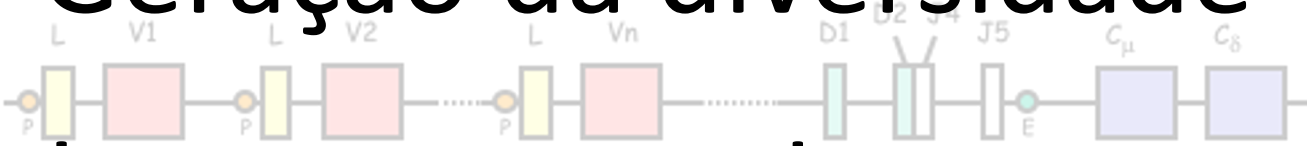


Geração da diversidade dos receptores de LB e LT

Rearranjo DJ



DNA

Rearranjo VDJ

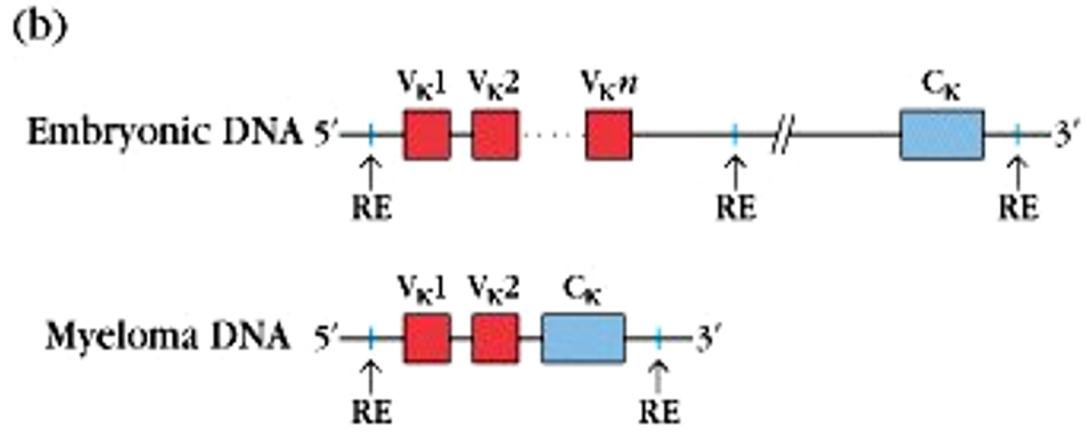
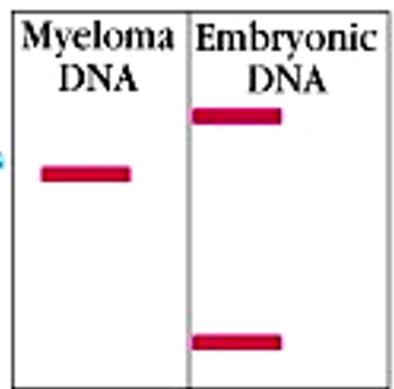
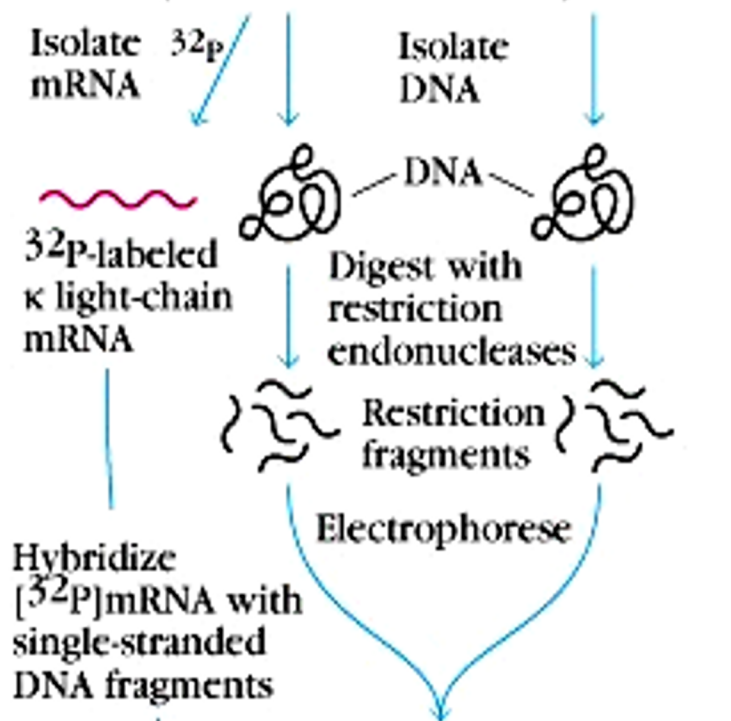
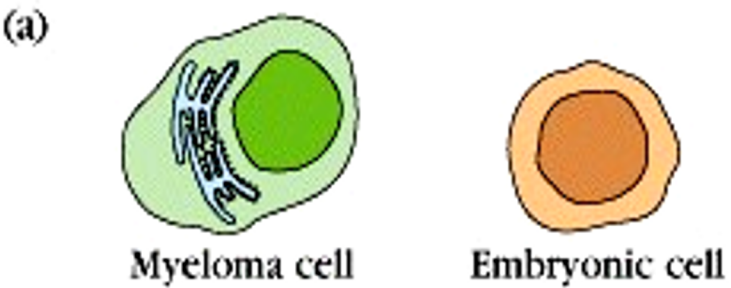
Prof. Dr. Gustavo P. Amarante-Mendes
Disciplina BMI-0256 – Imunologia
Nutrição Noturno - 2021

DNA

Tre

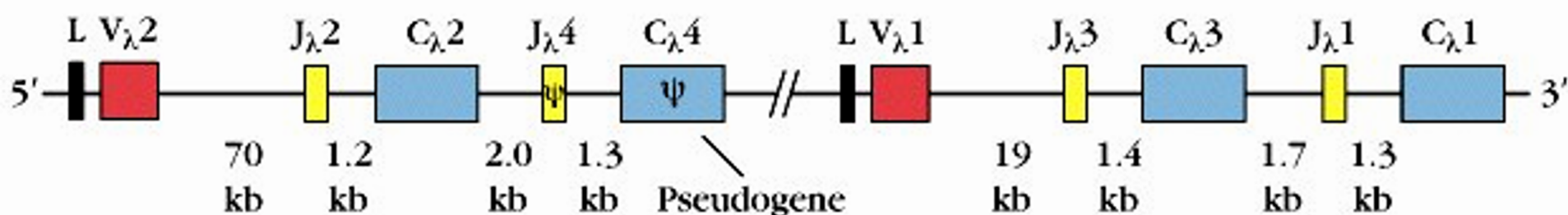


RNA



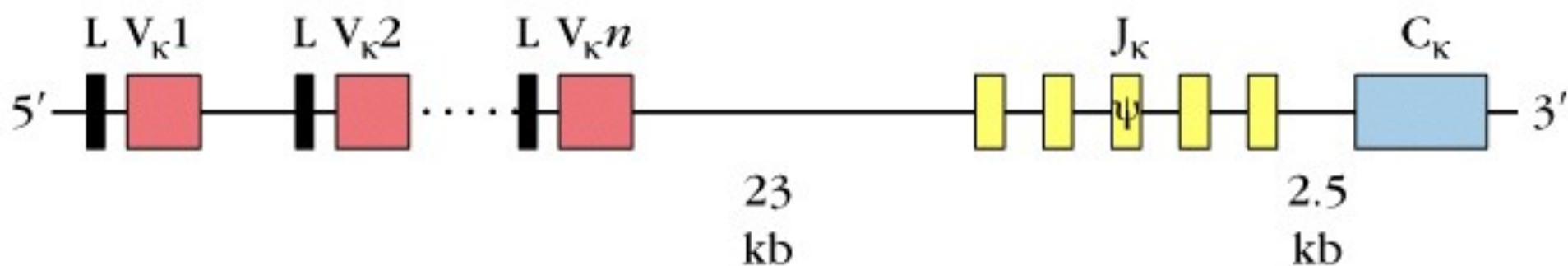
Susumo Tonegawa
(Nobel em 1987)

