

Day 4. Cancer Genome Analysis - Latin America and the Caribbean

Mutational Signatures Analysis



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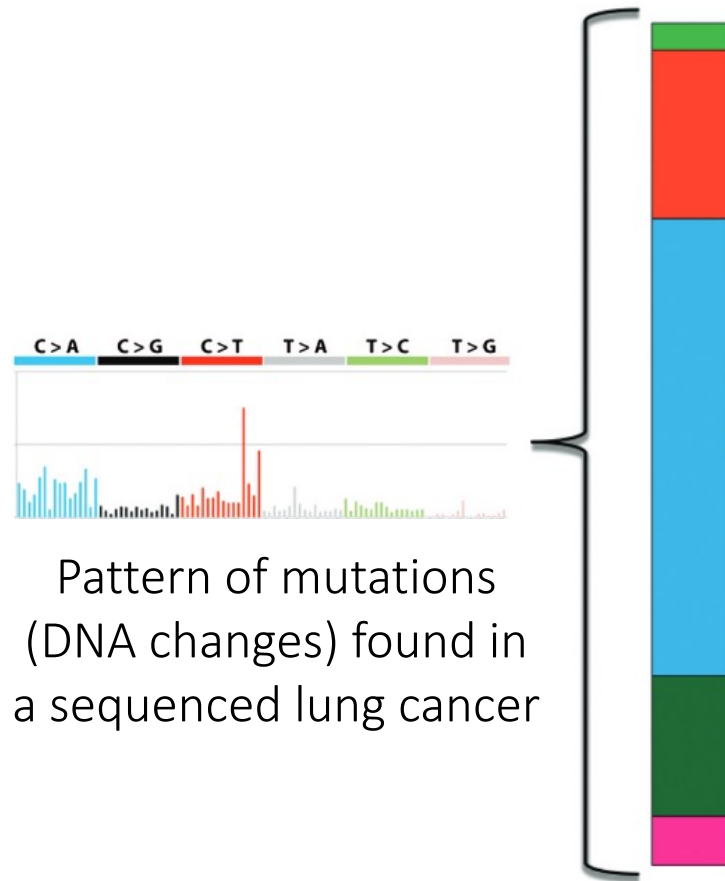
UC San Diego



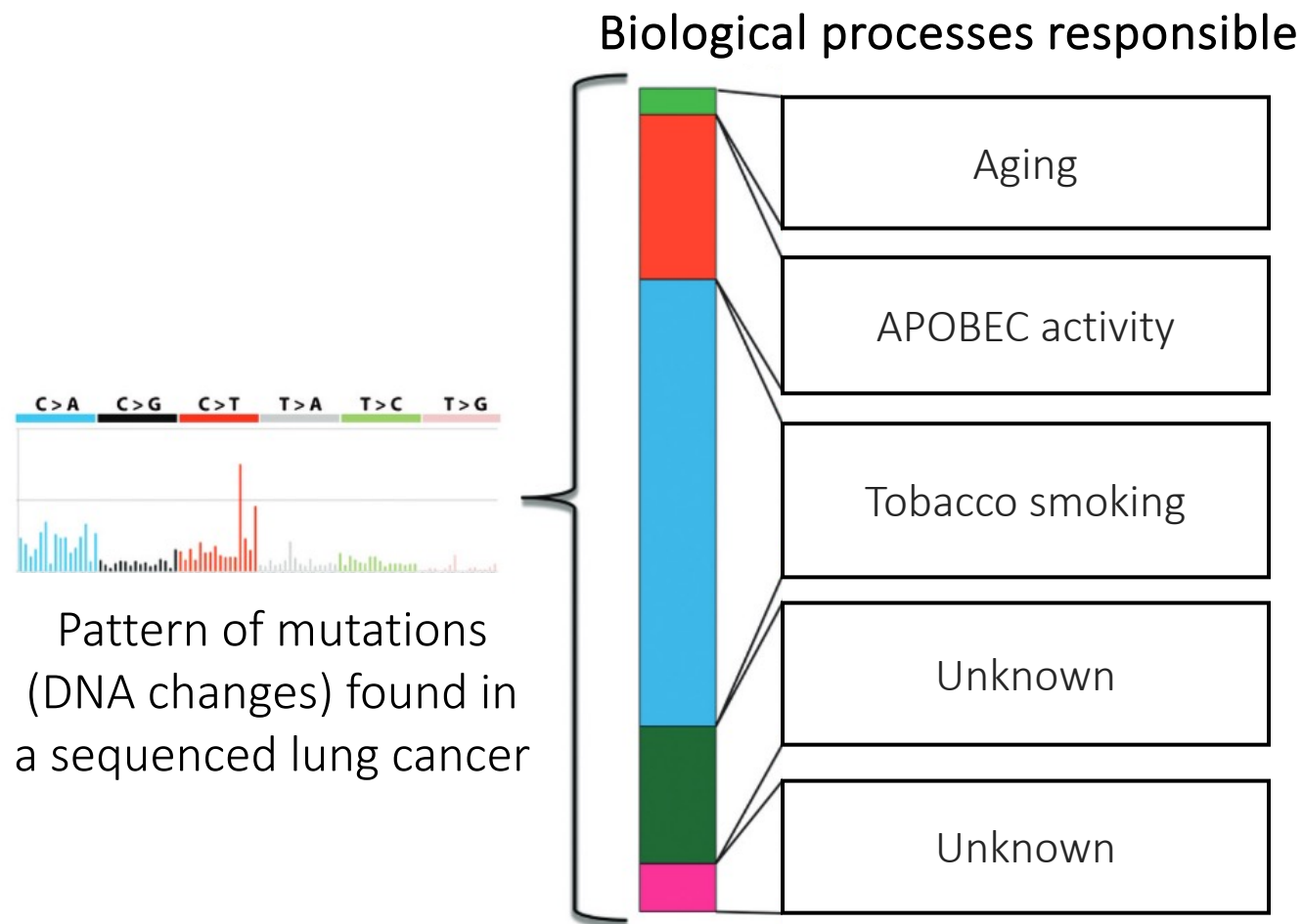
Spoiler alert!

