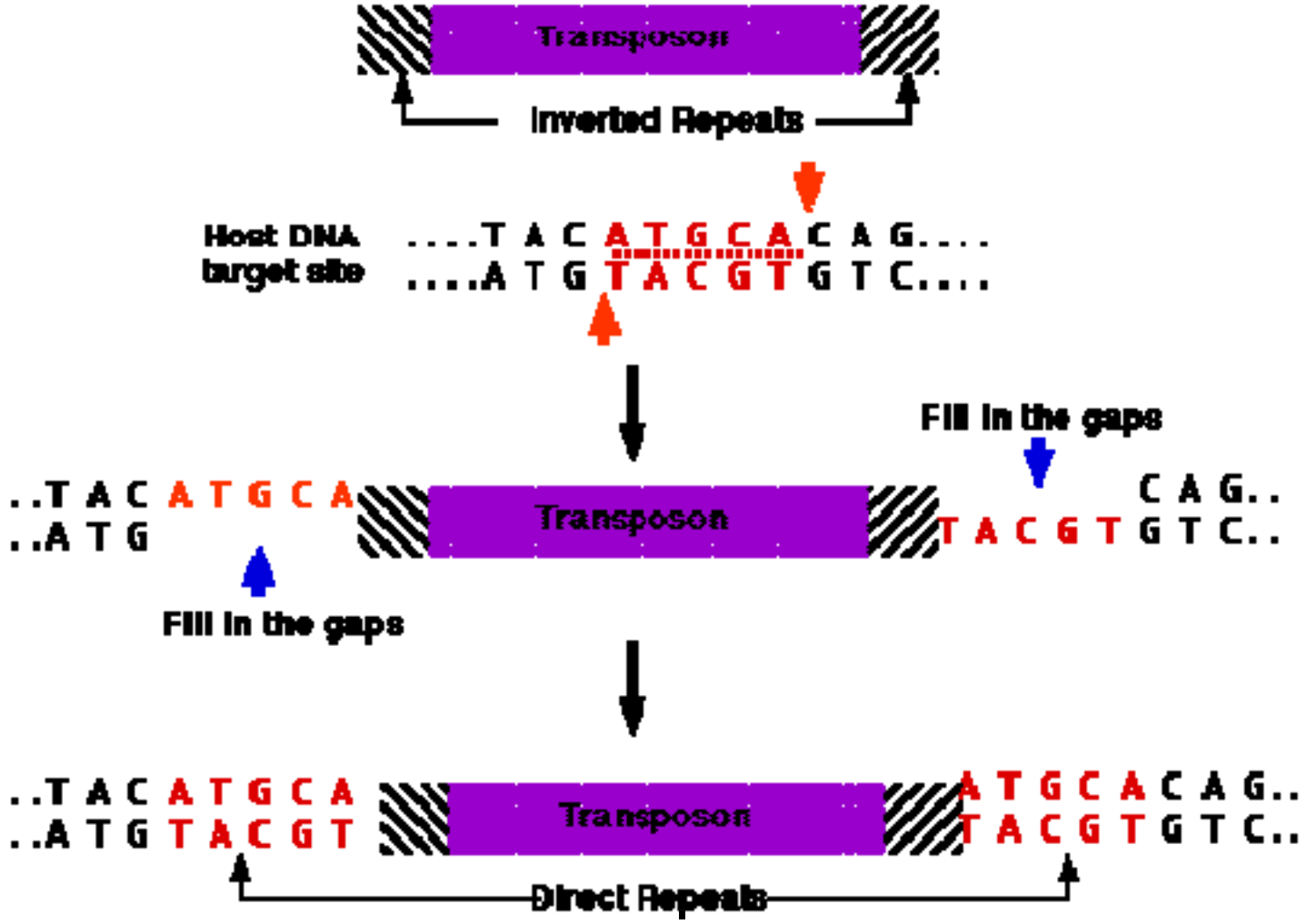
DNA-Transposons: Körnerfarbe bei Mais

Activator Element „Ac“ bei Mais

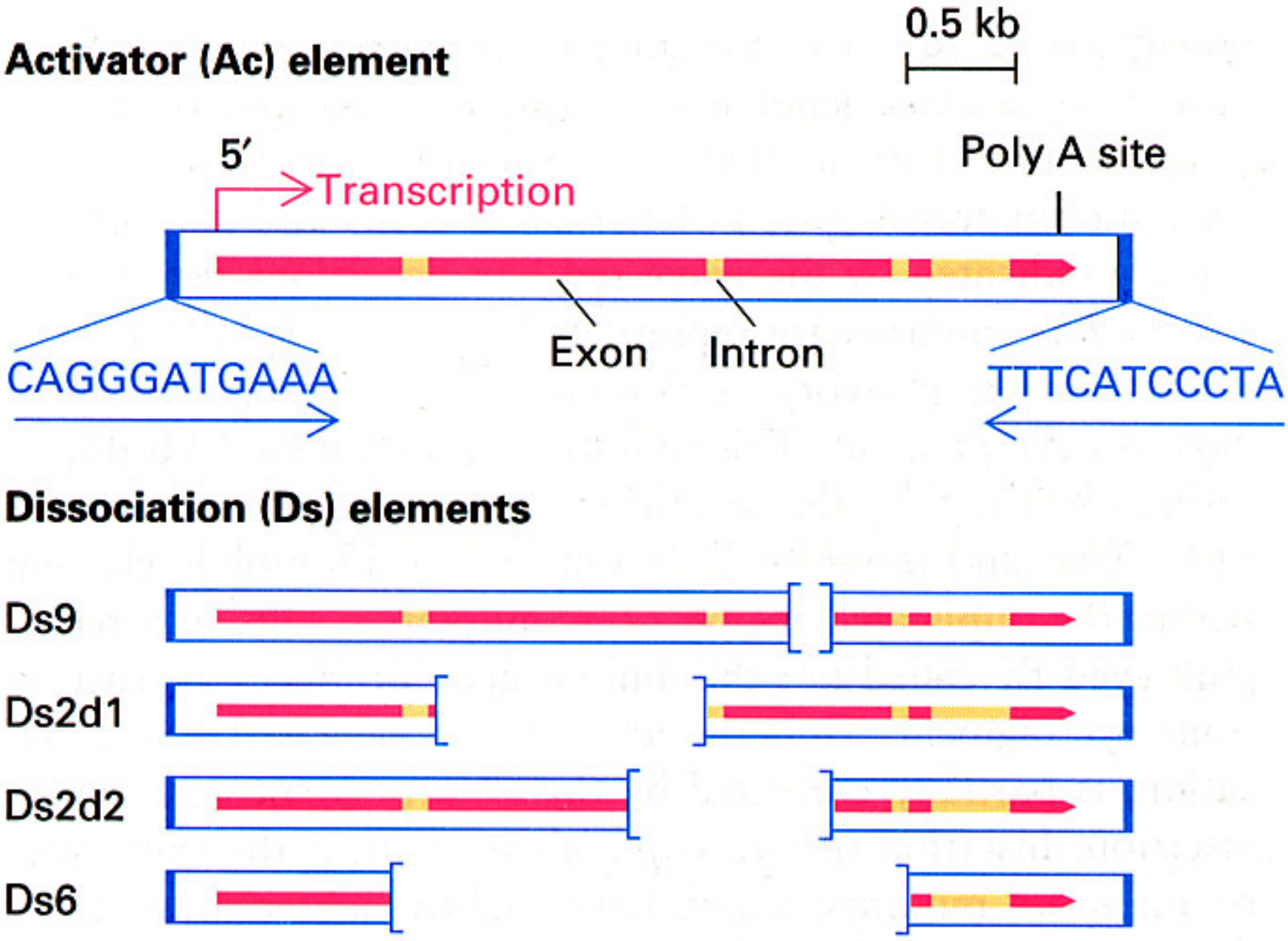


Das „Ac“-Element ist durch kurze „direct repeats“ flankiert

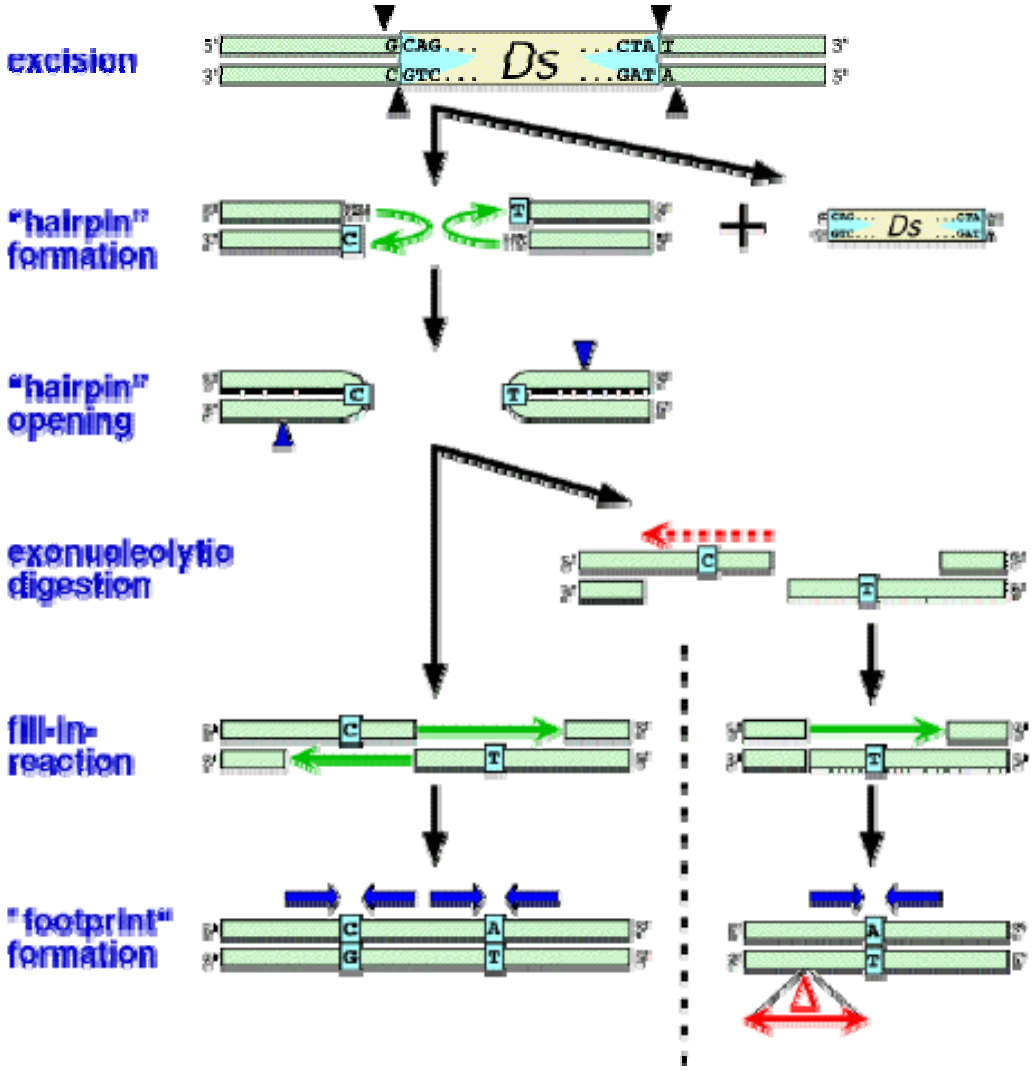
DNA-Transposons erzeugen „target site duplications“



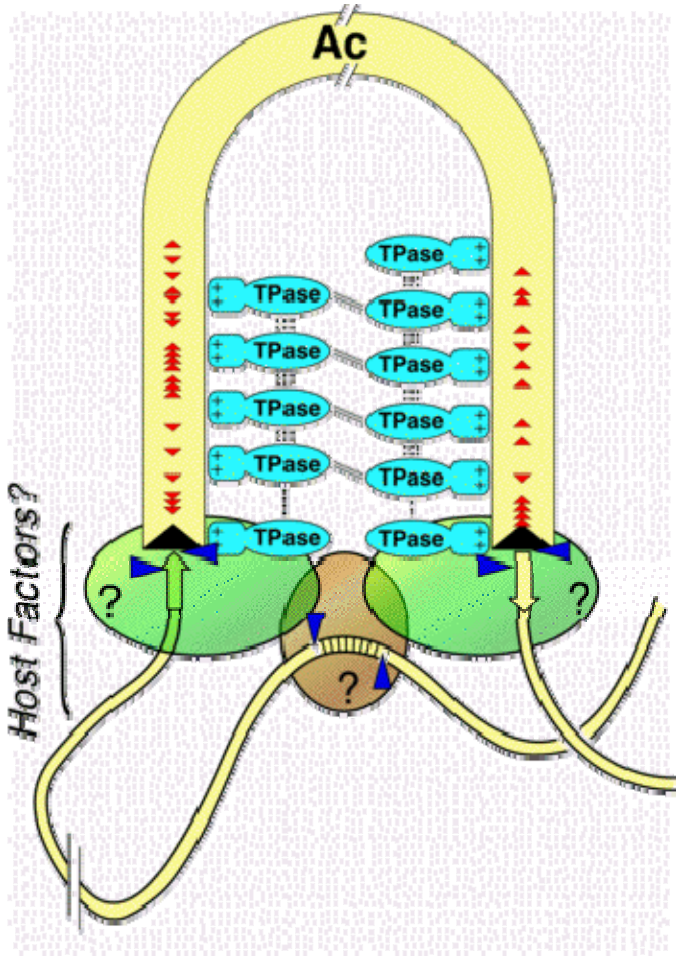
Das AC-Element besitzt eine aktive Transpsosase, Ds Elemente sind „nicht-autonom“