(a) λ -chain DNA



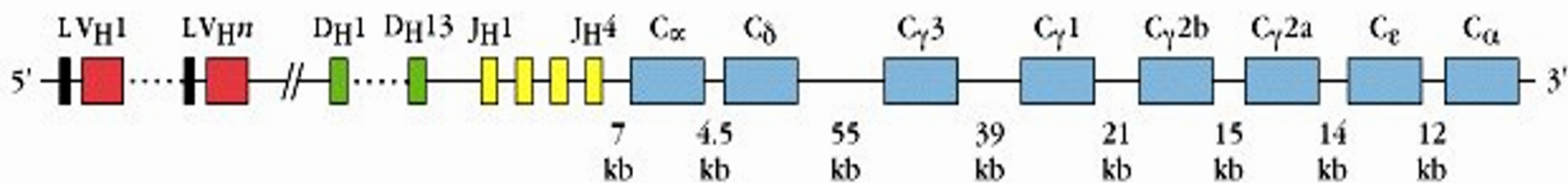
(b) κ -chain DNA

$n = \sim 85$



(c) Heavy-chain DNA

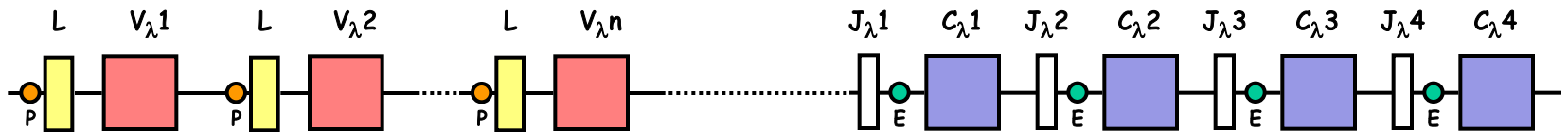
$n = \sim 134$



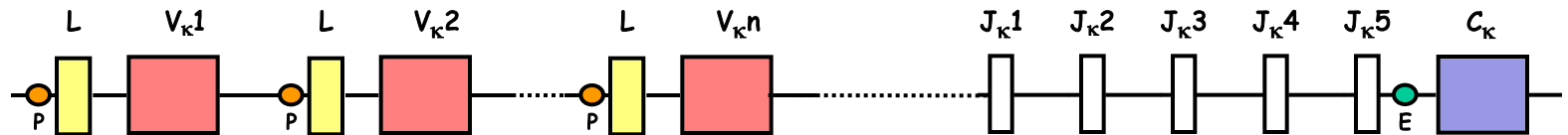
Genes das Cadeias Leves

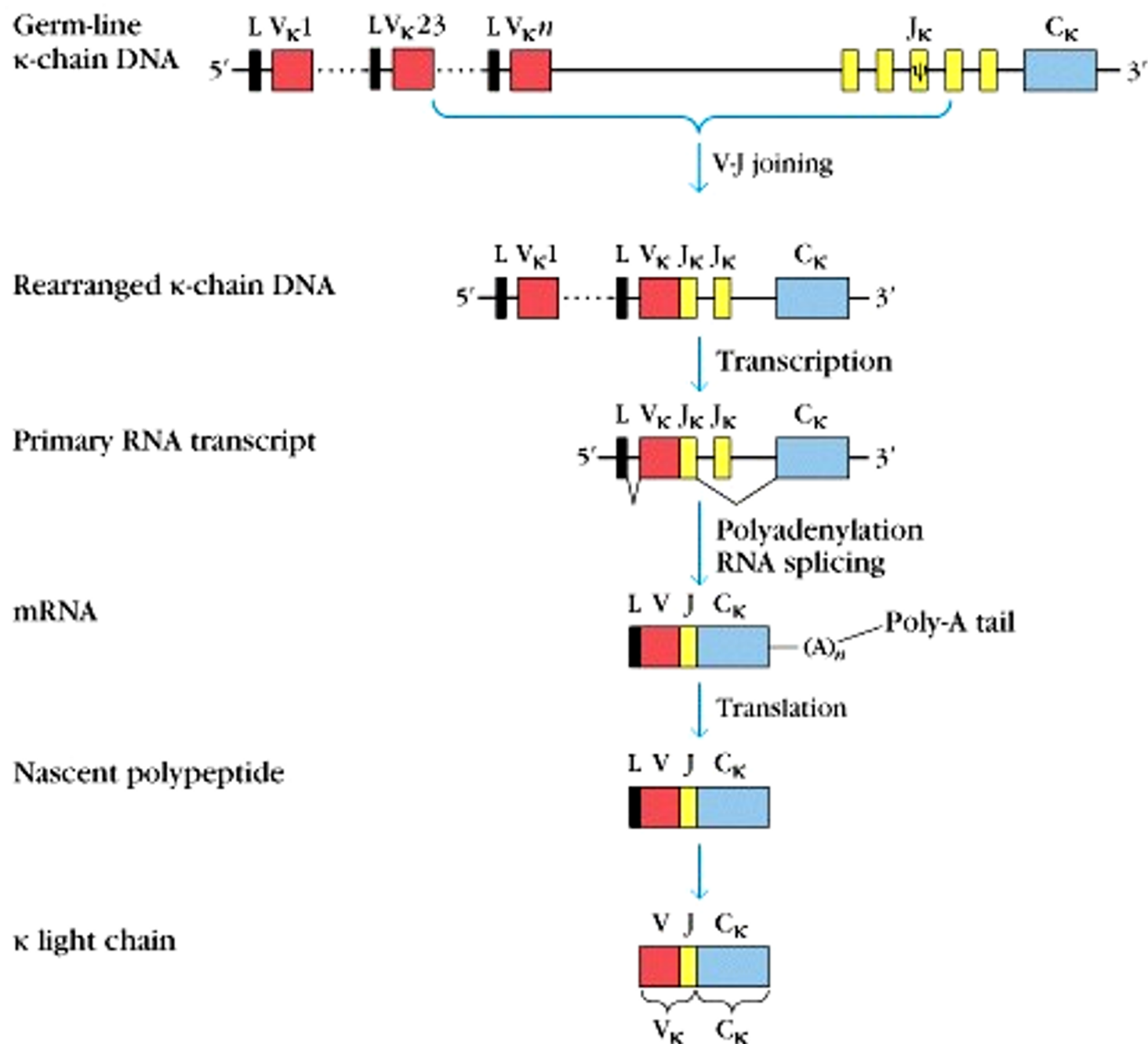
Organização na linhagem germinativa

Lambda light chain genes; $n=30$



Kappa light chain genes; $n=300$

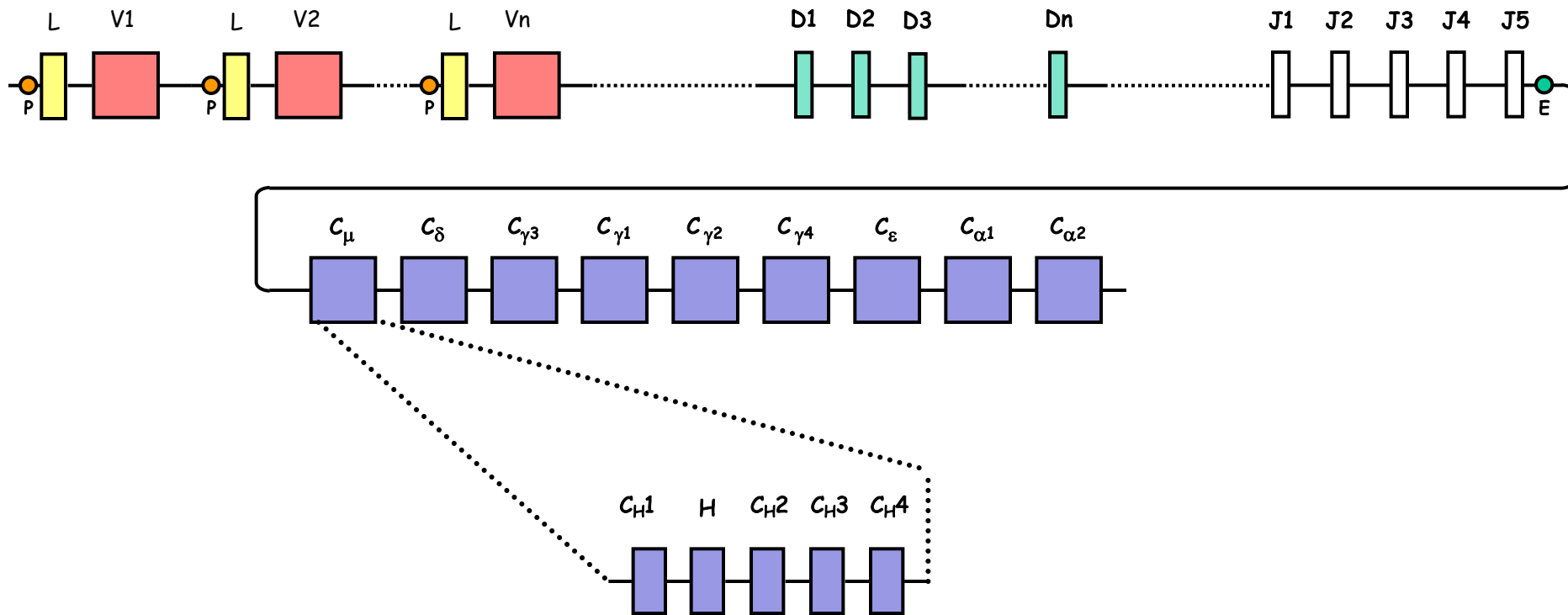




Gene da Cadeia Pesada

Organização na linhagem germinativa

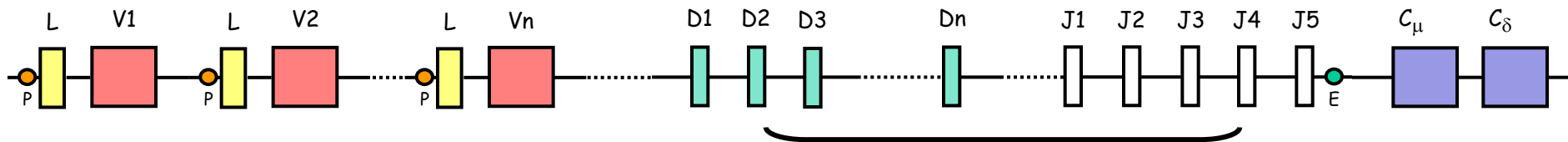
Genes da Cadeia Pesada; $V_n=1000$, $D_n=15$



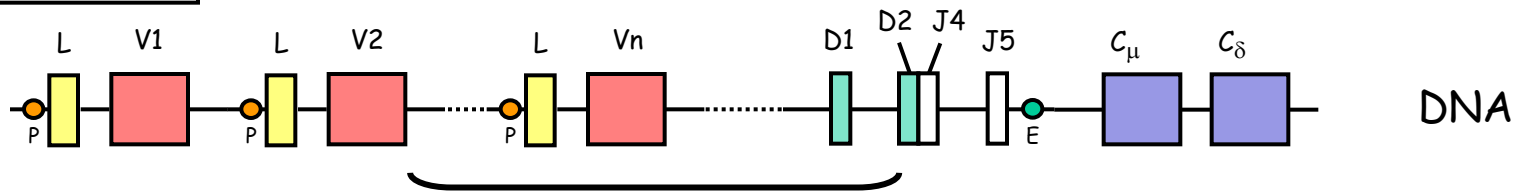
Existem introns separando os exons que codificam cada domínio da cadeia pesada