Pattern of mutations
(DNA changes) found in
a sequenced lung cancer

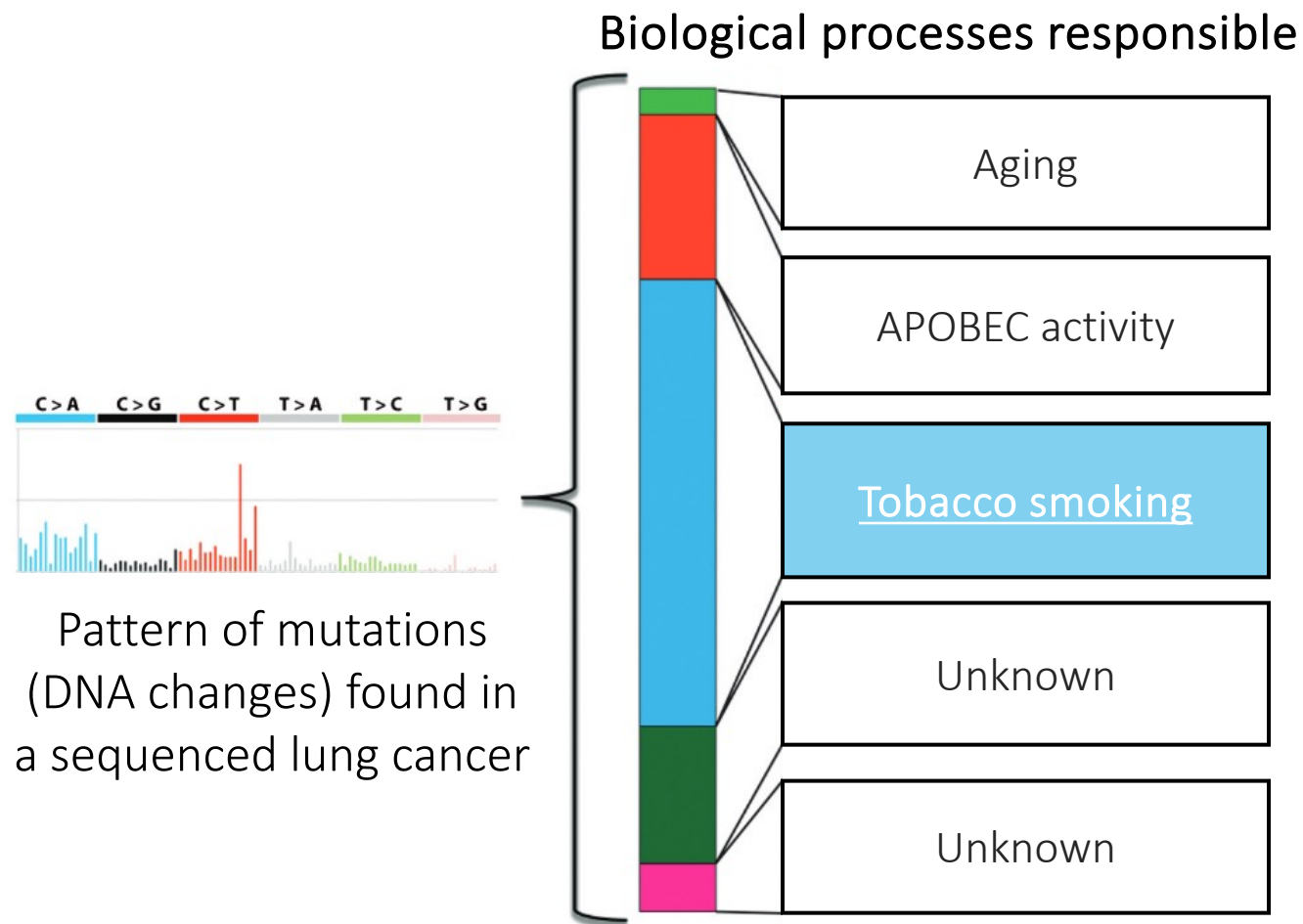
Spoiler alert!