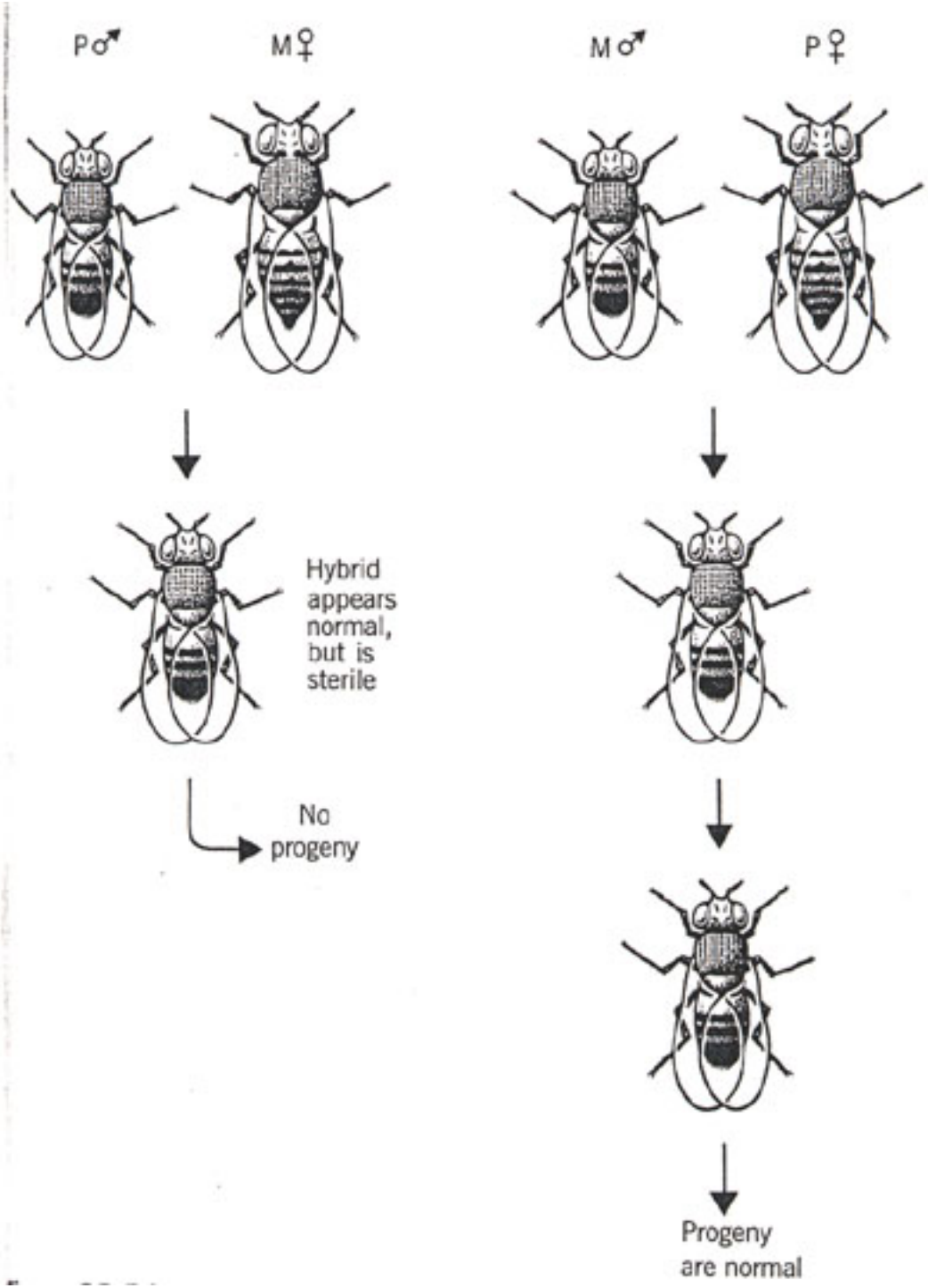
Bei der Exzision entstehen „footprints“



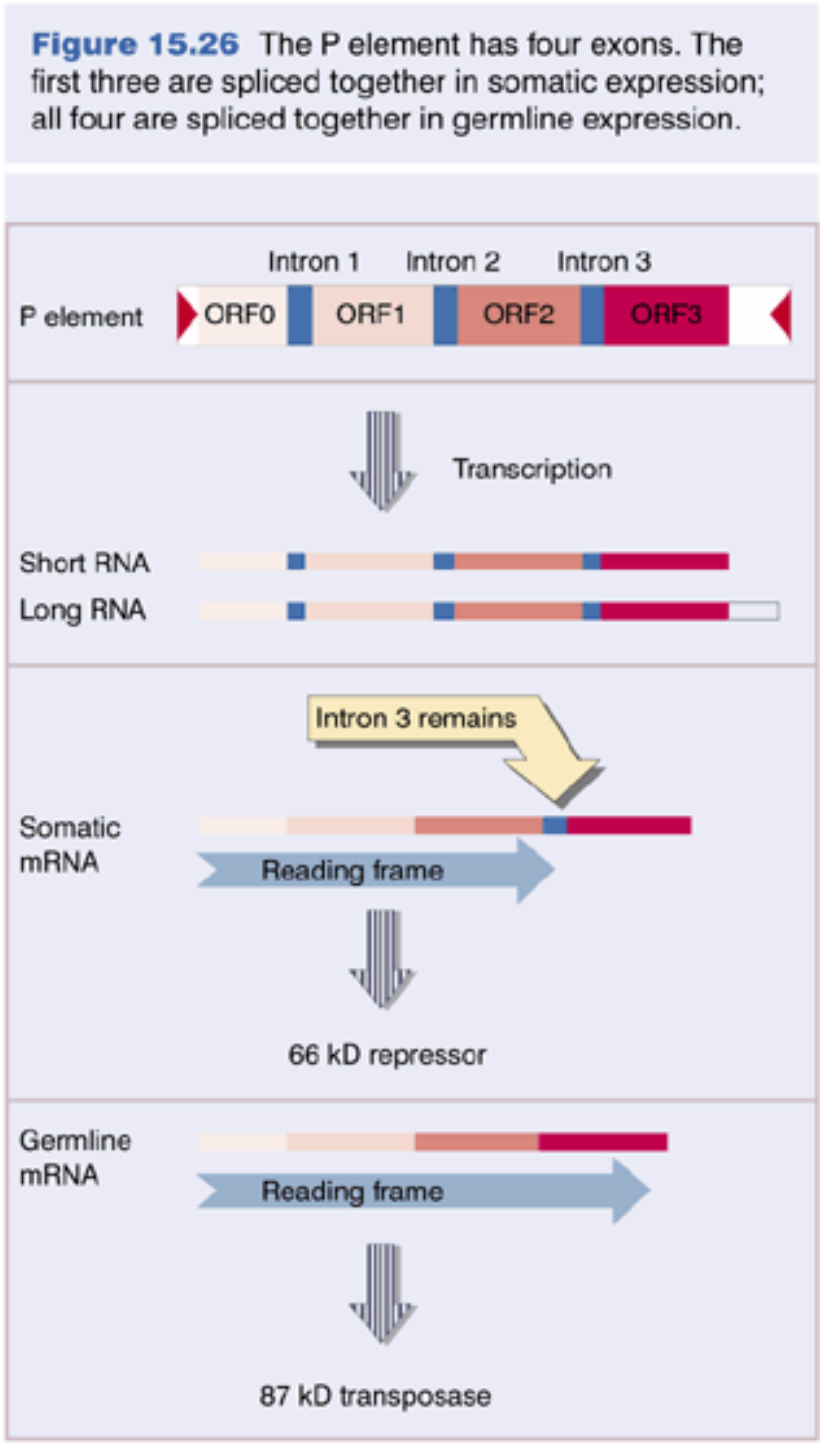
Bei der Transposition spielen die „inverted repeats“ ein große Rolle



Die P-Elemente von Drosophila erzeugen „hybrid dysgenesis“



Die P-Elemente von Drosophila:



Die P-Elemente von Drosophila:

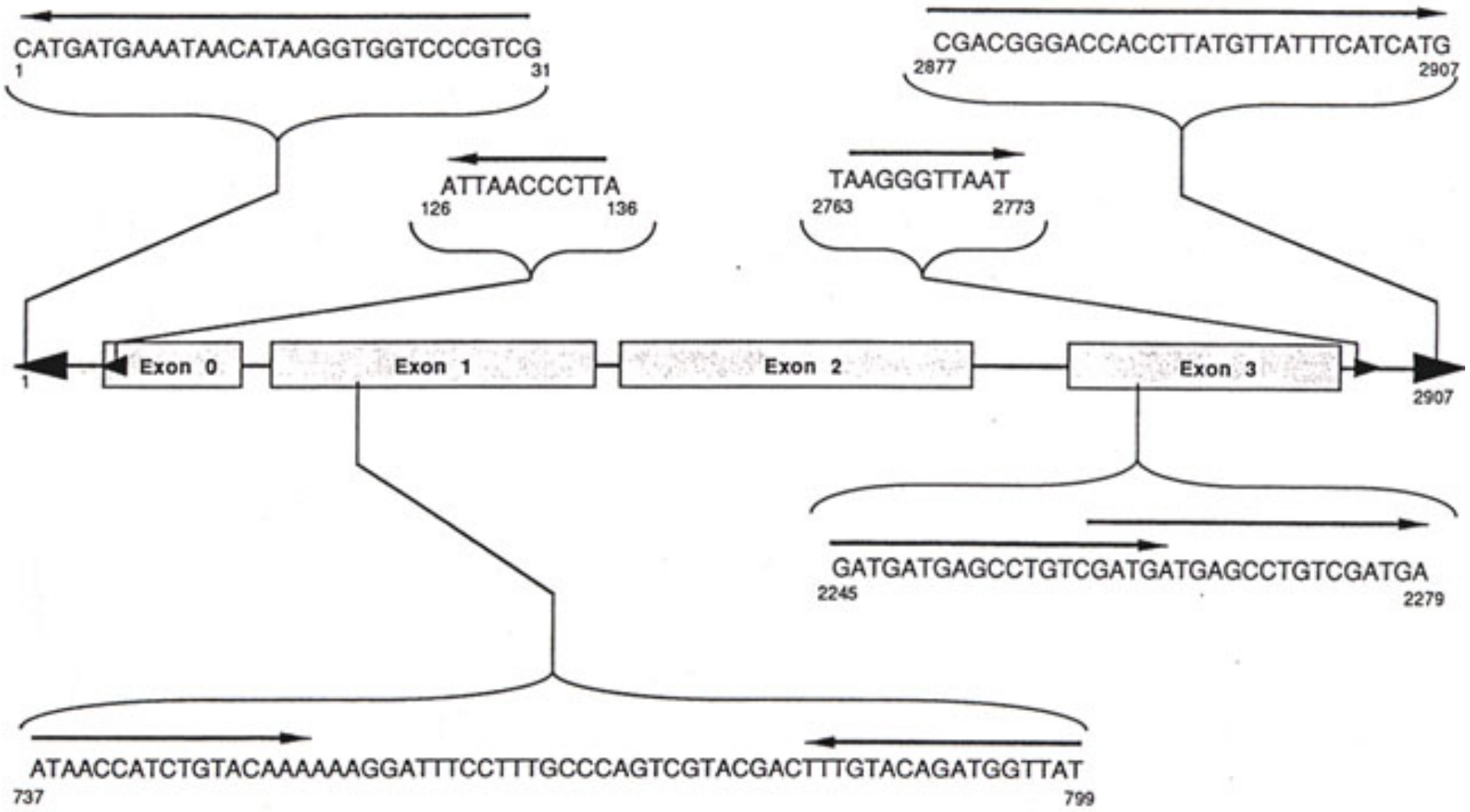
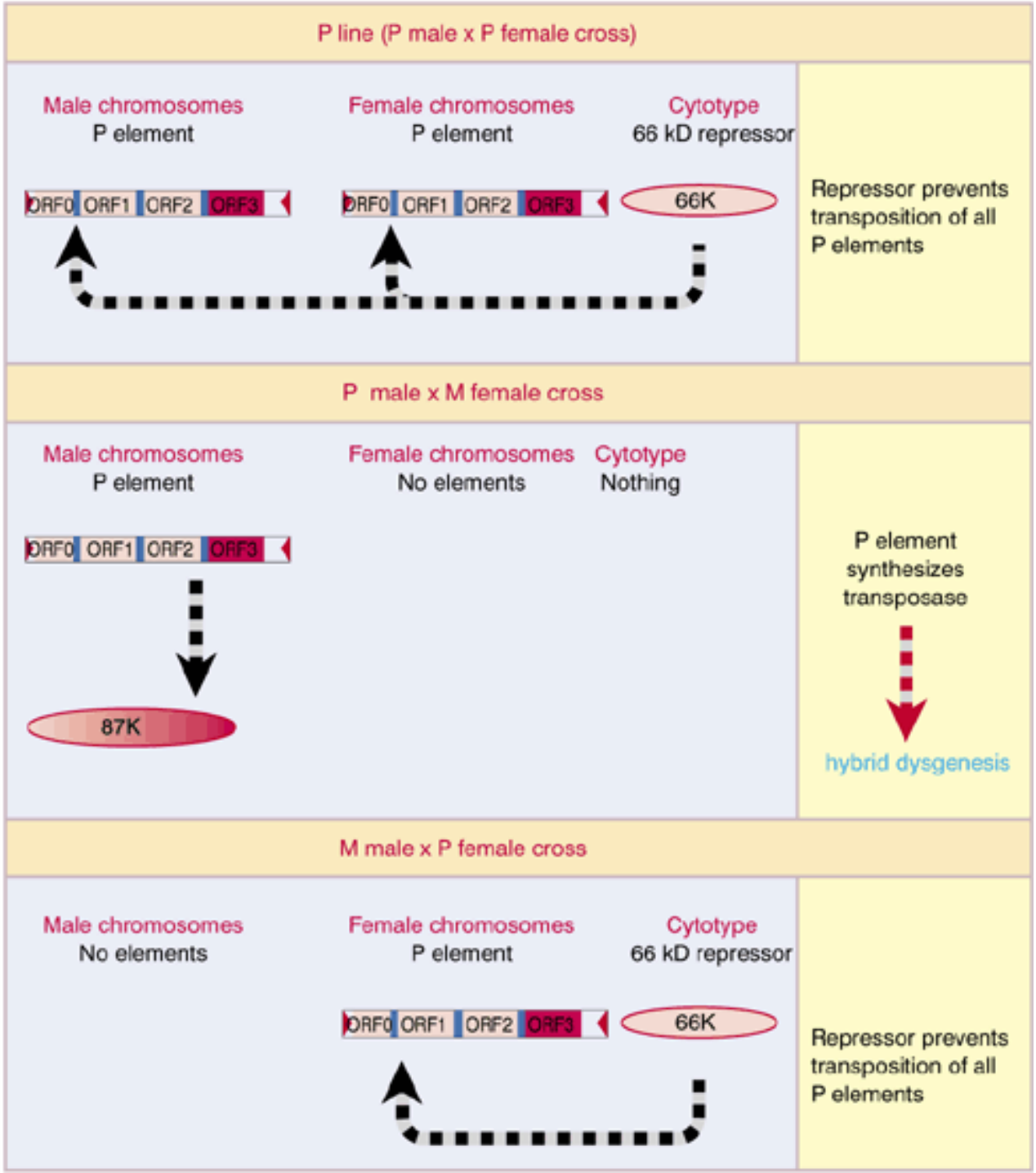


Figure 3. The complete P element and its repeat structures. The sequence was obtained by O'Hare and Rubin (155).

Figure 15.27 Hybrid dysgenesis is determined by the interactions between P elements in the genome and 66 kD repressor in the cytotype.