Gene da Cadeia Pesada

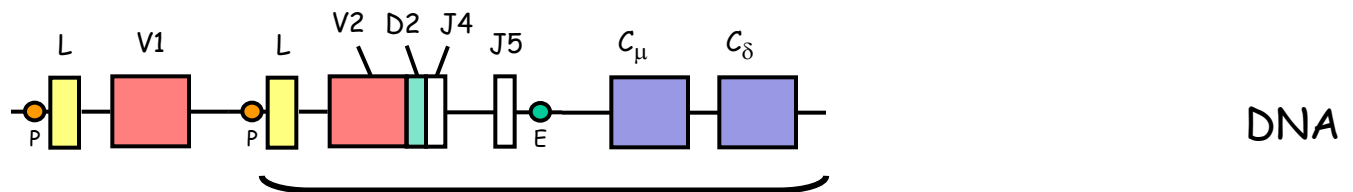
Rearranjo e expressão gênica



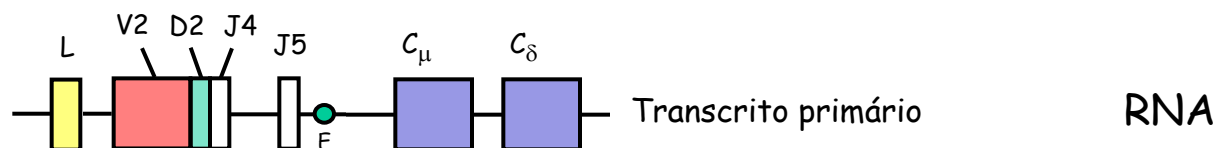
Rearranjo DJ



Rearranjo VDJ