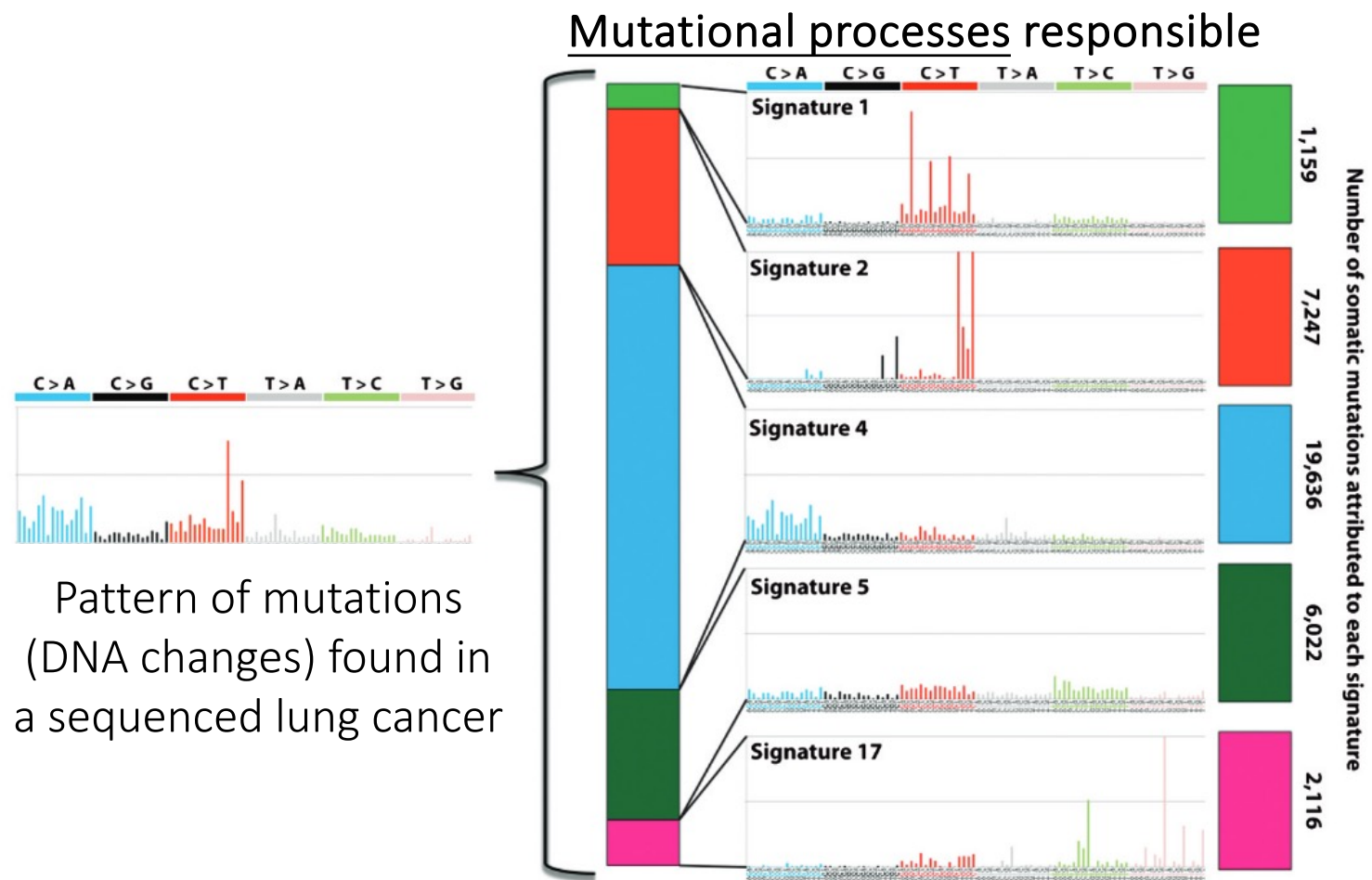
Spoiler alert!