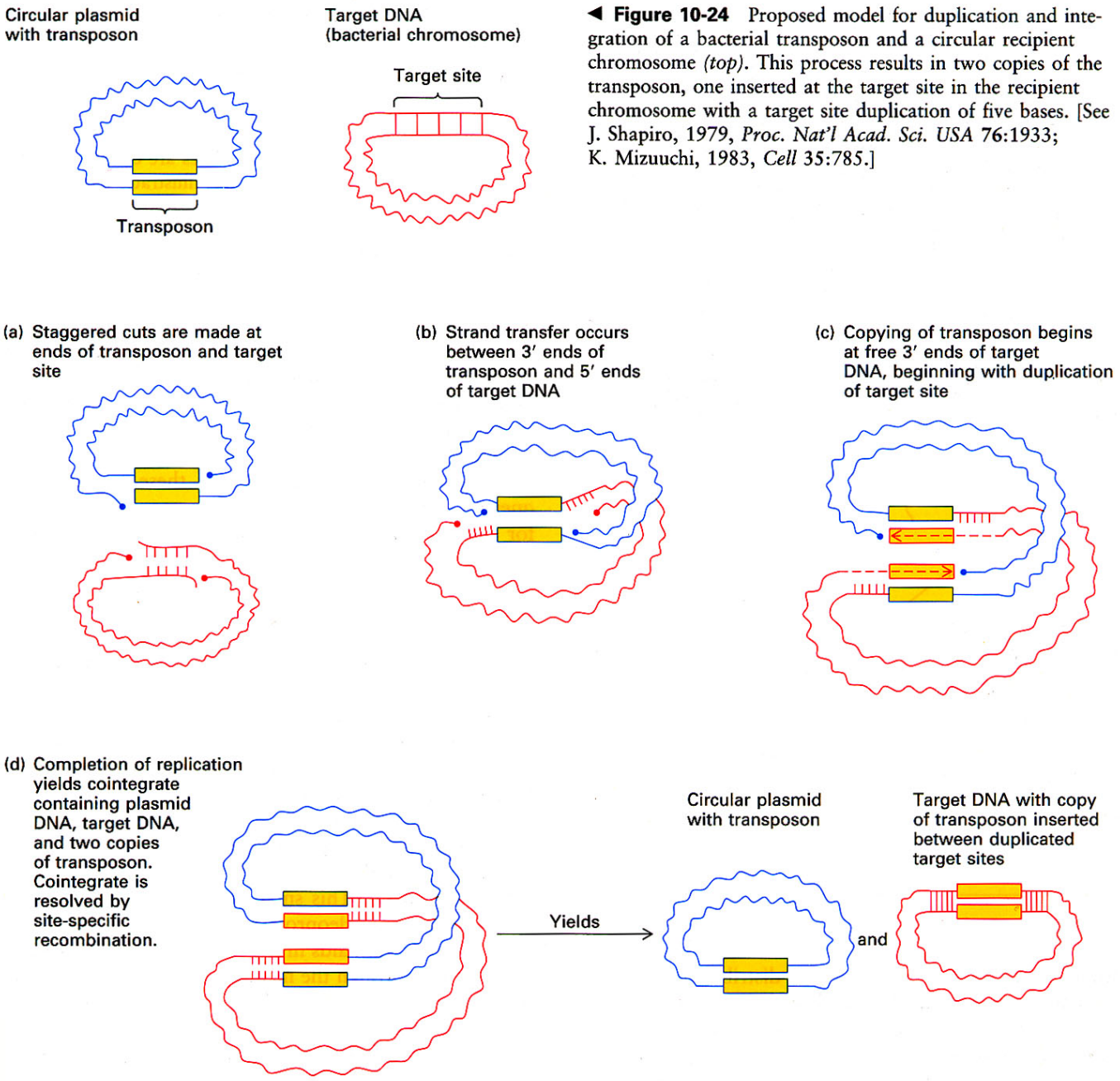
Die
„hybrid dysgenesis“
Ist die Folge von einem
Wechselspiel von
aktiver Transposase
In Keimzellen von P-freien
Tieren und dem Repressor
In P-haltigen Tieren

DNA-Transposons beim Menschen

Table 11 Number of copies and fraction of genome for classes of interspersed repeat

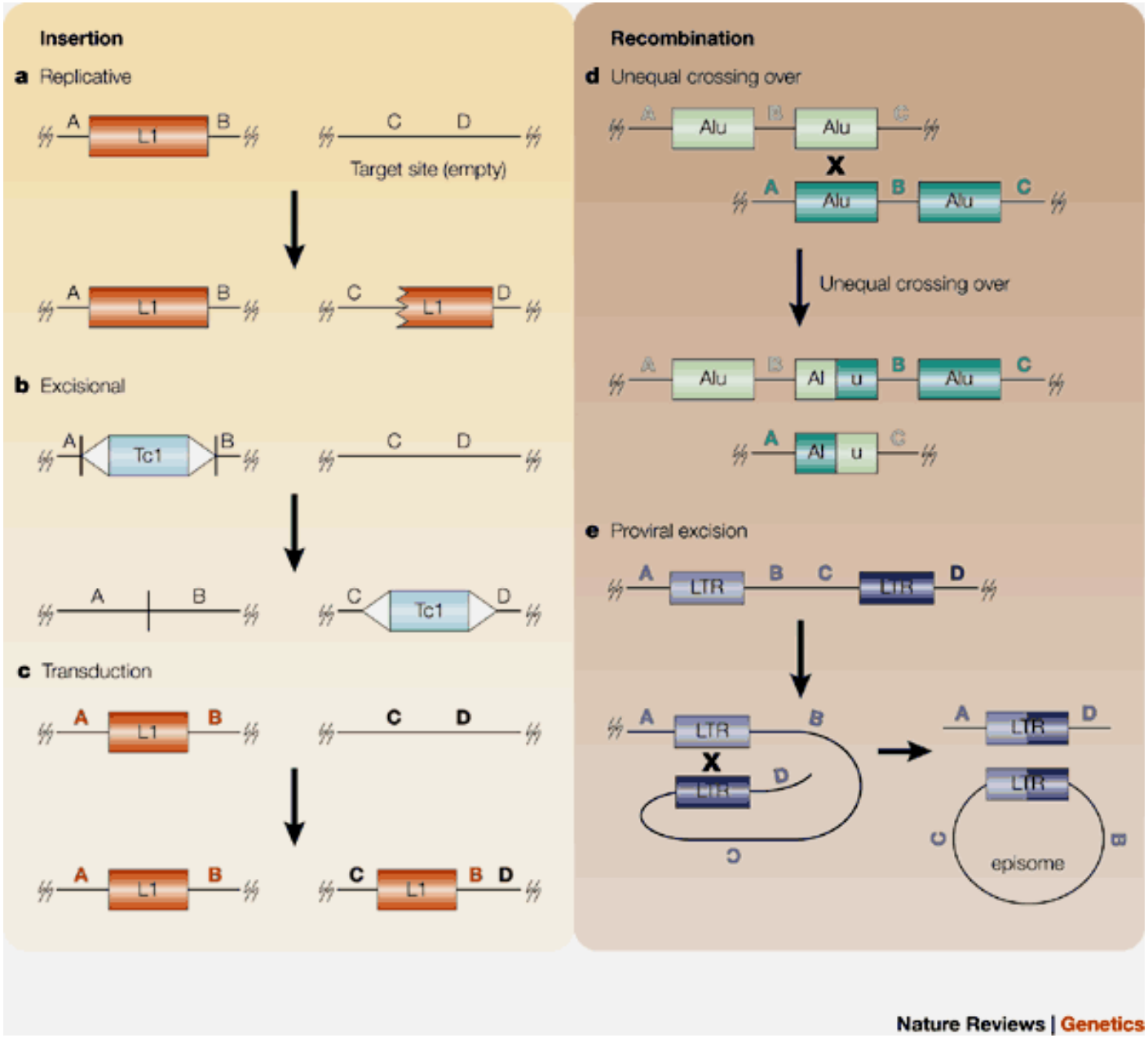
	Number of copies (× 1,000)	Total number of bases in the draft genome	Fraction of the draft genome sequence (%)	Number of families (subfamilies)
DNA elements	294	77.6	2.84	
hAT group				
MER1-Charlie	182	38.1	1.39	25 (50)
Zaphod	13	4.3	0.16	4 (10)
Tc-1 group				
MER2-Tigger	57	28.0	1.02	12 (28)
Tc2	4	0.9	0.03	1 (5)
Mariner	14	2.6	0.10	4 (5)
PiggyBac-like	2	0.5	0.02	10 (20)
Unclassified	22	3.2	0.12	7 (7)

Mechanismus der replikativen Transpososition

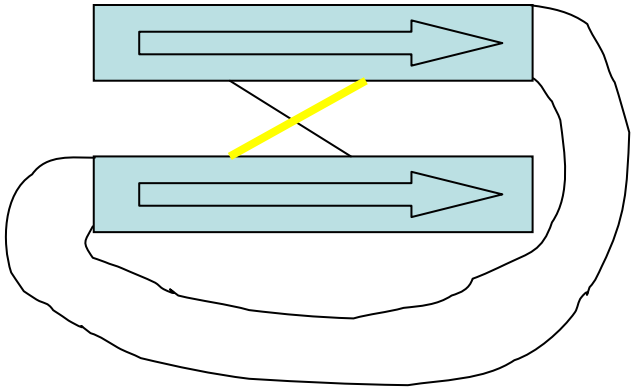


◀ **Figure 10-24** Proposed model for duplication and integration of a bacterial transposon and a circular recipient chromosome *(top)*. This process results in two copies of the transposon, one inserted at the target site in the recipient chromosome with a target site duplication of five bases. [See J. Shapiro, 1979, *Proc. Nat'l Acad. Sci. USA* 76:1933; K. Mizuuchi, 1983, *Cell* 35:785.]

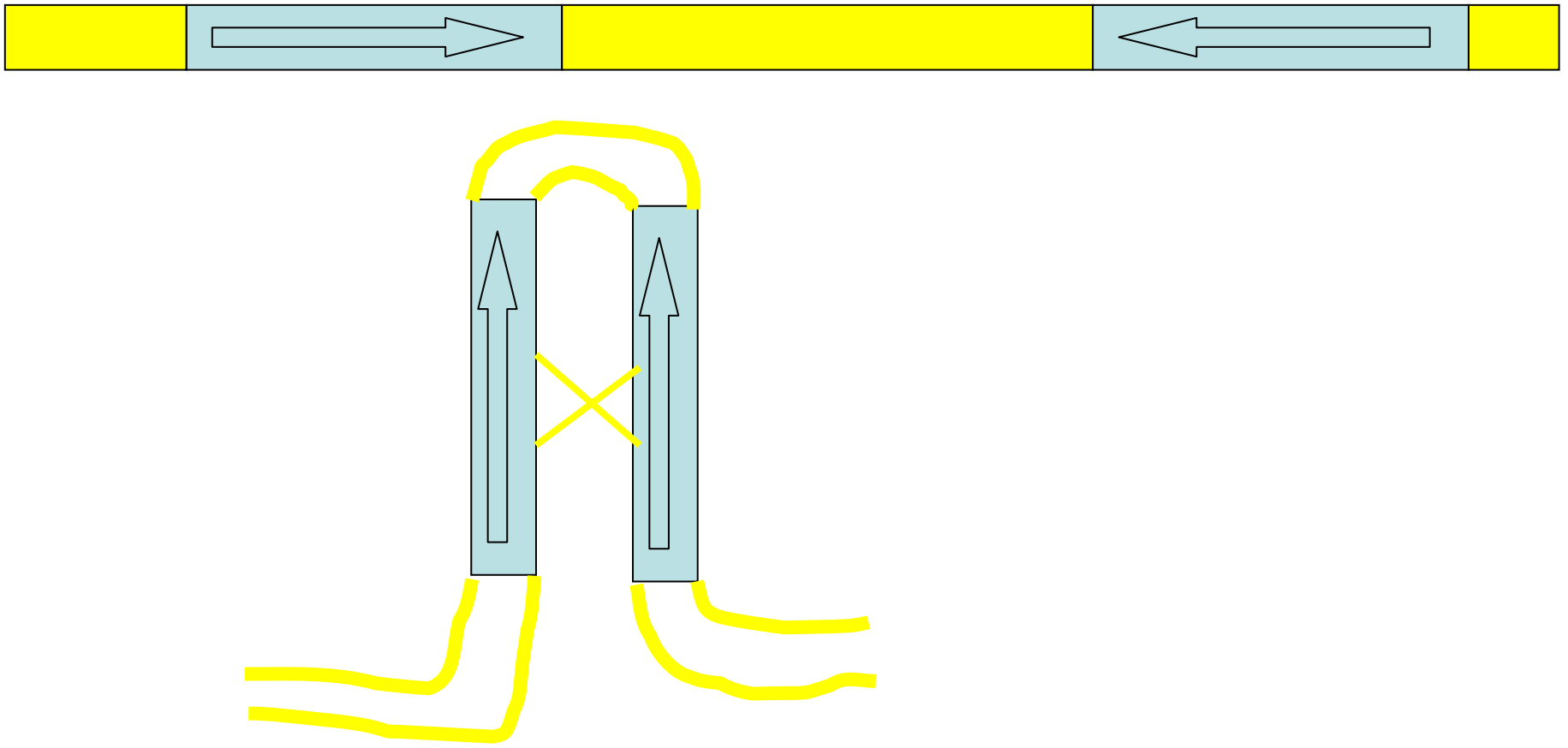
Vermehrung und Transposition von repetitiven Elementen