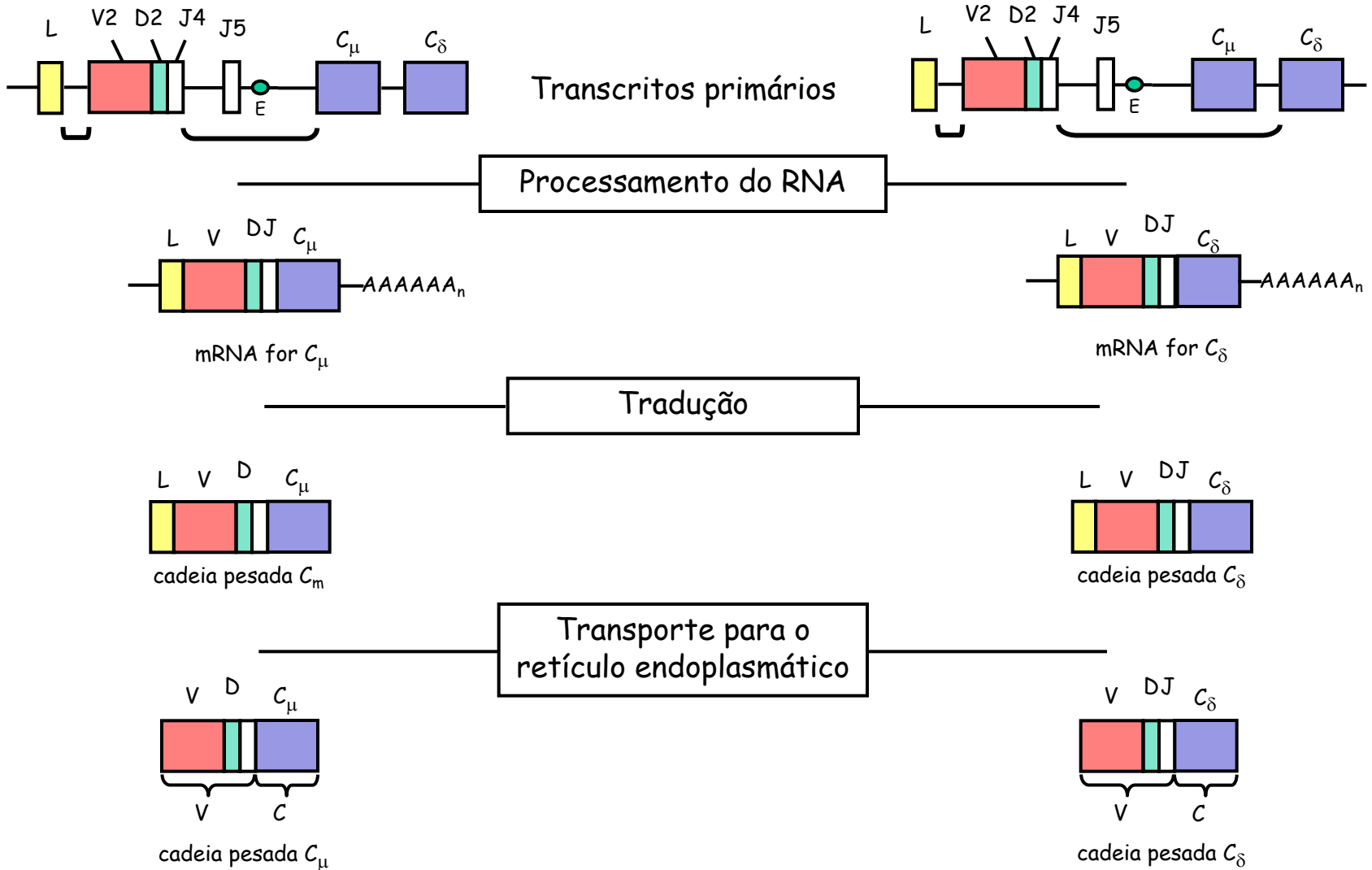


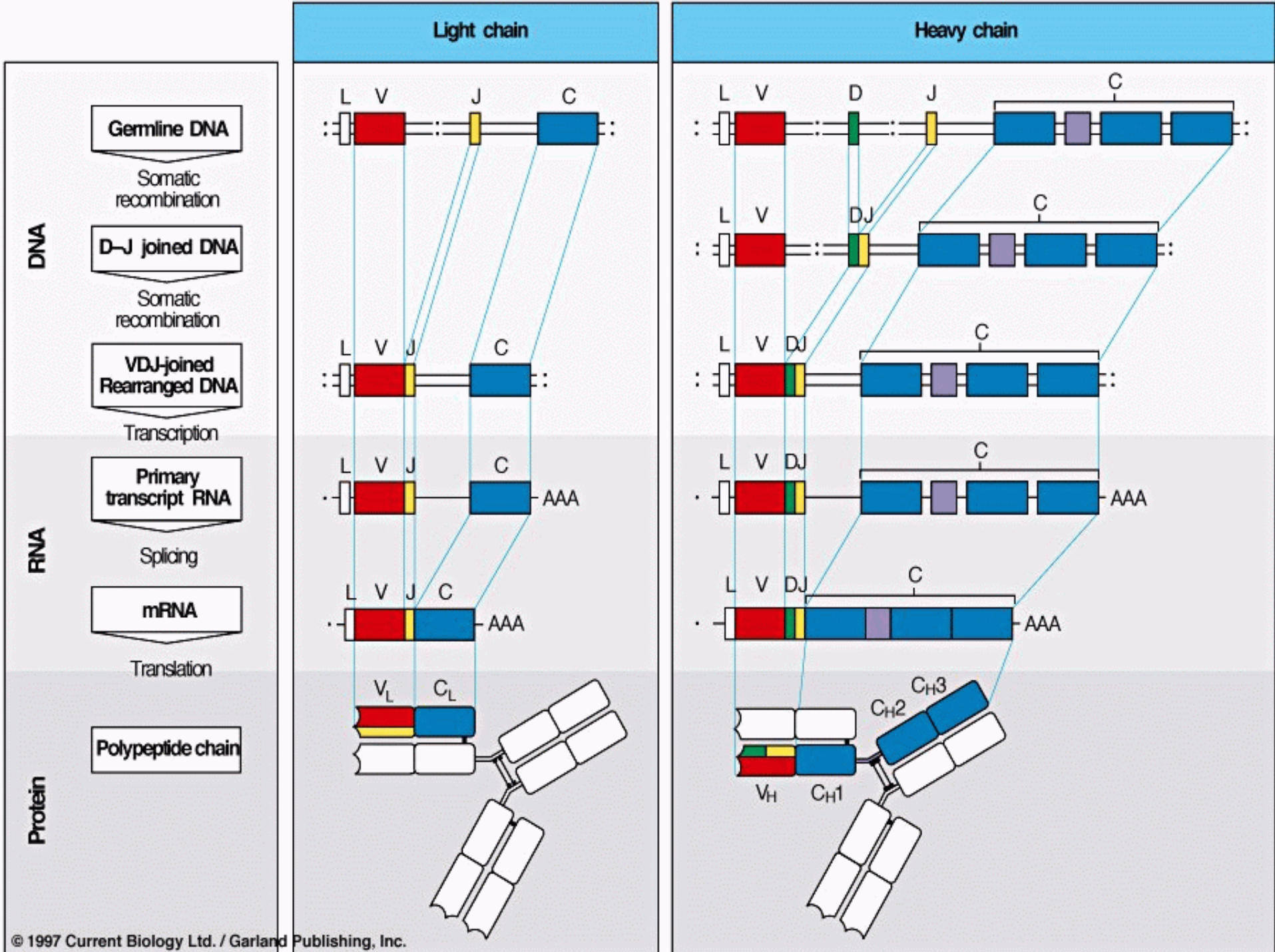
Transcrição



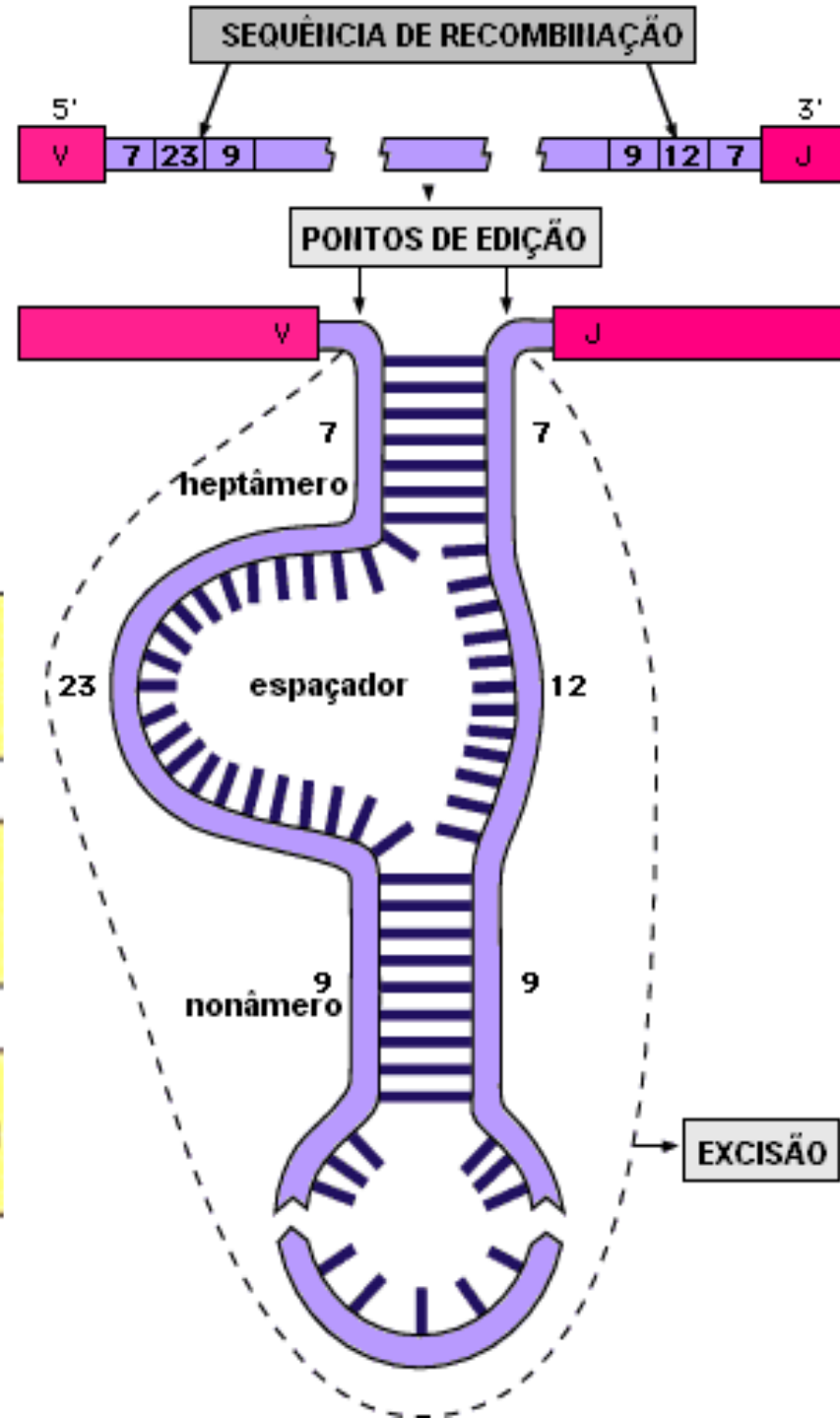
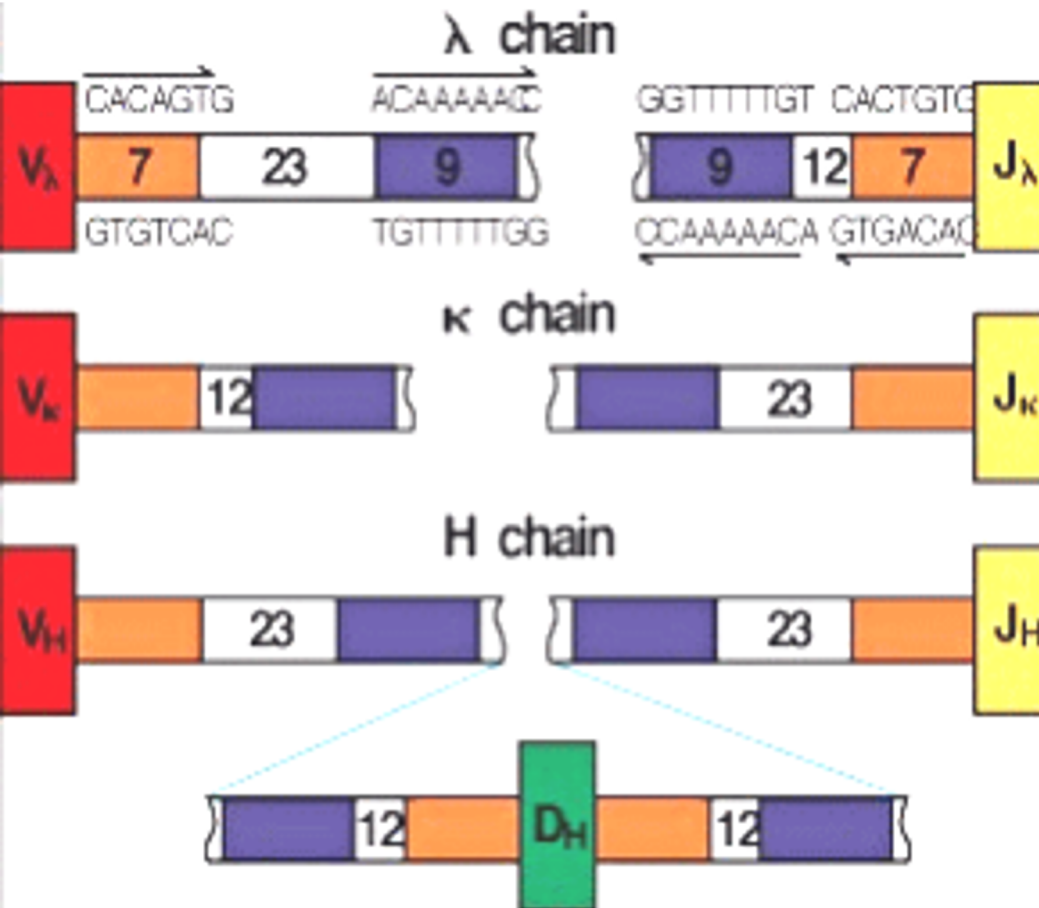
Gene da Cadeia Pesada