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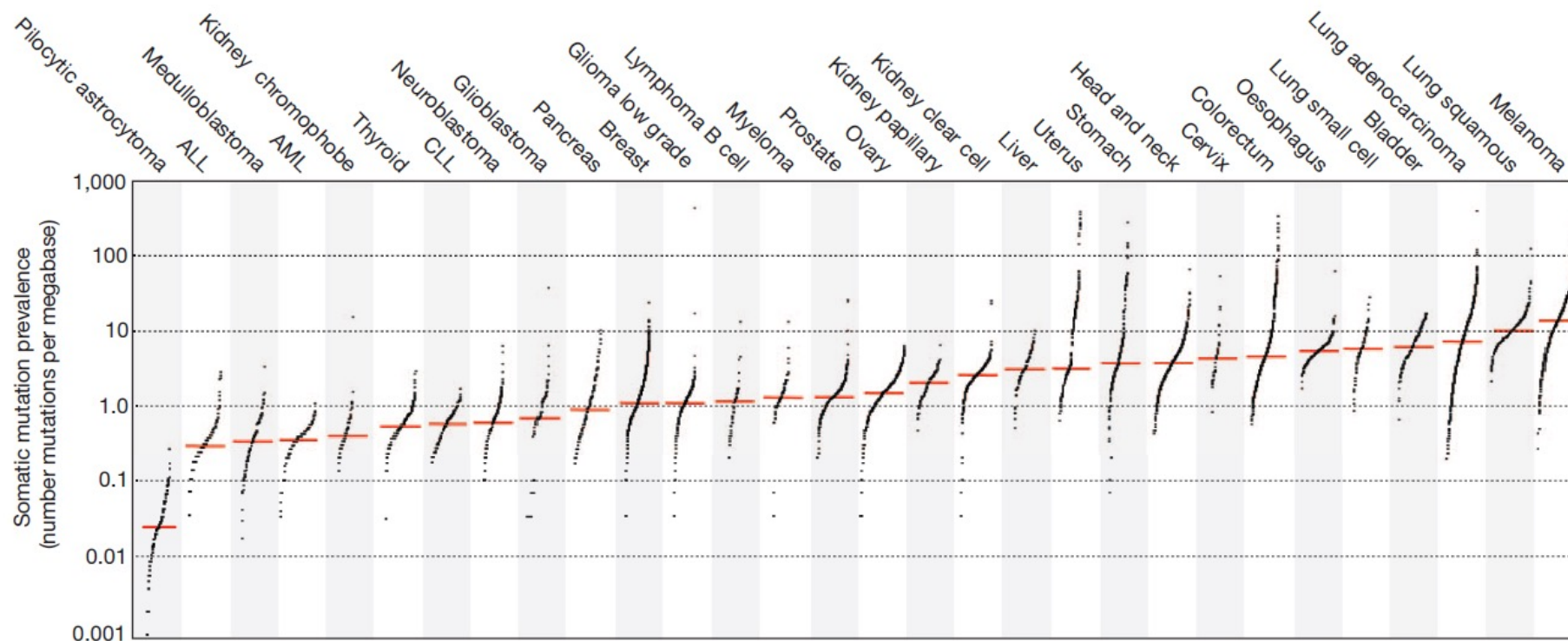