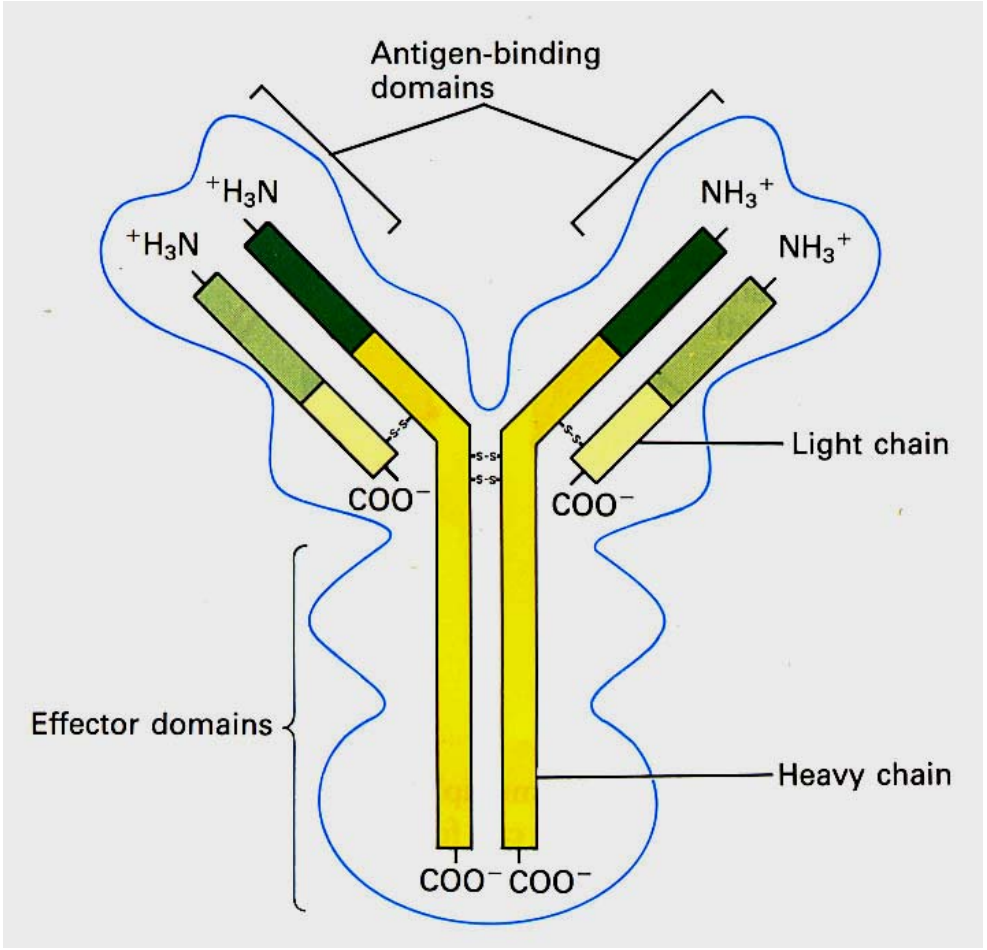
Interspergierte repetitive Elemente können Inversionen und Deletionen erzeugen



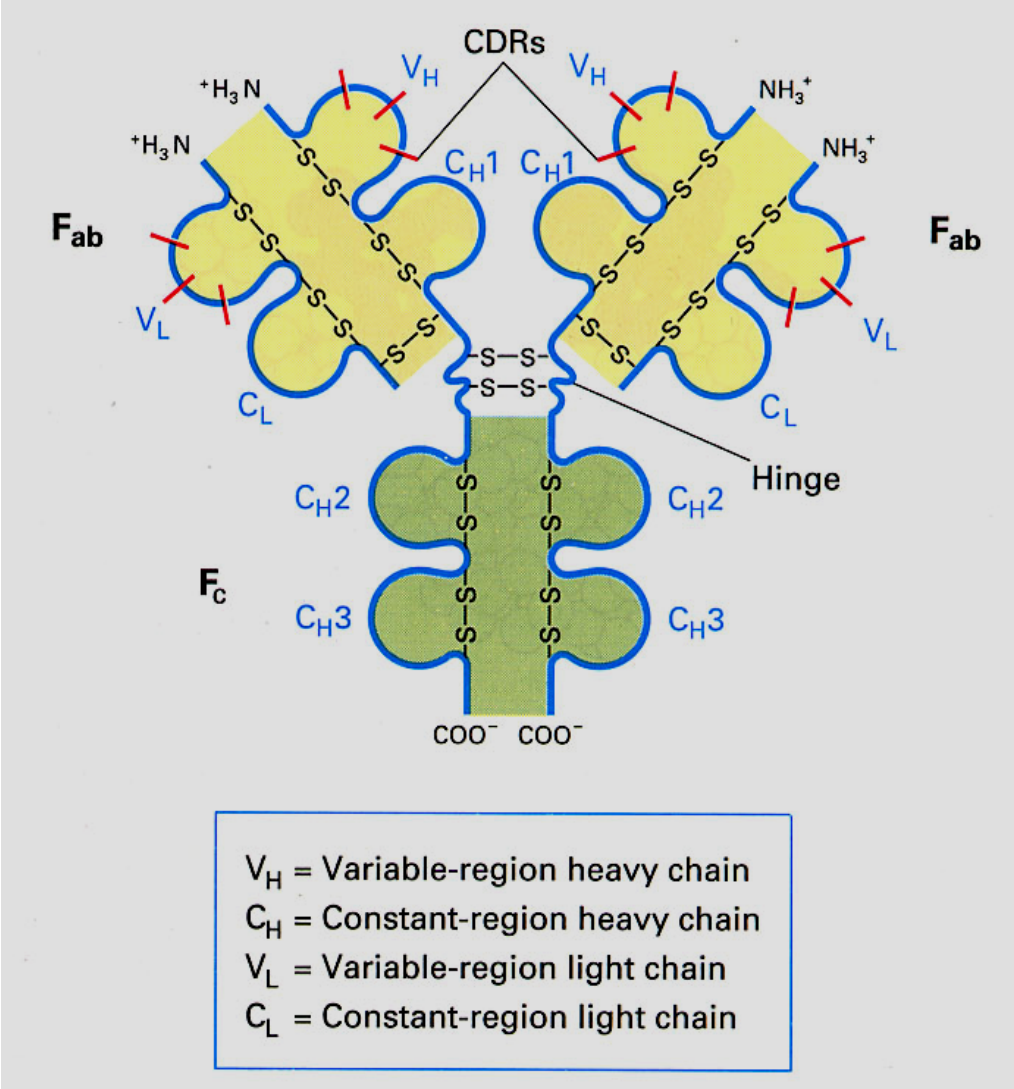
Interspergierte repetitive Elemente können Inversionen und Deletionen erzeugen



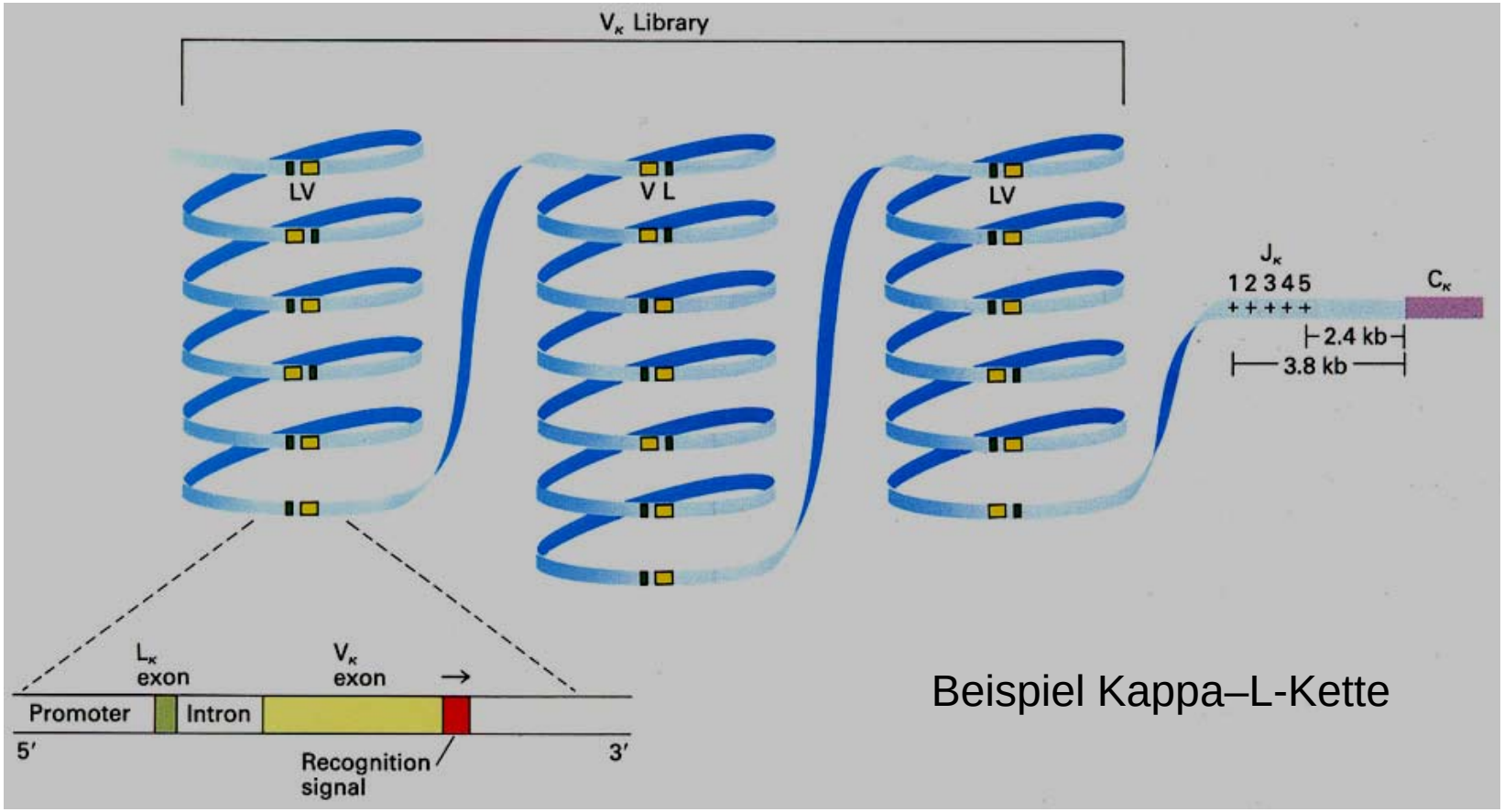
Die Variabilität der Immunglobuline:



Die Immunglobuline bestehen aus zwei Ketten, L und H, die über Disulfidbrücken verknüpft sind

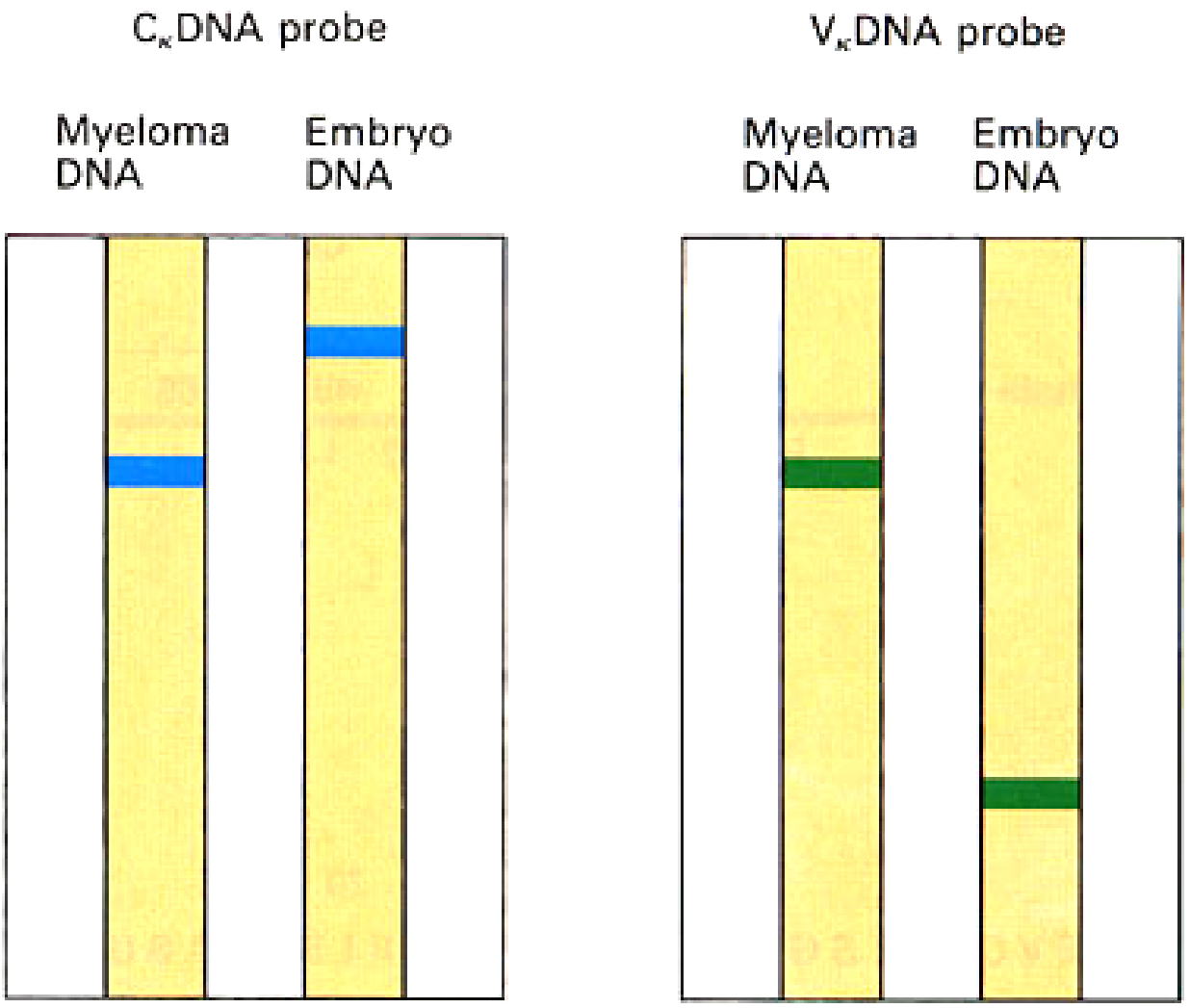


Die Gene für Immunglobuline bestehen aus verschiedenen Teilen, die in den Chromosomen nicht unmittelbar zusammen liegen