Rearranjo e expressão gênica





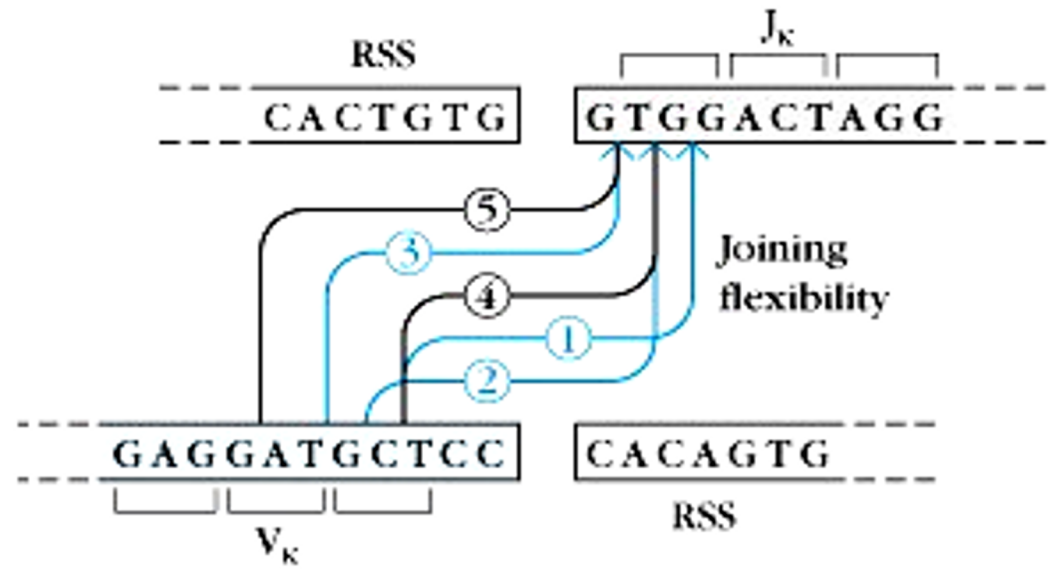
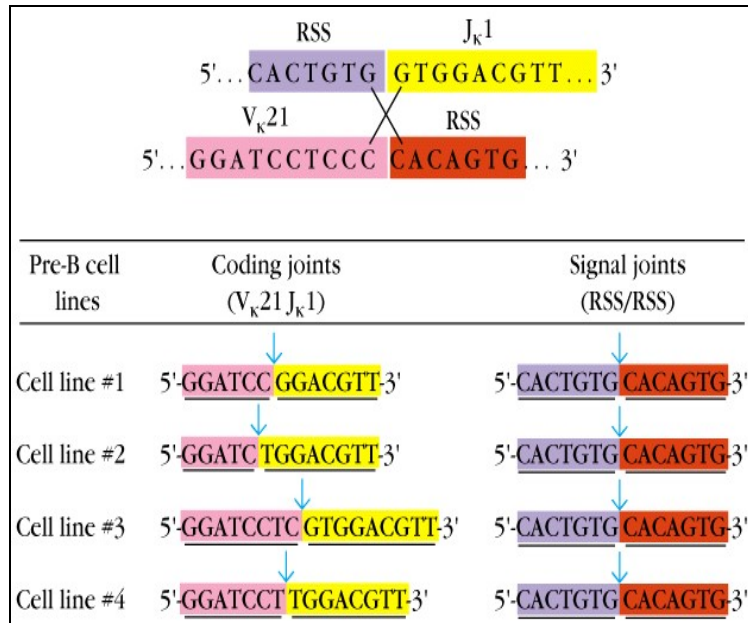
Lei dos heptâmeros e nonâmeros



**TABLE 5-2 COMBINATORIAL ANTIBODY DIVERSITY
IN HUMANS AND MICE**

| Multiple germ-line segments | Heavy chain | Light chains | |
|---|--|---------------------|---------------------|
| | | κ | λ |
| Estimated number of segments in humans* | | | |
| V | 51 | 40 | 30 |
| D | 27 | 0 | 0 |
| J | 6 | 5 | 4 |
| Combinatorial V-D-J and V-J joining (possible number of combinations) | $51 \times 27 \times 6 = 8262$ | $40 \times 5 = 200$ | $30 \times 4 = 120$ |
| Possible combinatorial associations of heavy and light chains [†] | $8262 \times (200 + 120) = 2.64 \times 10^6$ | | |
| Estimated number of segments in mice* | | | |
| V | 134 | 85 | 2 |
| D | 13 | 0 | 0 |
| J | 4 | 4 | 3 |
| Combinatorial V-D-J and V-J joining (possible number of combinations) | $134 \times 13 \times 4 = 6968$ | $85 \times 4 = 340$ | $2 \times 3 = 6$ |
| Possible combinatorial associations of heavy and light chains [†] | $6968 \times (340 + 6) = 2.41 \times 10^6$ | | |

Flexibilidade Juncional



Productive rearrangements

- ①

| | | | | |
|-----------------|-----|-----|-----|-----|
| Glu | Asp | Ala | Thr | Arg |
| GAGGATGCGACTAGG | | | | |
- ②

| | | | | |
|-----------------|-----|-----|-----|-----|
| Glu | Asp | Gly | Thr | Arg |
| GAGGATGGGACTAGG | | | | |
- ③

| | | | | |
|-----------------|-----|-----|-----|-----|
| Glu | Asp | Trp | Thr | Arg |
| GAGGATTGGACTAGG | | | | |

Nonproductive rearrangements

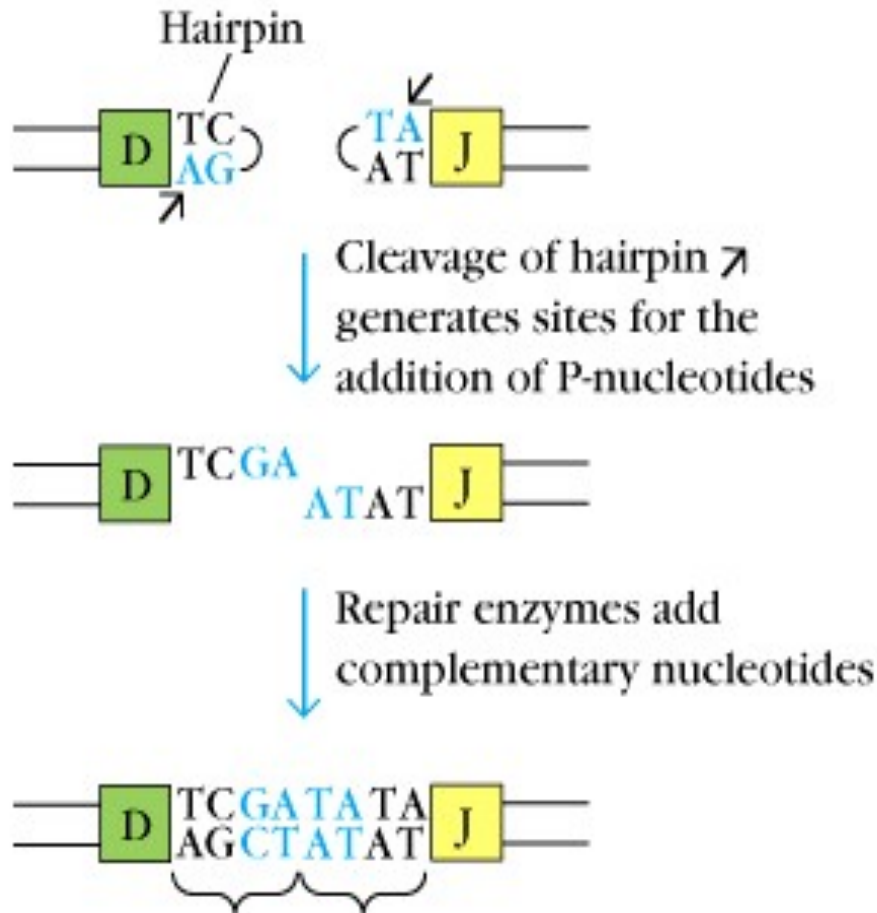
- ④

| | | | | |
|------------------|-----|-----|-----|------|
| Glu | Asp | Ala | Asp | Stop |
| GAGGATGCGGACTAGG | | | | |
- ⑤