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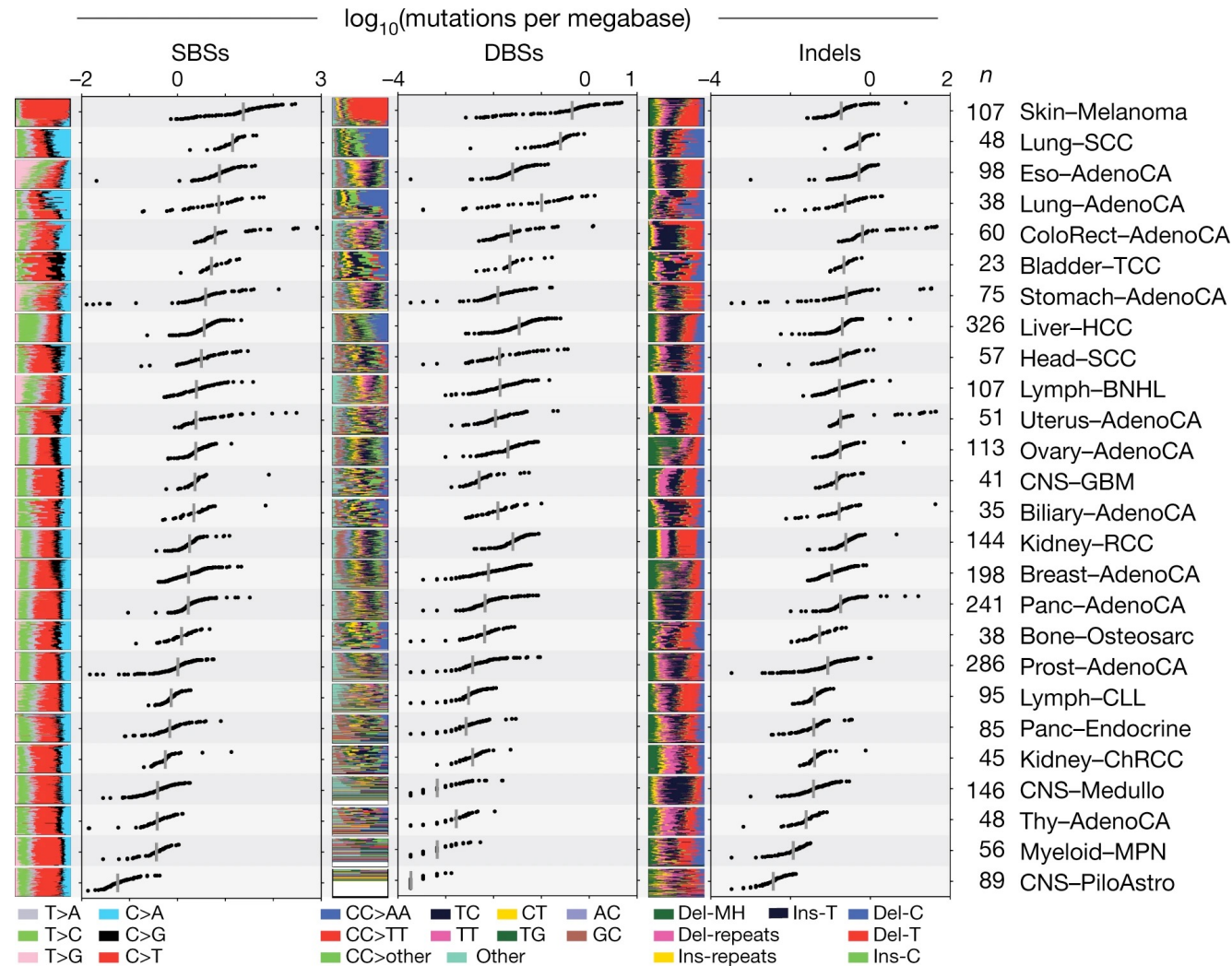