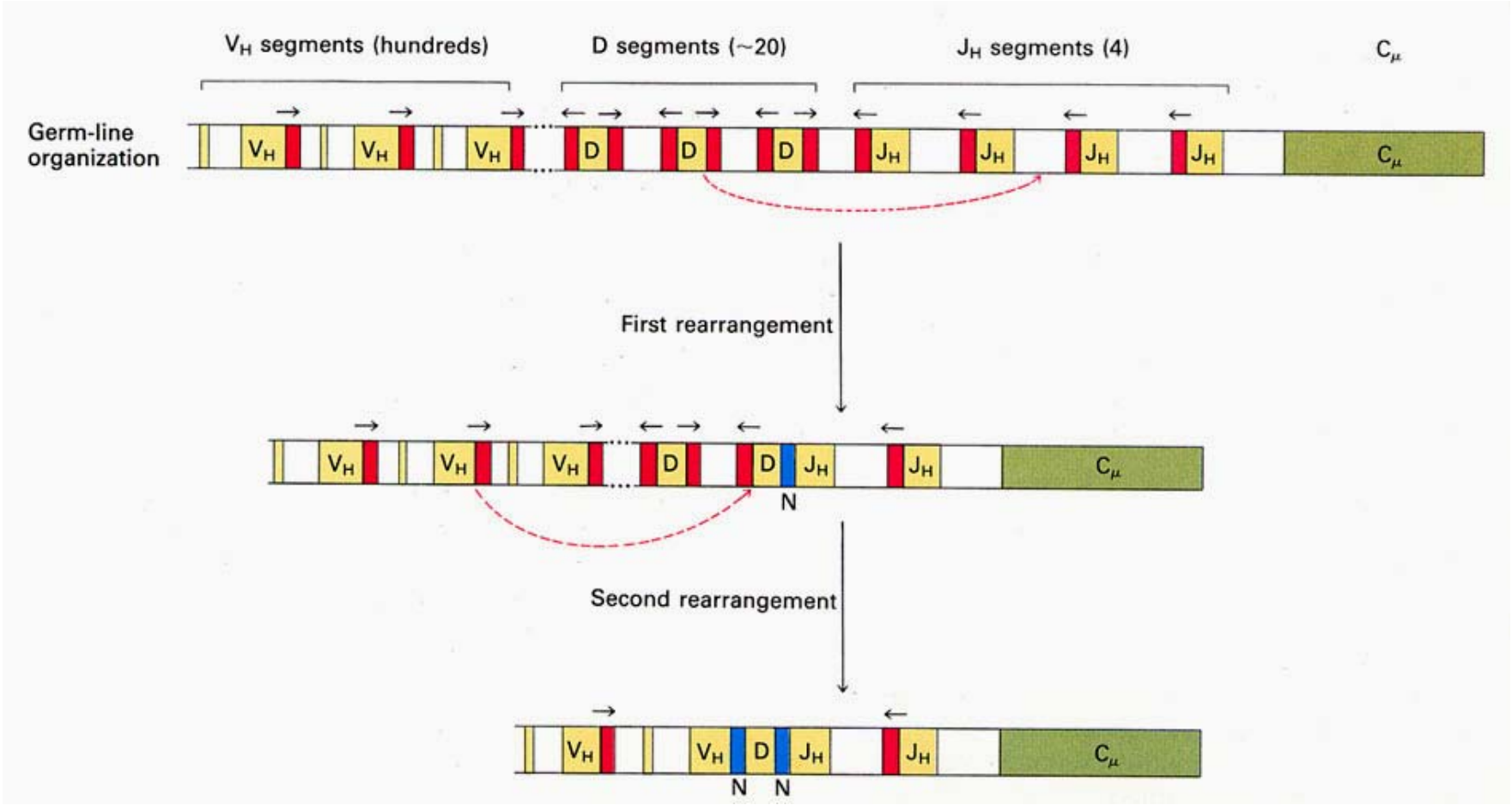


Beispiel Kappa–L-Kette

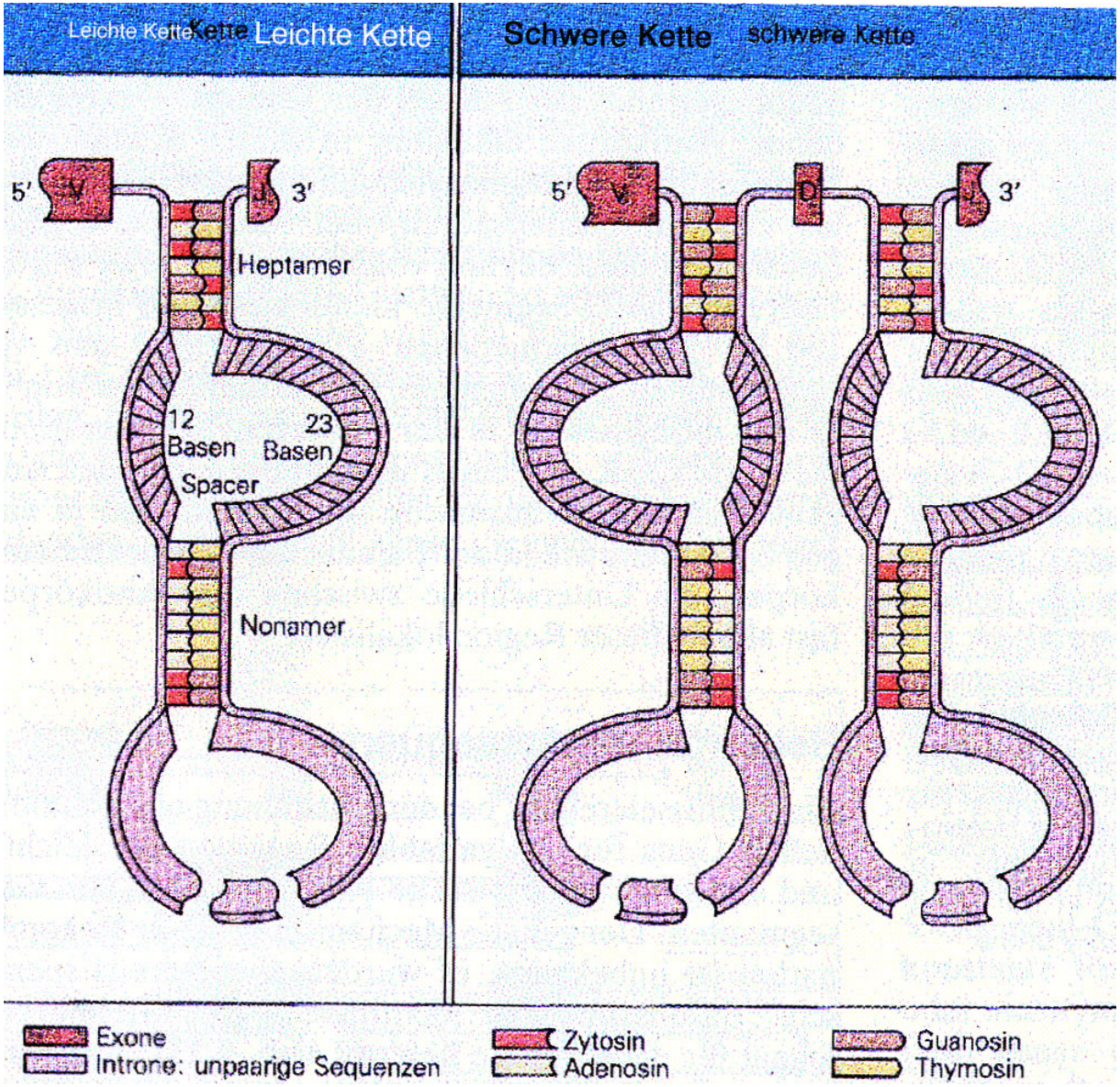
Die Variabilität der Antikörper wird durch „Rearrangements“ der Genteile während der Immunzellenreifung erzeugt: die Southern-Analyse zeigt Unterschiede zwischen Embryo und „reifen“ Immunzellen



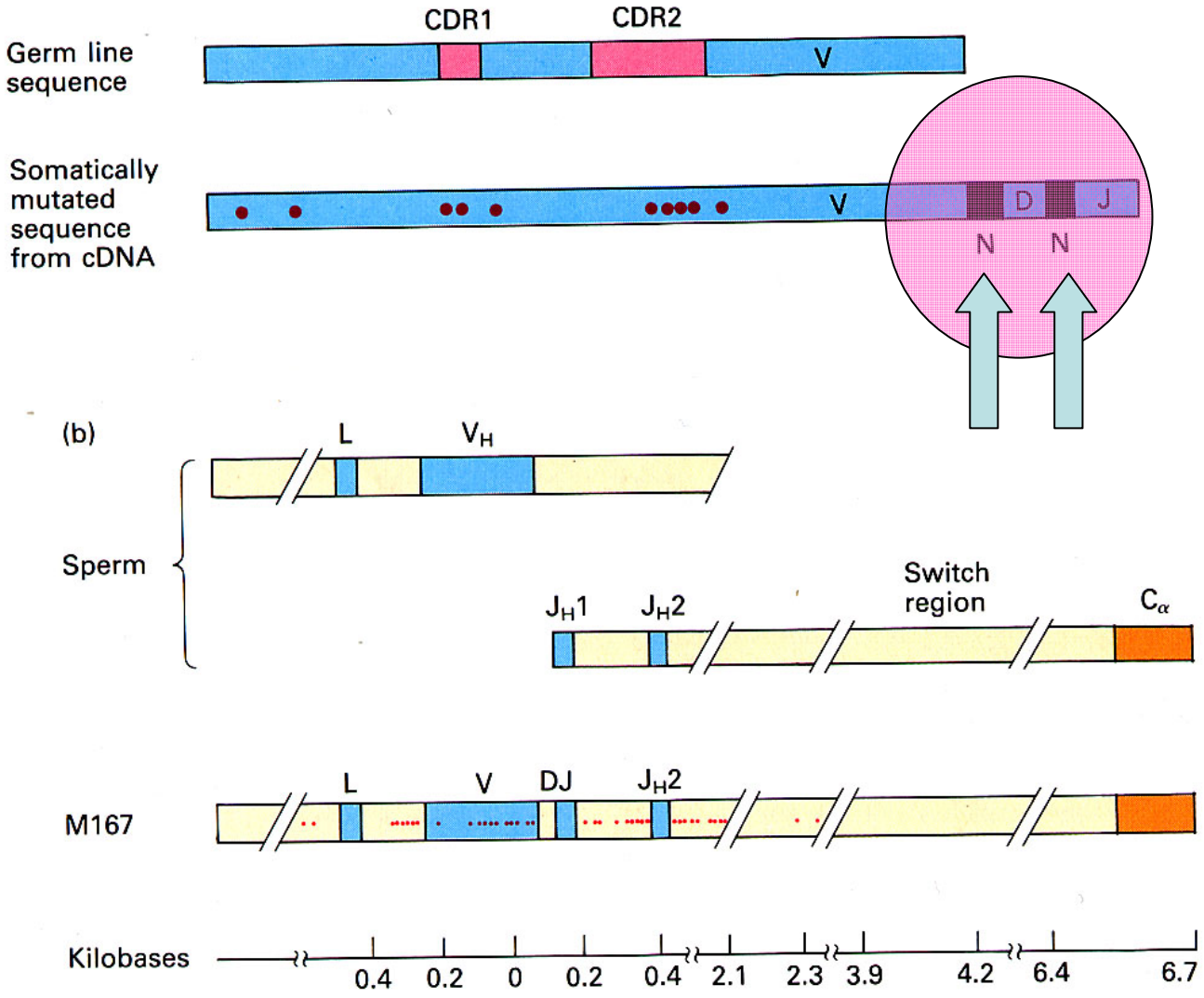
Beim „Rearrangement“ werden jeweils einzelne der Genteile „rekombiniert“



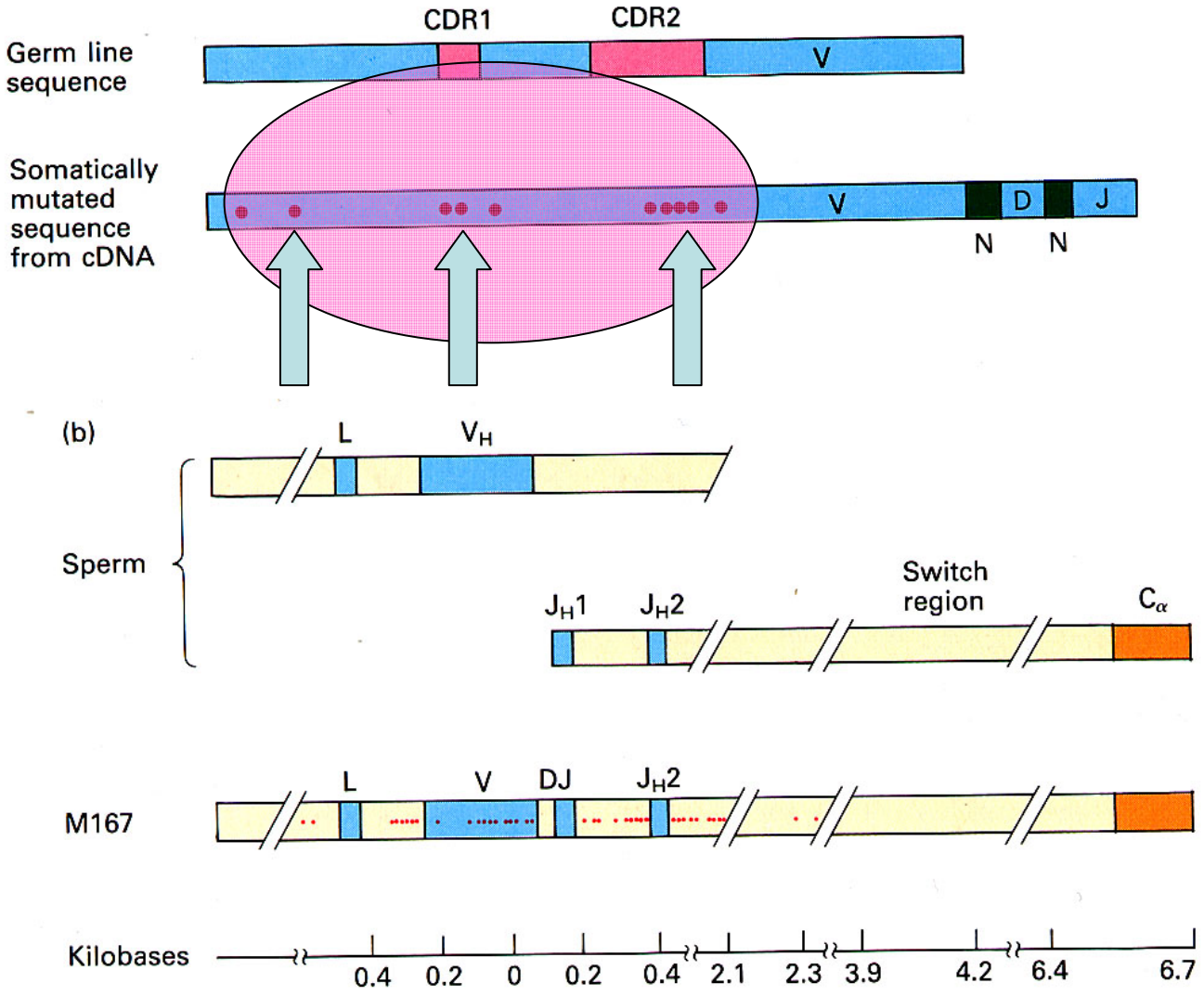
Die Rekombination wird vermittelt durch die „Rekombinationssequenz“ am Ende der Genteile