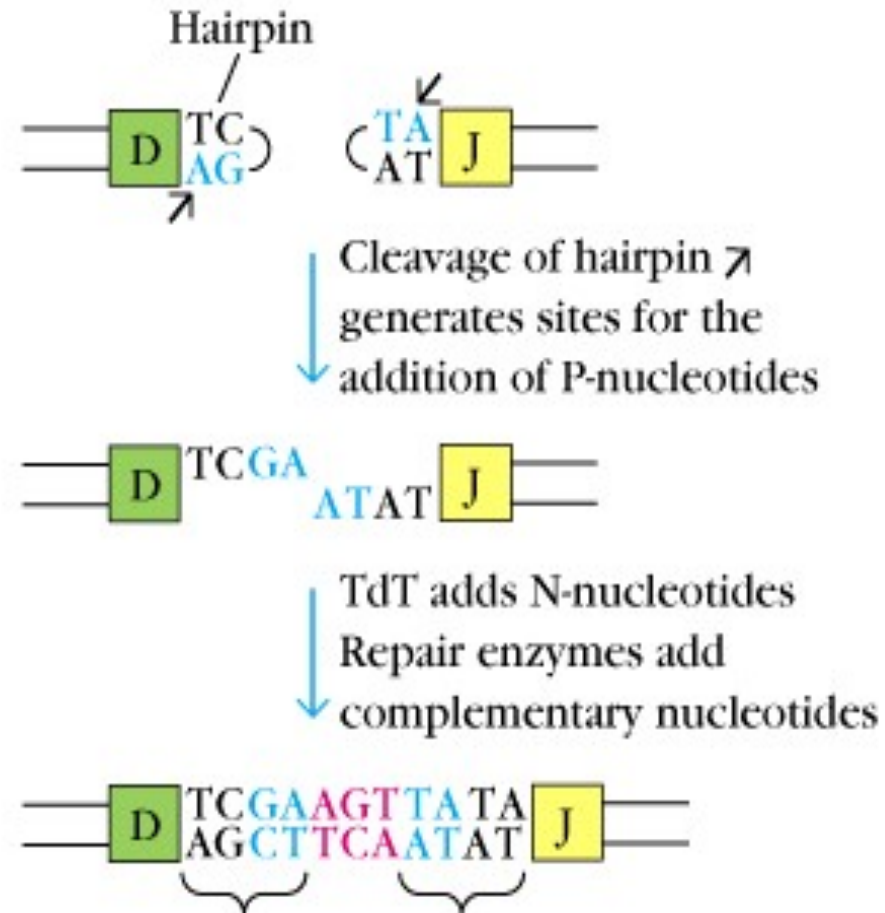
| | | | |
|---------------|-----|-----|------|
| Glu | Val | Asp | Stop |
| GAGGTGGACTAGG | | | |