Somatic mutations in cancer

- The burden of somatic mutations is highly variable among different cancer types
- The most mutated cancer types (lung and skin cancers) are associated with well-known environmental mutagens (tobacco smoking and UV light exposure, respectively)

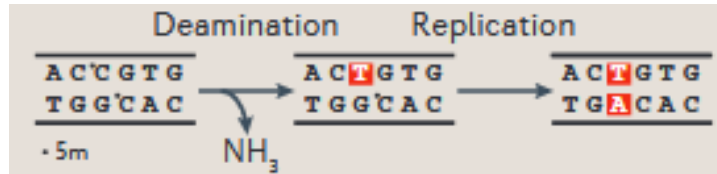
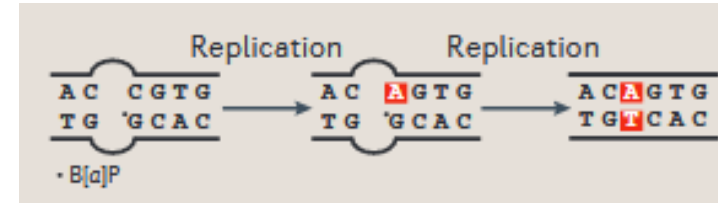


Burden of somatic mutations is highly variable among cancer classes



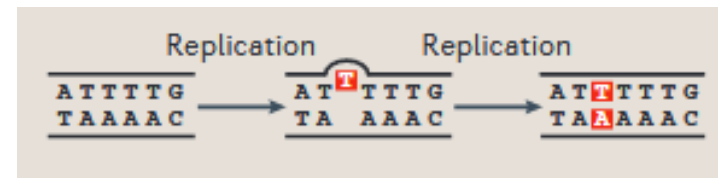
Different patterns of mutations are linked to different sources of DNA damage

Environmental exposures
Tobacco smoking or chewing



Normal cellular activities
Spontaneous deamination of methylated cytosines

Failure in DNA replication or repair
Aberrant mismatch repair pathway



Classification of base substitution mutations

.....ATCGGGAAT**C**GGACCCGATG.....
 ↓
.....ATCGGGAAT**T**GGACCCGATG.....

Classification of base substitution mutations

.....ATCGGGAA**T****C**GGACCCGATG.....
 ↓
.....ATCGGGAA**T****T**GGACCCGATG.....

Classification of base substitution mutations

.....ATCGGGAA**T****C**GGACCCGATG.....



.....ATCGGGAA**T****T**GGACCCGATG.....

.....ATCGGGAA**A****C**GGACCCGATG.....



.....ATCGGGAA**A****T**GGACCCGATG.....

Classification of base substitution mutations

.....ATCGGGAA**TC**GGACCCGATG.....



.....ATCGGGAA**TT**GGACCCGATG.....

.....ATCGGGAA**AC**GGACCCGATG.....



.....ATCGGGAA**AT**GGACCCGATG.....

.....ATCGGGAA**ACC**GGACCCGATG.....



.....ATCGGGAA**ATC**GGACCCGATG.....