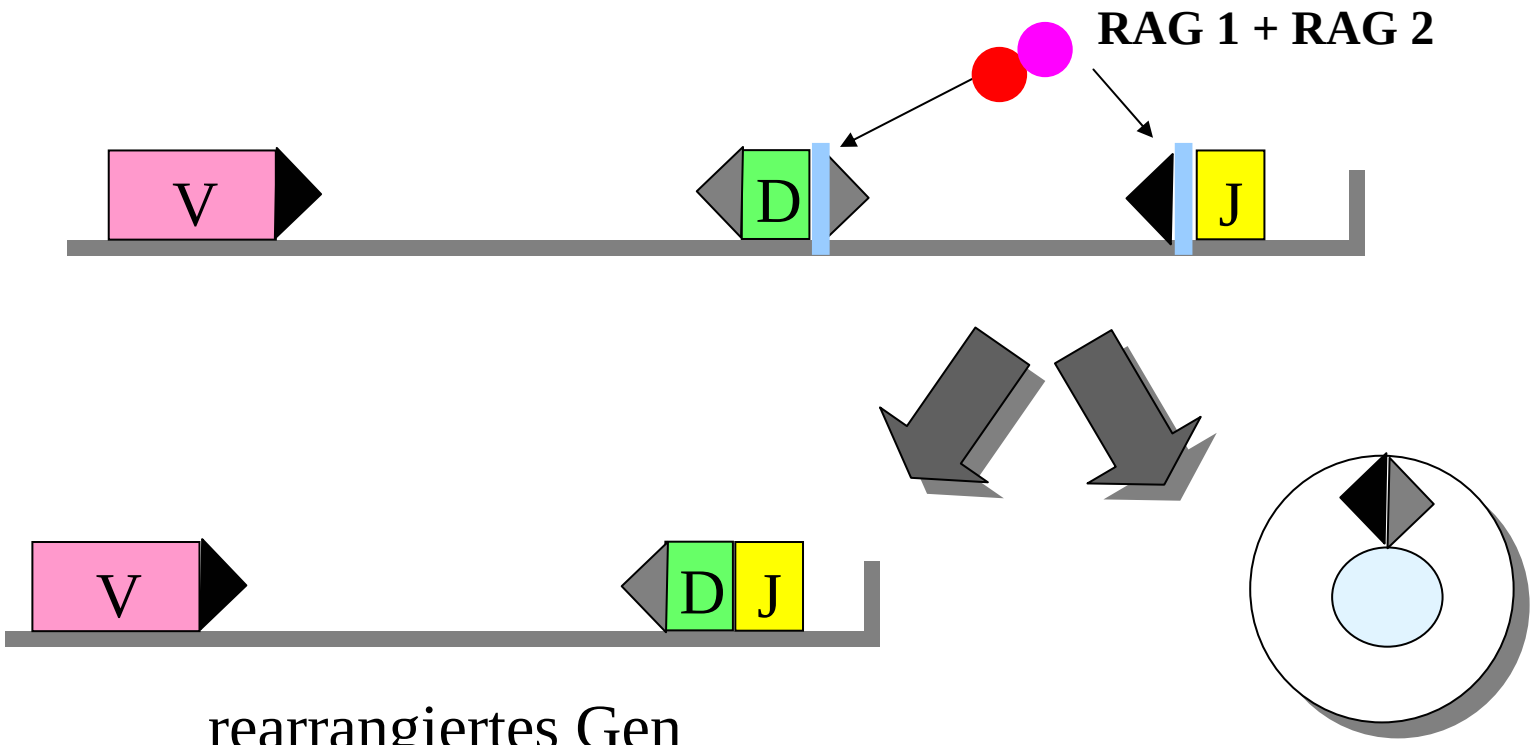
Bei der VDJ- Rekombination werden noch zusätzlich Nukleotide von der terminalen Nukleotidyltransferase Basen eingefügt,



Bei der VDJ- Rekombination entstehen außerdem „somatische Mutationen“



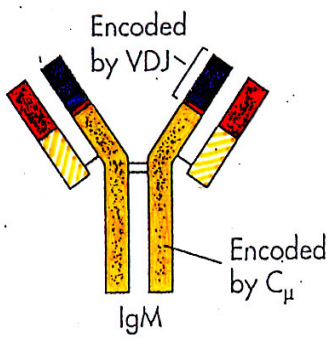
Molekulares Geschehen bei der V-D-J-Rekombination /

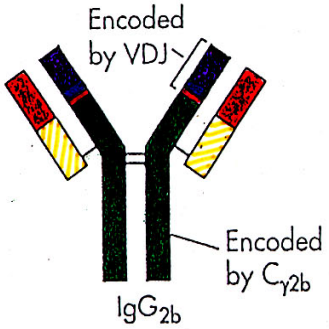


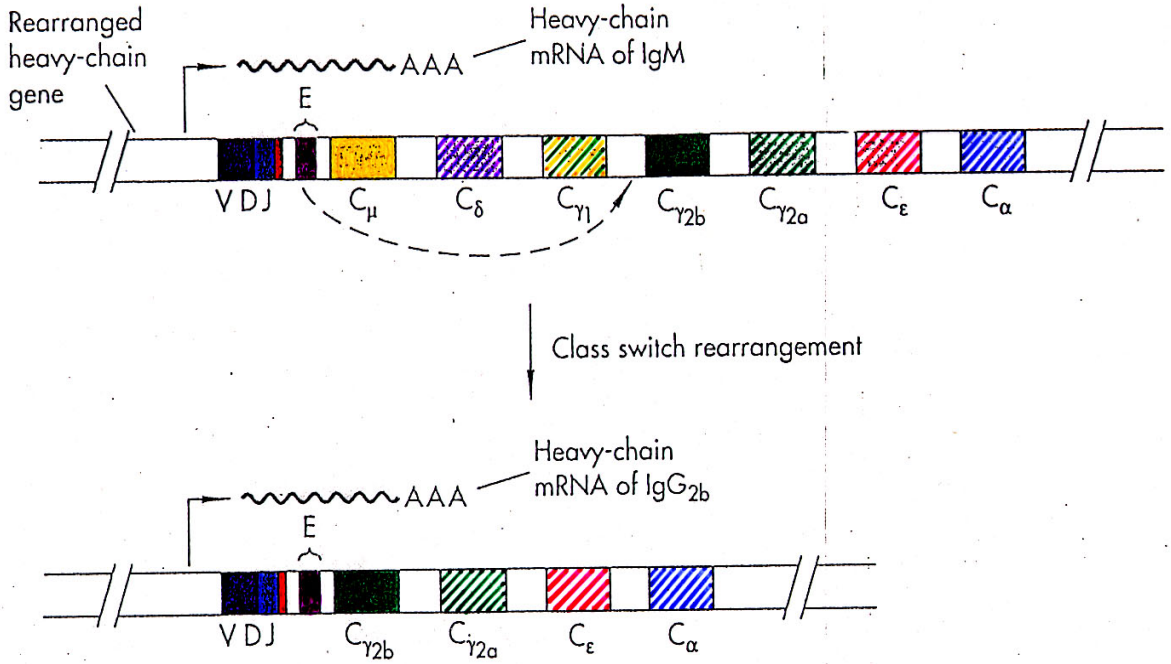
rearrangiertes Gen

extrachromosomale, zirkuläre DNA

Es gibt zusätzlich verschiedene Antikörperklassen. Die Klasse wird durch die C-Region bestimmt







18.3 Antibody Classes (Part 1)

CLASS	GENERAL STRUCTURE		LOCATION	FUNCTION
IgG	Monomer		Free in plasma; about 80 percent of circulating antibodies	Most abundant antibody in primary and secondary responses; crosses placenta and provides passive immunization to fetus
IgM	Pentamer		Surface of B cell; free in plasma	Antigen receptor on B cell membrane; first class of antibodies released by B cells during primary response
IgD	Monomer		Surface of B cell	Cell surface receptor of mature B cell; important in B cell activation

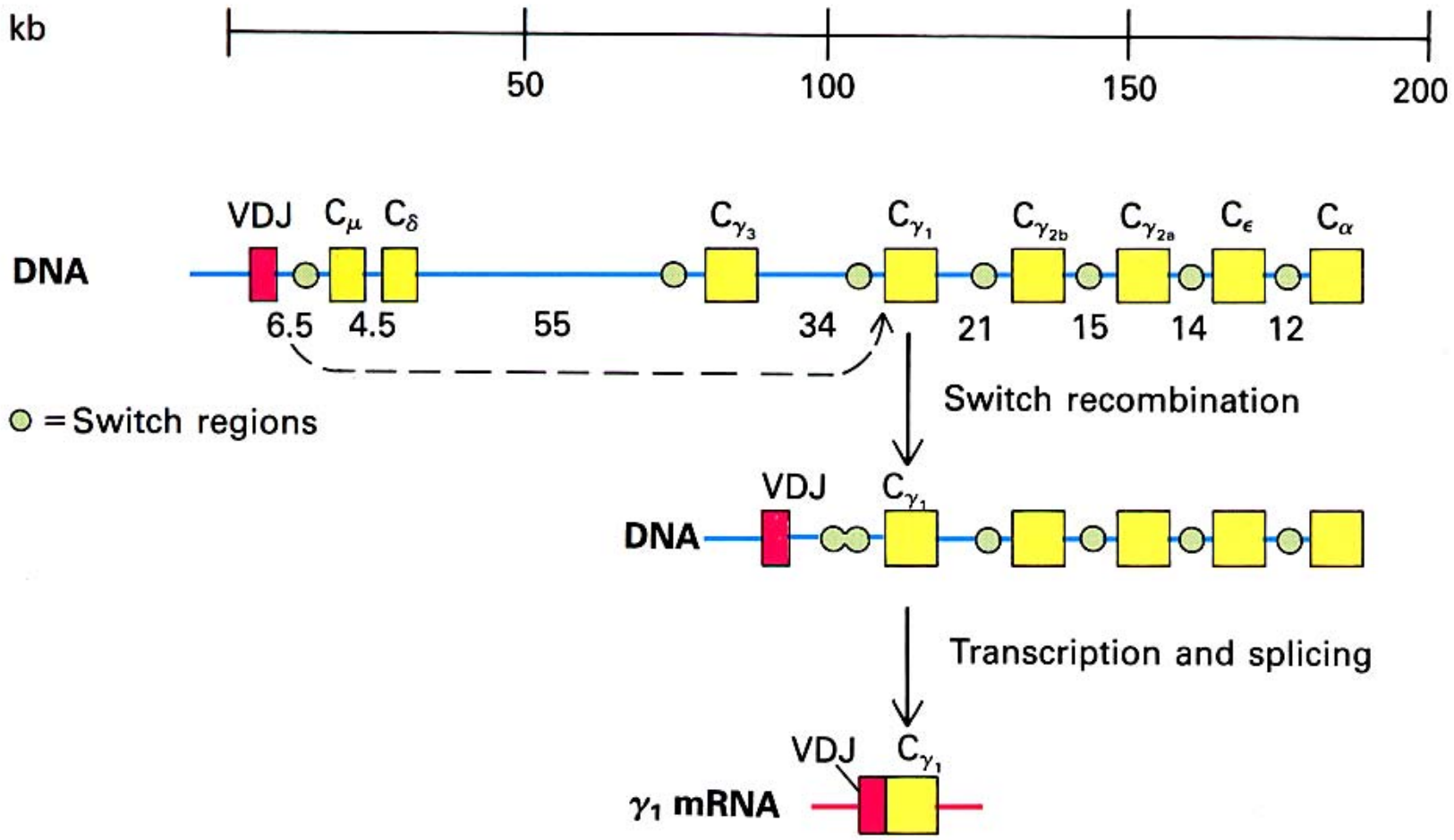
LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Table 18.3 (Part 1)

18.3 *Antibody Classes (Part 1)*

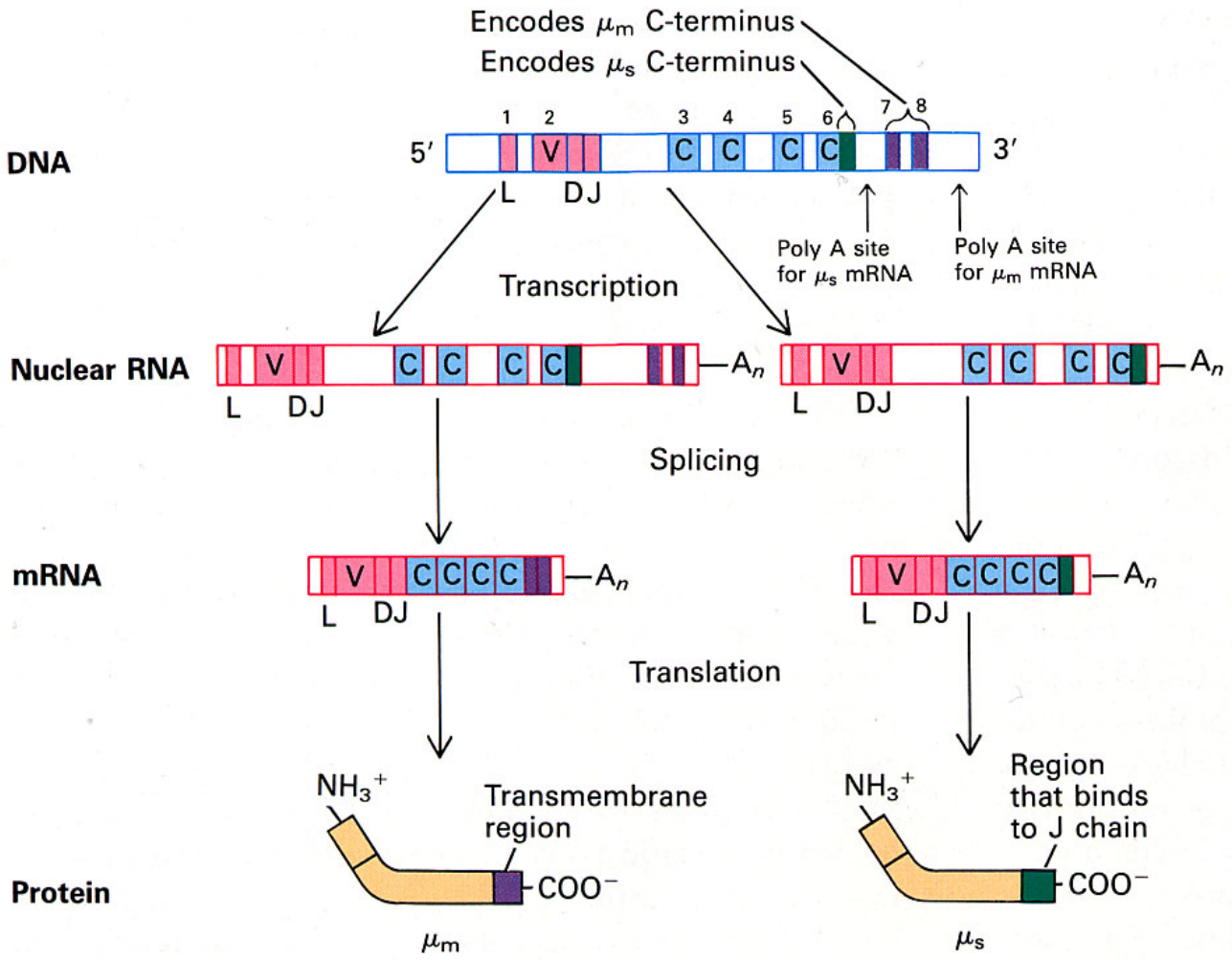
CLASS	GENERAL STRUCTURE		LOCATION	FUNCTION
IgG	Monomer		Free in plasma; about 80 percent of circulating antibodies	Most abundant antibody in primary and secondary responses; crosses placenta and provides passive immunization to fetus
IgM	Pentamer		Surface of B cell; free in plasma	Antigen receptor on B cell membrane; first class of antibodies released by B cells during primary response
IgD	Monomer		Surface of B cell	Cell surface receptor of mature B cell; important in B cell activation
IgA	Dimer		Monomer found in plasma; polymers in saliva, tears, milk, and other body secretions	Protects mucosal surfaces; prevents attachment of pathogens to epithelial cells
IgE	Monomer		Secreted by plasma cells in skin and tissues lining gastrointestinal and respiratory tracts	Found on mast cells and basophils; when bound to antigens, triggers release of histamine from mast cell or basophil that contributes to inflammation and some allergic responses

LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Table 18.3 (Part 1)

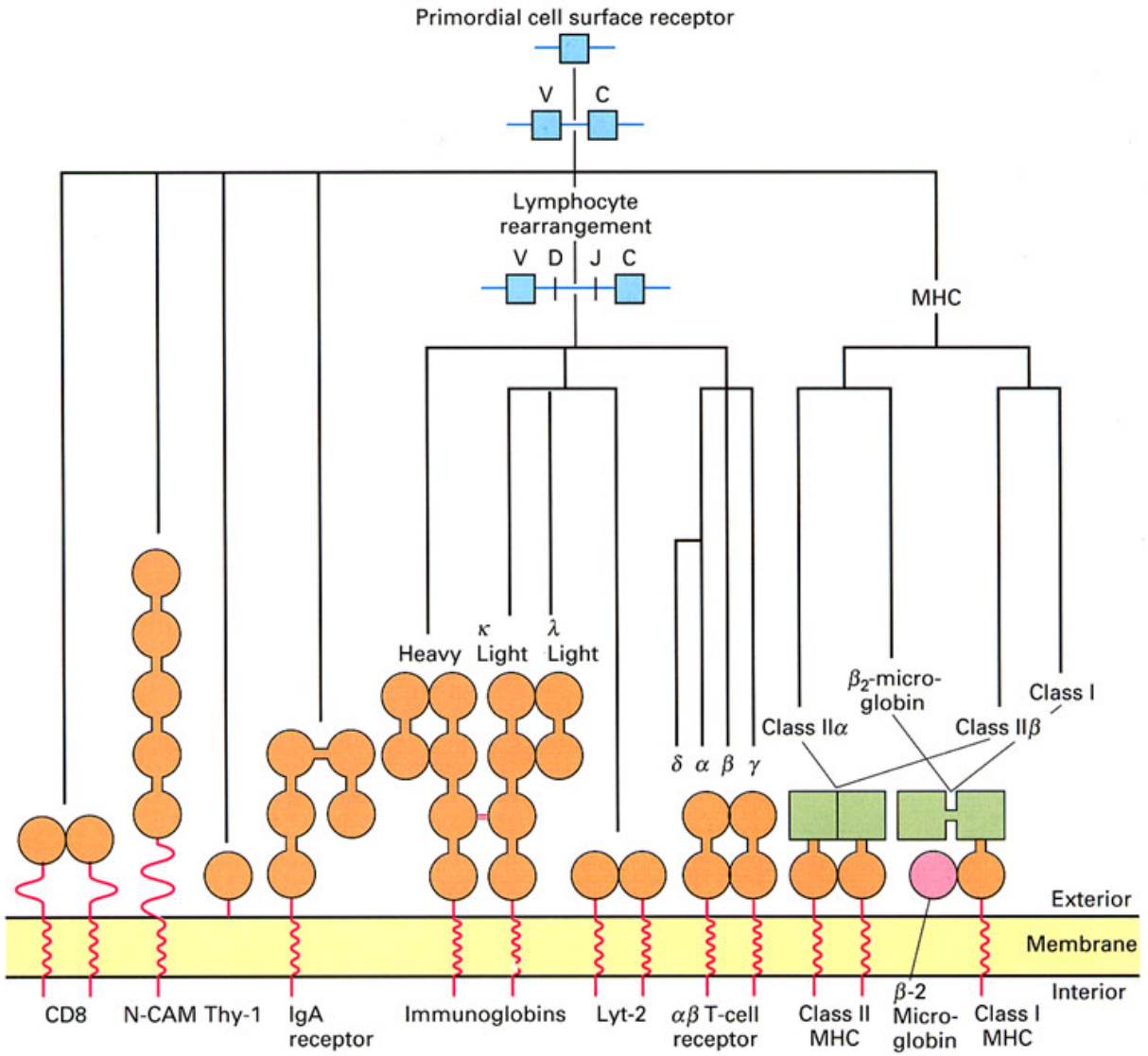
Der Antikörper “switch“ erfolgt durch Rekombination zwischen verschiedenen C-Abschnitten in der „switch“-Region



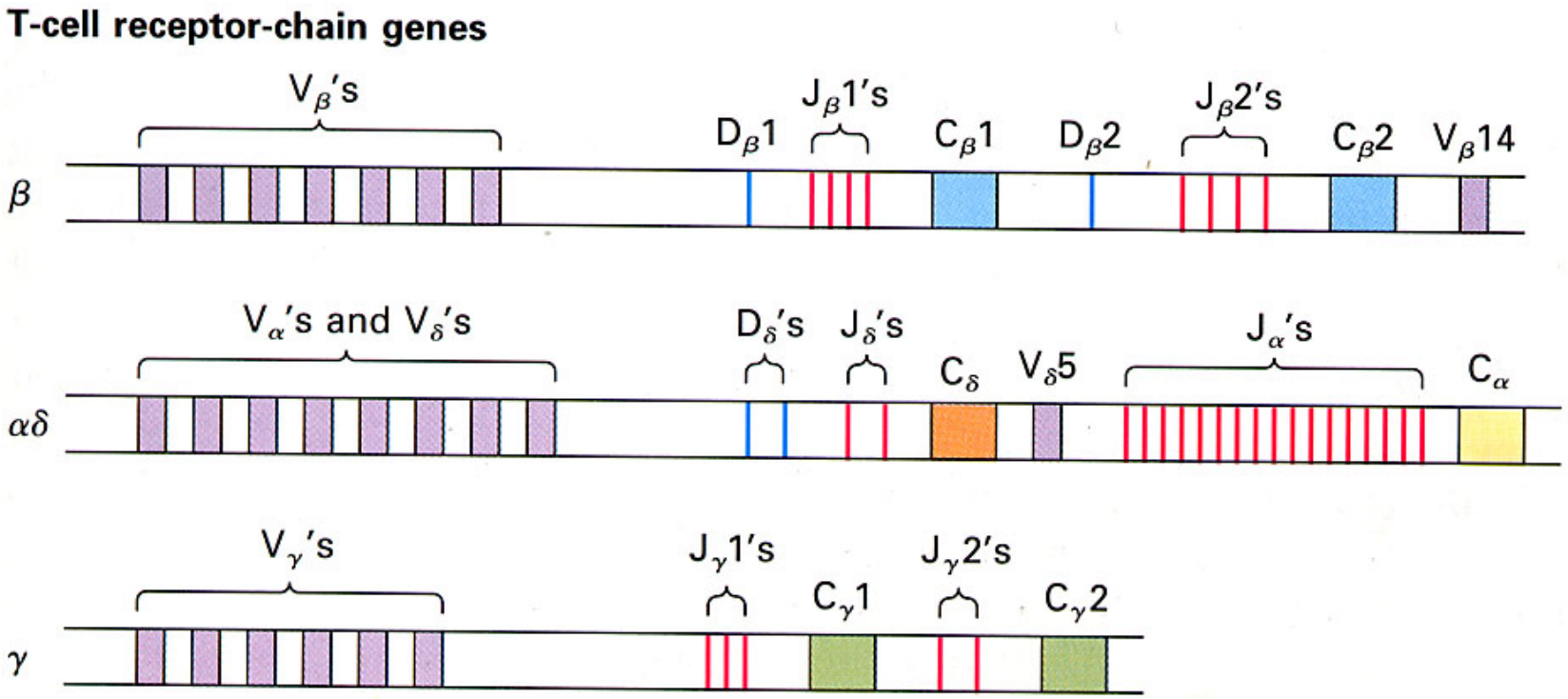
Durch Verwendung unterschiedlicher Polyadenylierungsstellen kann entweder die lösliche oder die membranständige Form erzeugt werden



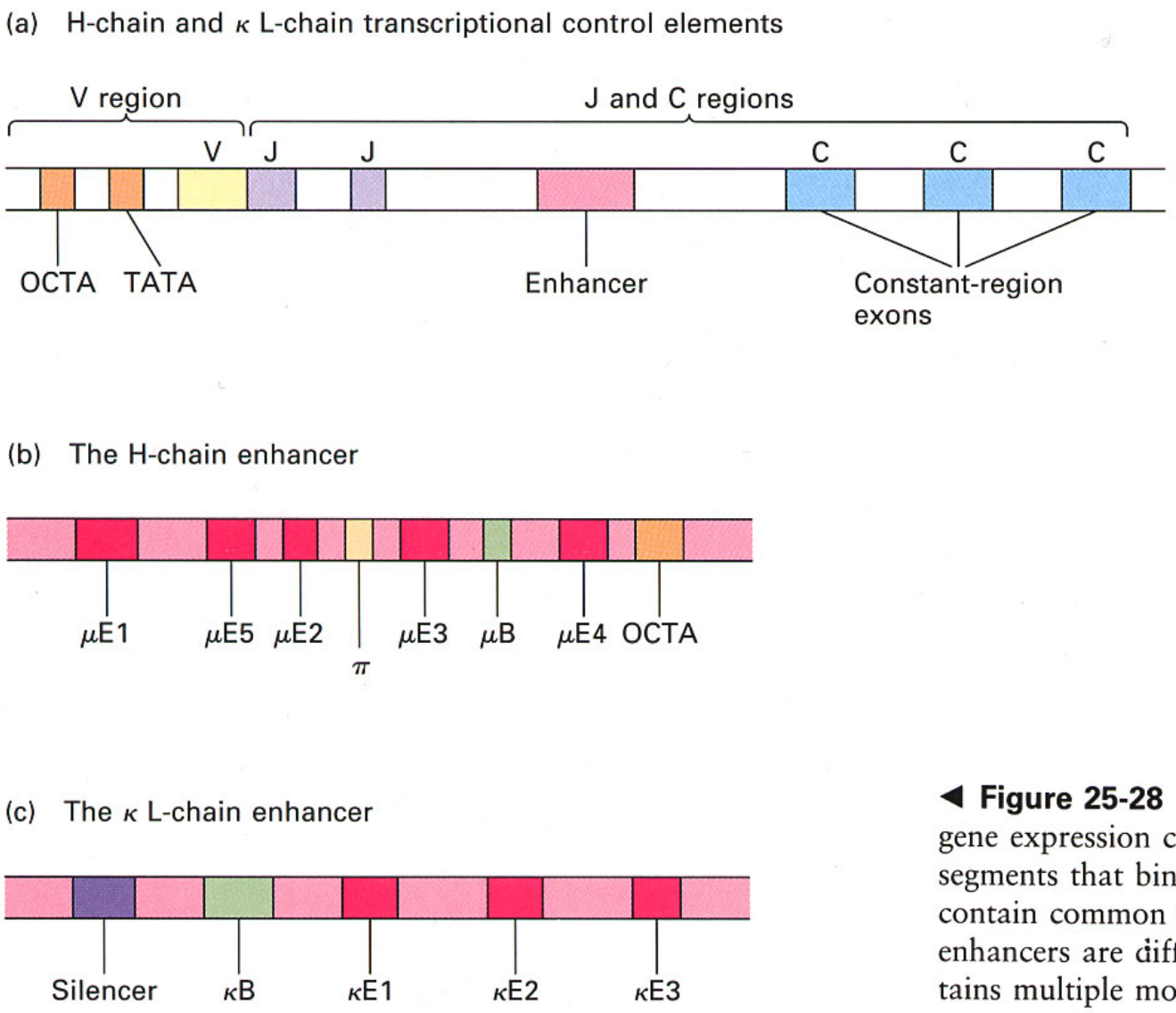
Die IG-Genfamilie hat sehr viele verschieden Mitglieder:



Noch komplizierter sind die Gene für die T-Zell-Rezeptor Ketten



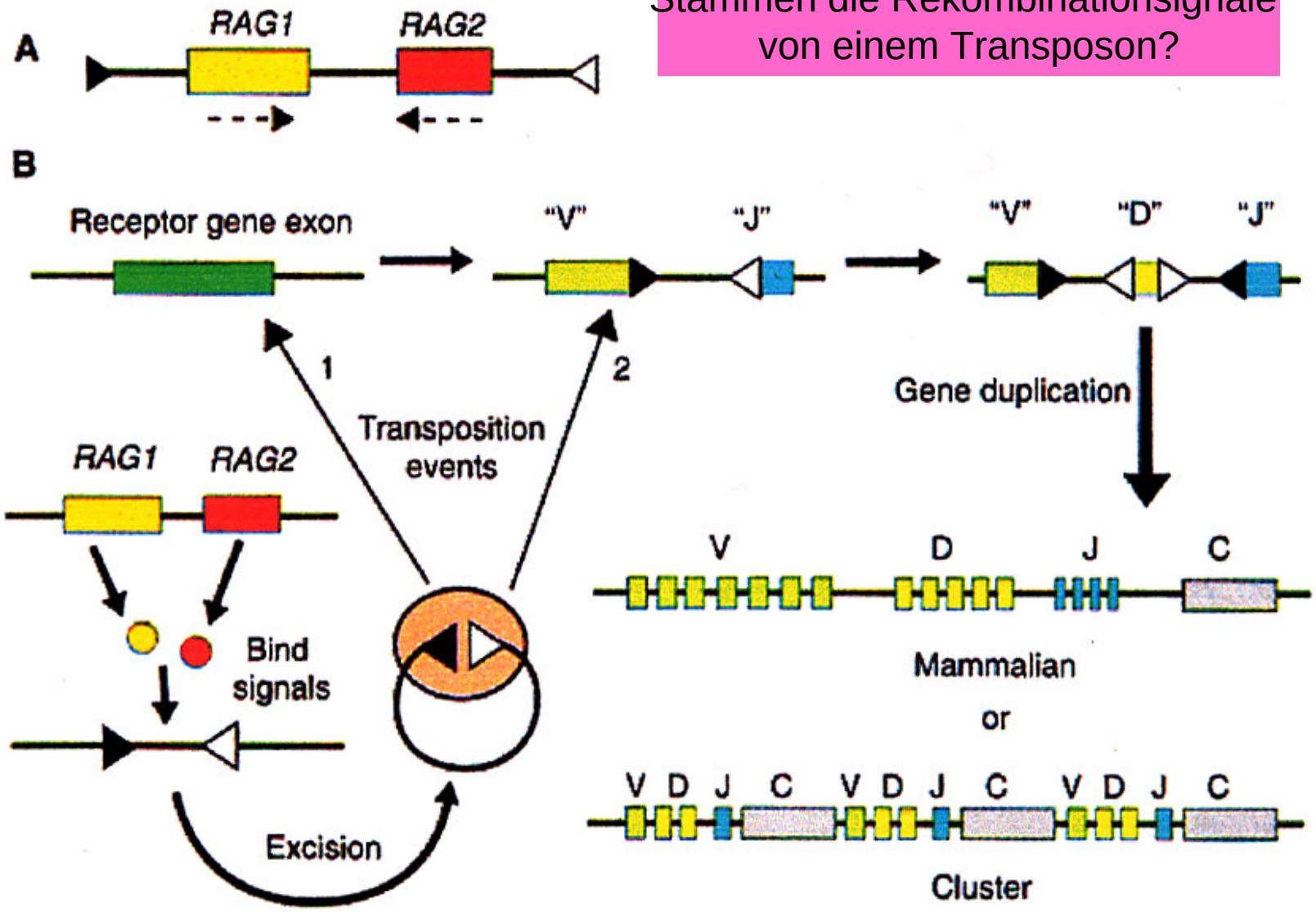
Für die Genregulation ist ein Enhancer im ersten Intron entscheidend:



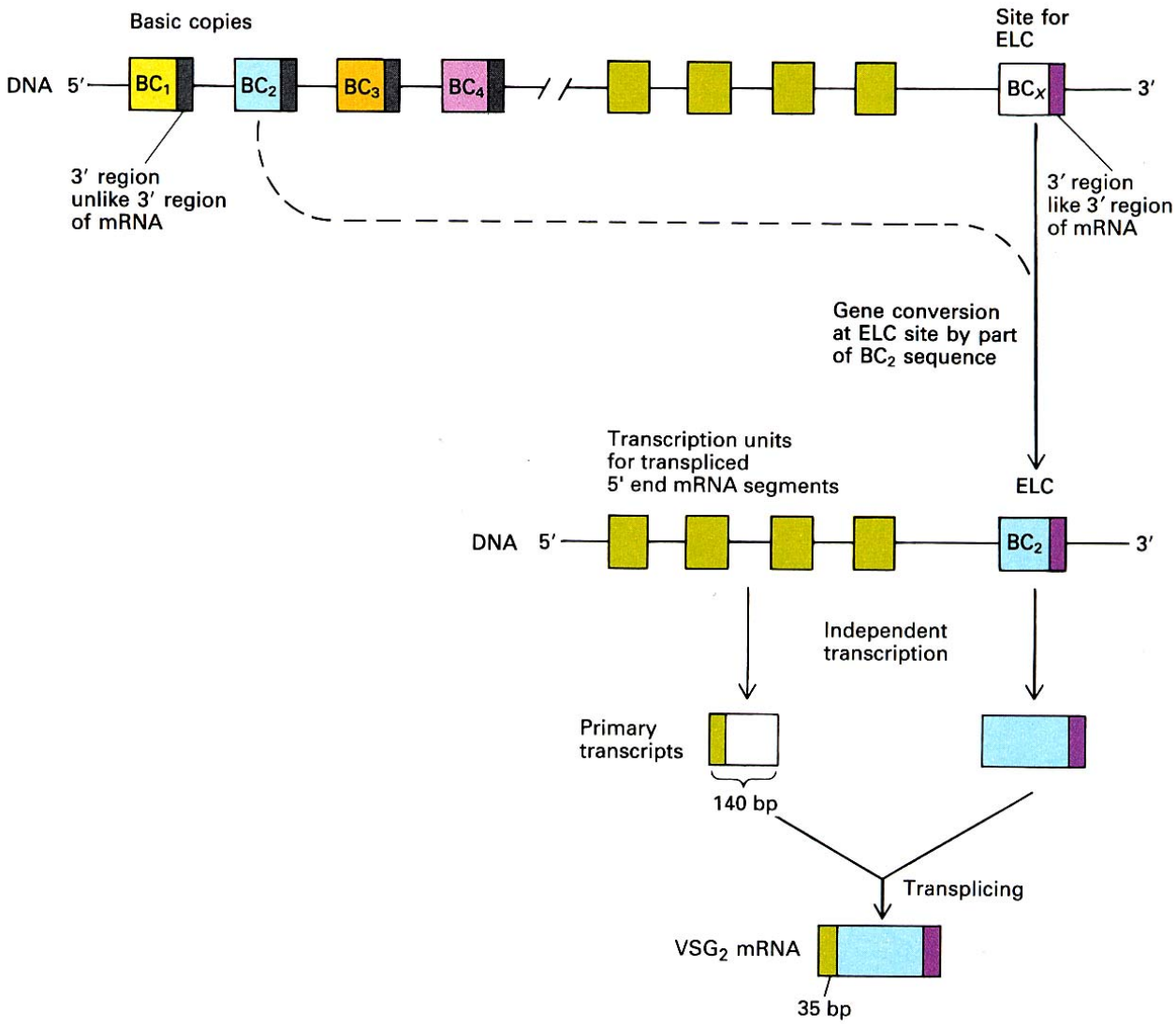
◀ **Figure 25-28** T
gene expression con
segments that bind
contain common pr
enhancers are differ
tains multiple motif

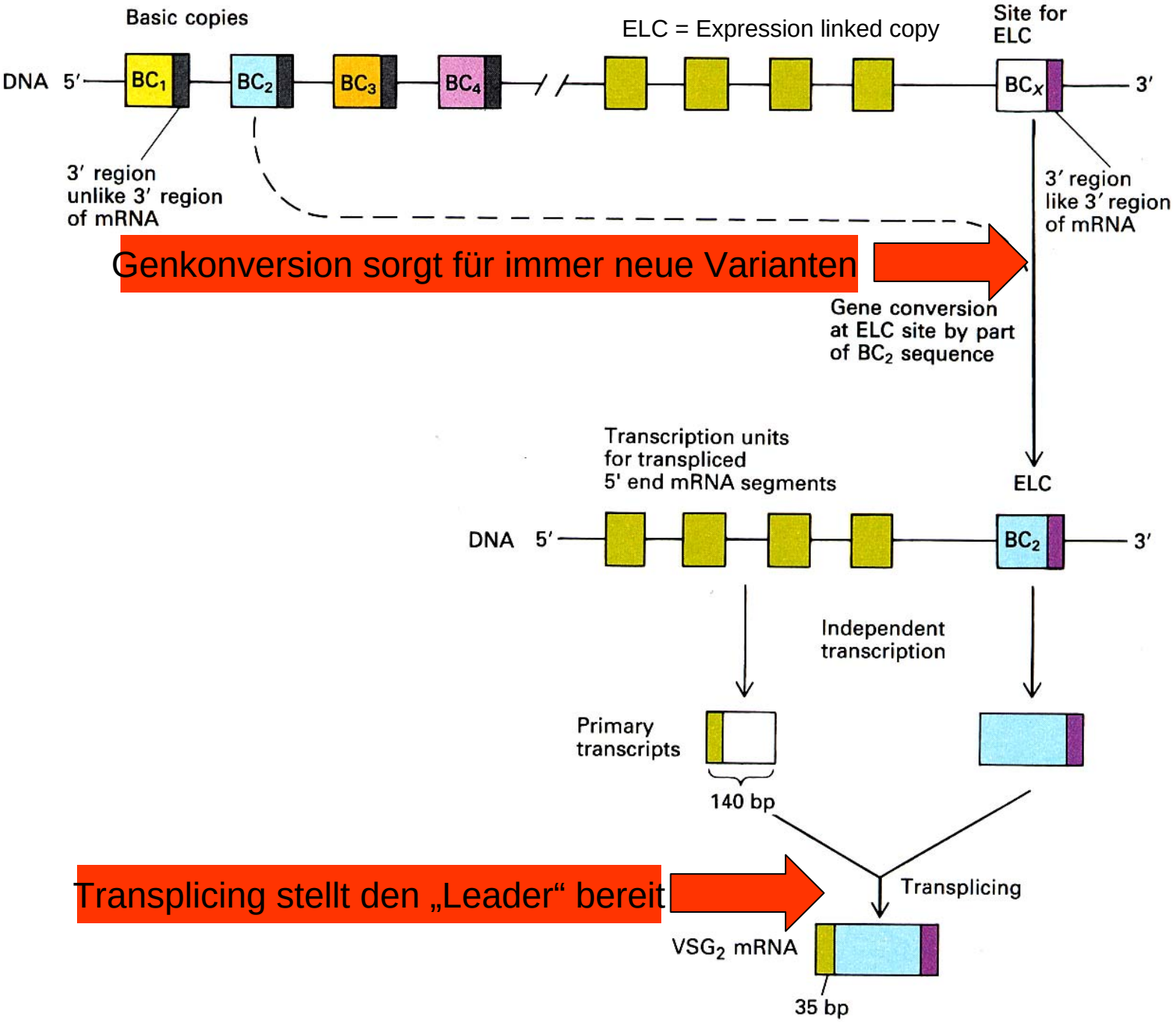
Was hat das alles mit Transposons zu tun?

Stammen die Rekombinationsignale von einem Transposon?

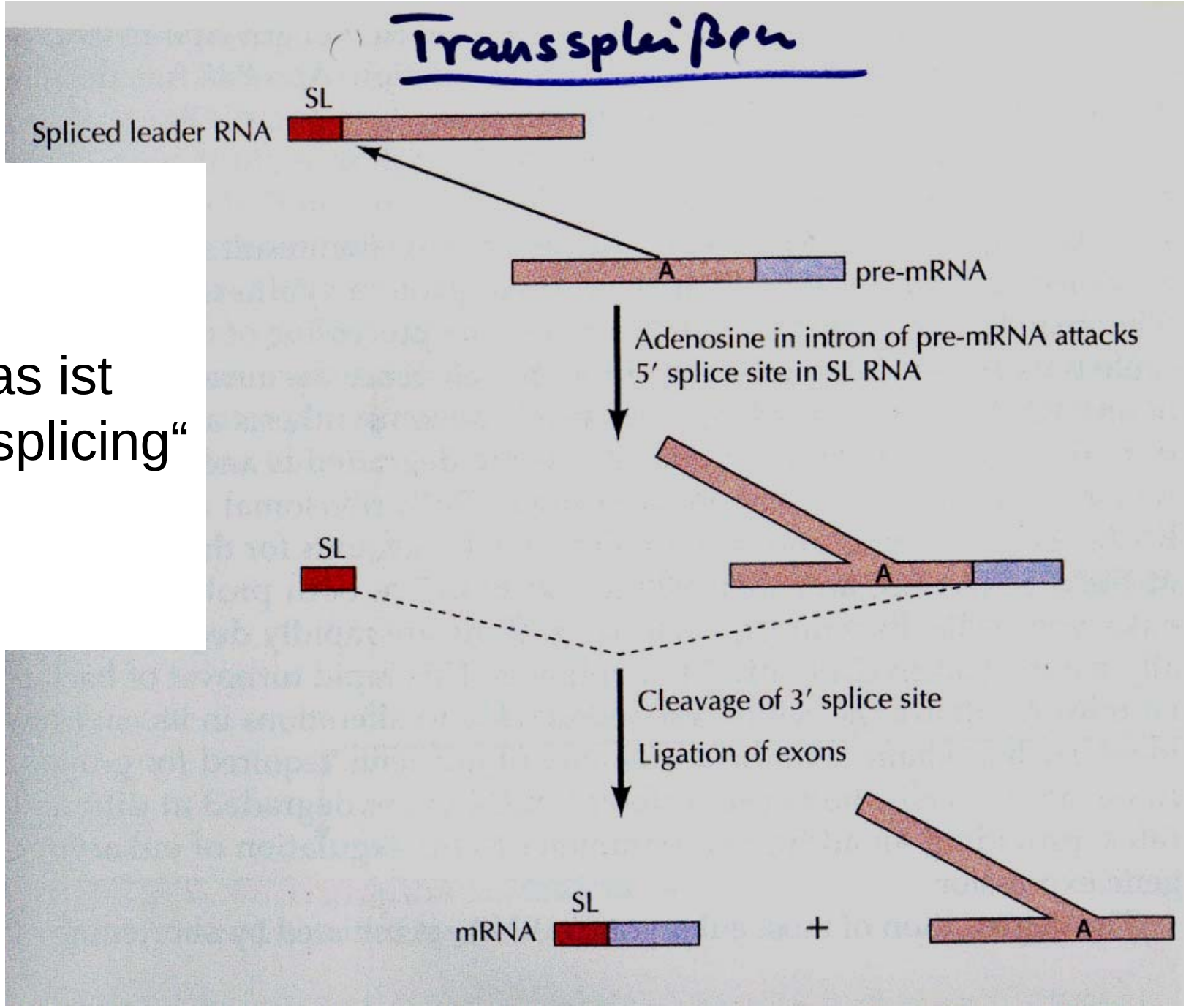


Variabilität bei Oberflächenproteinen von Trypanosomen („VSGs“)




Basic copies
ELC = Expression linked copy
Site for ELC
DNA 5′
BC1
BC2
BC3
BC4
BCX
3′
3′ region unlike 3′ region of mRNA
3′ region like 3′ region of mRNA
Genkonversion sorgt für immer neue Varianten
Gene conversion at ELC site by part of BC2 sequence
Transcription units for transpliced 5' end mRNA segments
ELC
DNA 5′
BC2
3′
Independent transcription
Primary transcripts
140 bp
Transplicing
Transplicing stellt den „Leader“ bereit
VSG2 mRNA
35 bp

Was ist „Transplicing“



Repetitive Gene:

- Immunglobulingenfamilie
- Gene für rRNA
- Gene für ribosomale Proteine
- Gene tRNA
- Histongene
- Gene für snRNA
- und viele andere