Adição de P- e N-nucleotídios

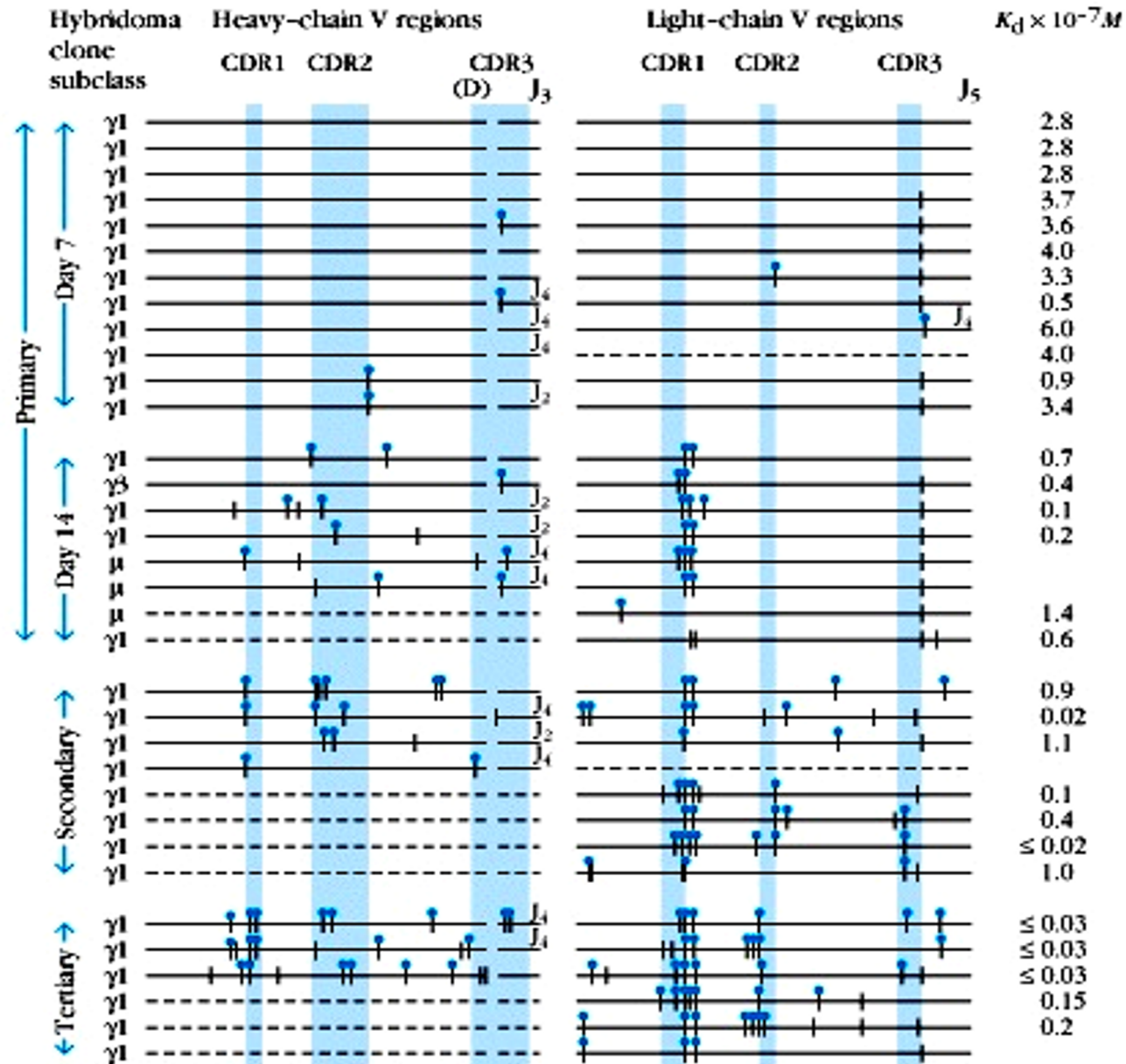
(a) P-nucleotide addition



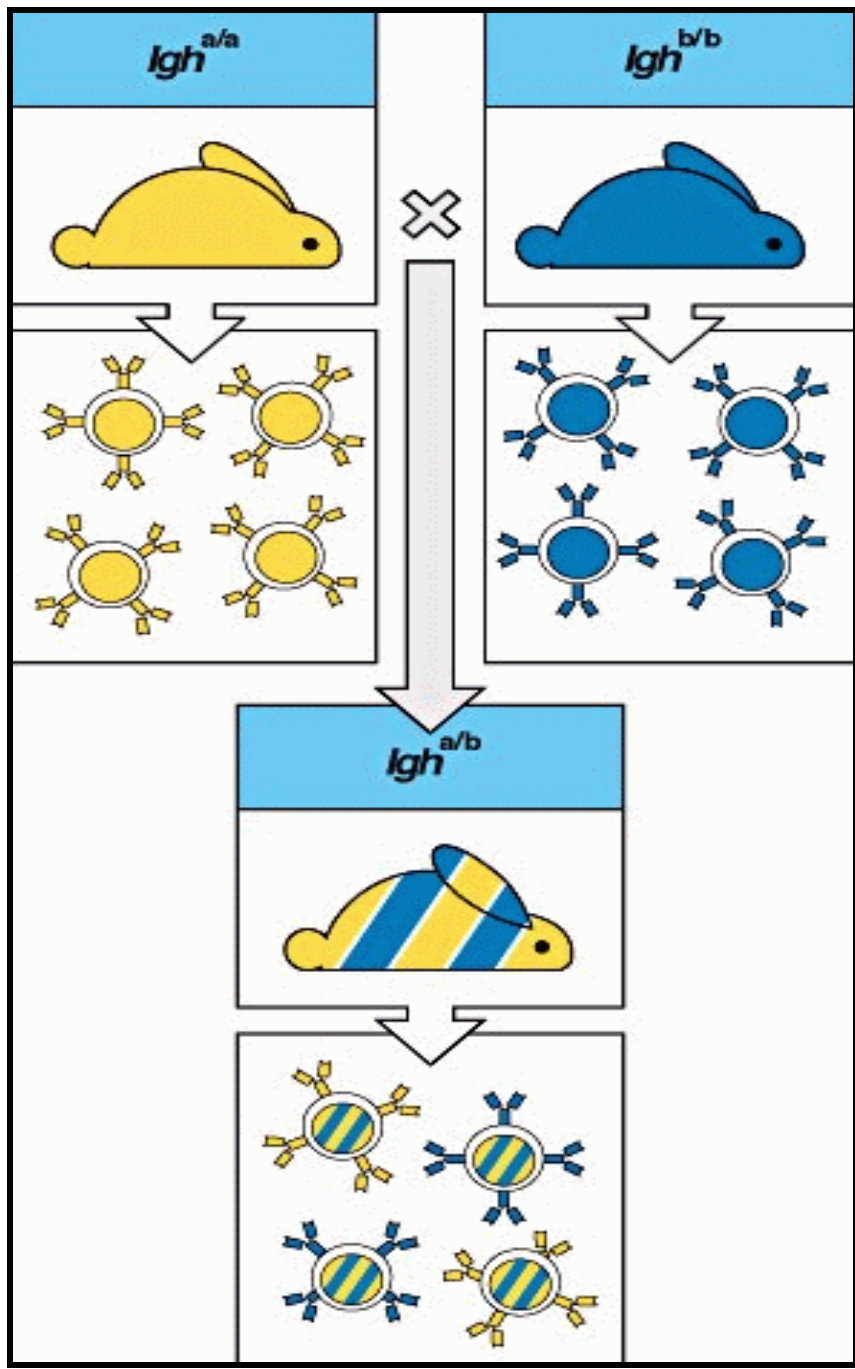
(b) N-nucleotide addition

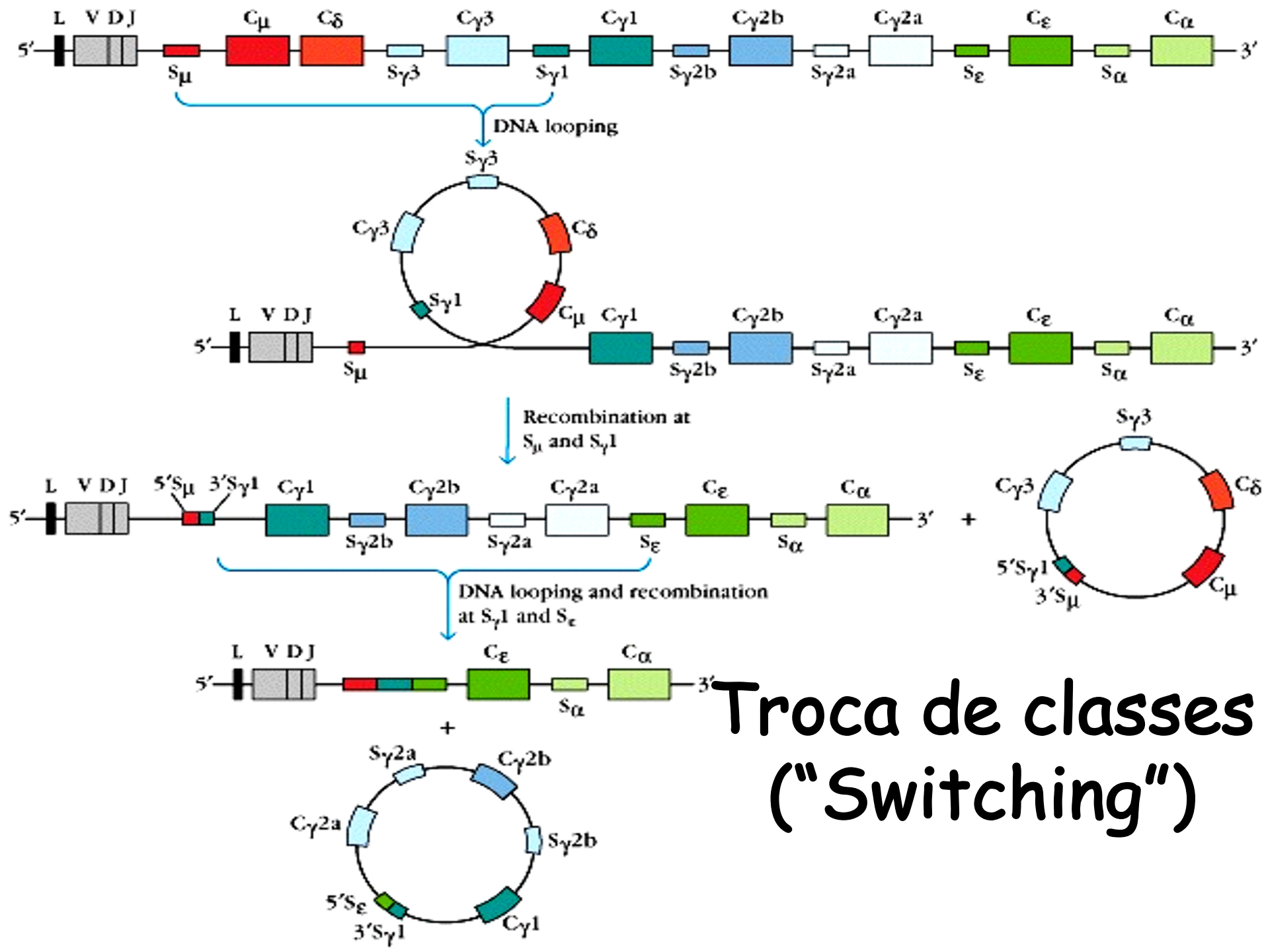


Hipermutação somática



Exclusão alélica da
expressão do gene
das
imunoglobulinas





"Splicing" Alternativo