Classification of base substitution mutations

C>T

C>A

C>G

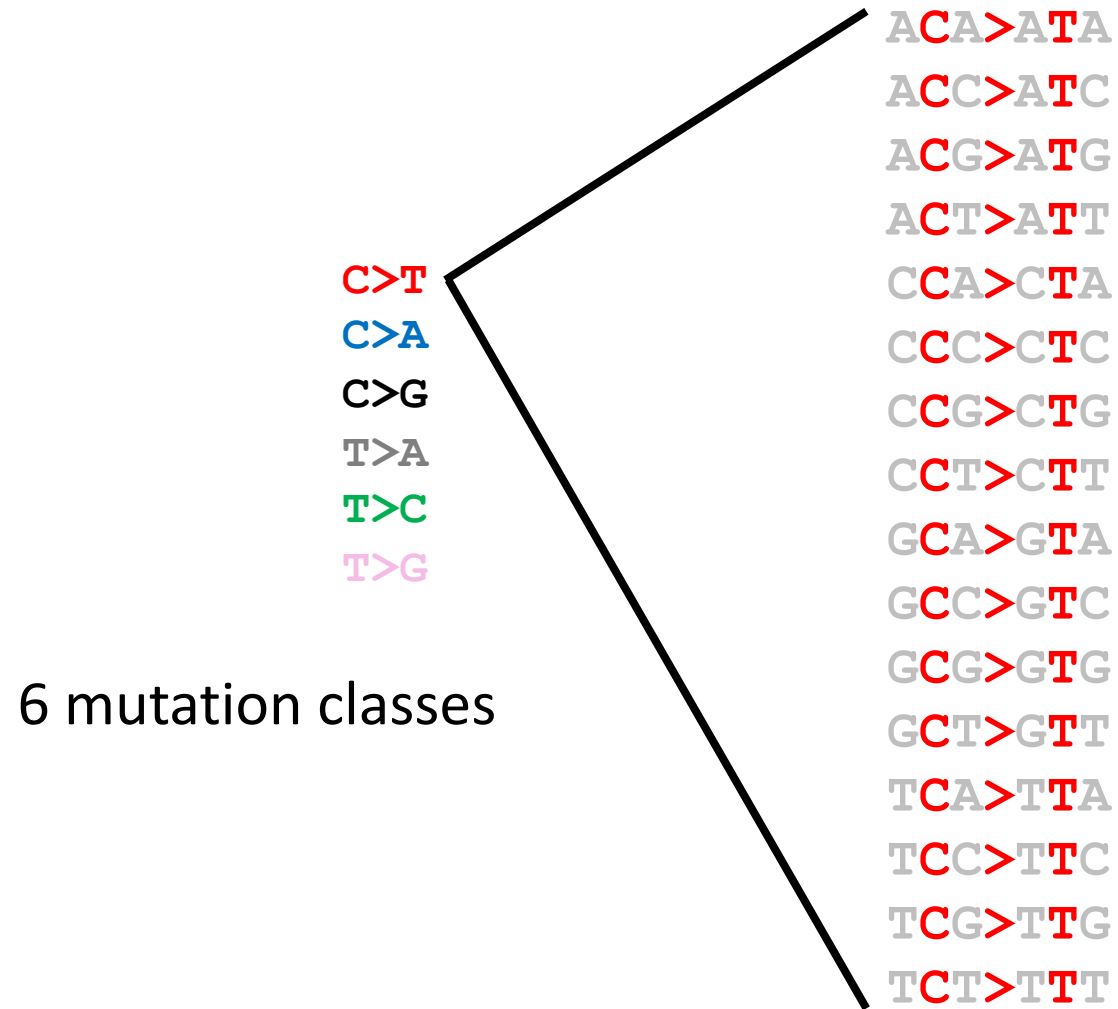
T>A

T>C

T>G

6 mutation classes

Classification of base substitution mutations



Classification of base substitution mutations

C>T

C>A

C>G

T>A

T>C

T>G

6 mutation classes

ACA>ATA
ACC>ATC
ACG>ATG
ACT>ATT
CCA>CTA
CCC>CTC
CCG>CTG
CCT>CTT
GCA>GTA
GCC>GTC
GCG>GTC
GCT>GTT
TCA>TTA
TCC>TTC
TCG>TTG
TCT>TTT

ACA>AAA
ACC>AAC
ACG>AAG
ACT>AAT
CCA>CAA
CCC>CAC
CCG>CAG
CCT>CAT
GCA>GAA
GCC>GAC
GCG>GAG
GCT>GAT
TCA>TAA
TCC>TAC
TCG>TAG
TCT>TAT

ACA>AGA
ACC>AGC
ACG>AGG
ACT>AGT
CCA>CGA
CCC>CGC
CCG>CGG
CCT>CGT
GCA>GGA
GCC>GGC
GCG>GGG
GCT>GGT
TCA>TGA
TCC>TGC
TCG>TGG
TCT>TGT

ATA>AAA
ATC>AAC
ATG>AAG
ATT>AAT
CTA>CAA
CTC>CAC
CTG>CAG
CTT>CAT
GTA>GAA
GTC>GAC
GTG>GAG
GTT>GAT
TTA>TAA
TTC>TAC
TTG>TAG
TTT>TAT

ATA>ACA
ATC>ACC
ATG>ACG
ATT>ACT
CTA>CCA
CTC>CCC
CTG>CCG
CTT>CCT
GTA>GCA
GTC>GCC
GTG>GCG
GTT>GCT
TTA>TCA
TTC>TCC
TTG>TCG
TTT>TCT

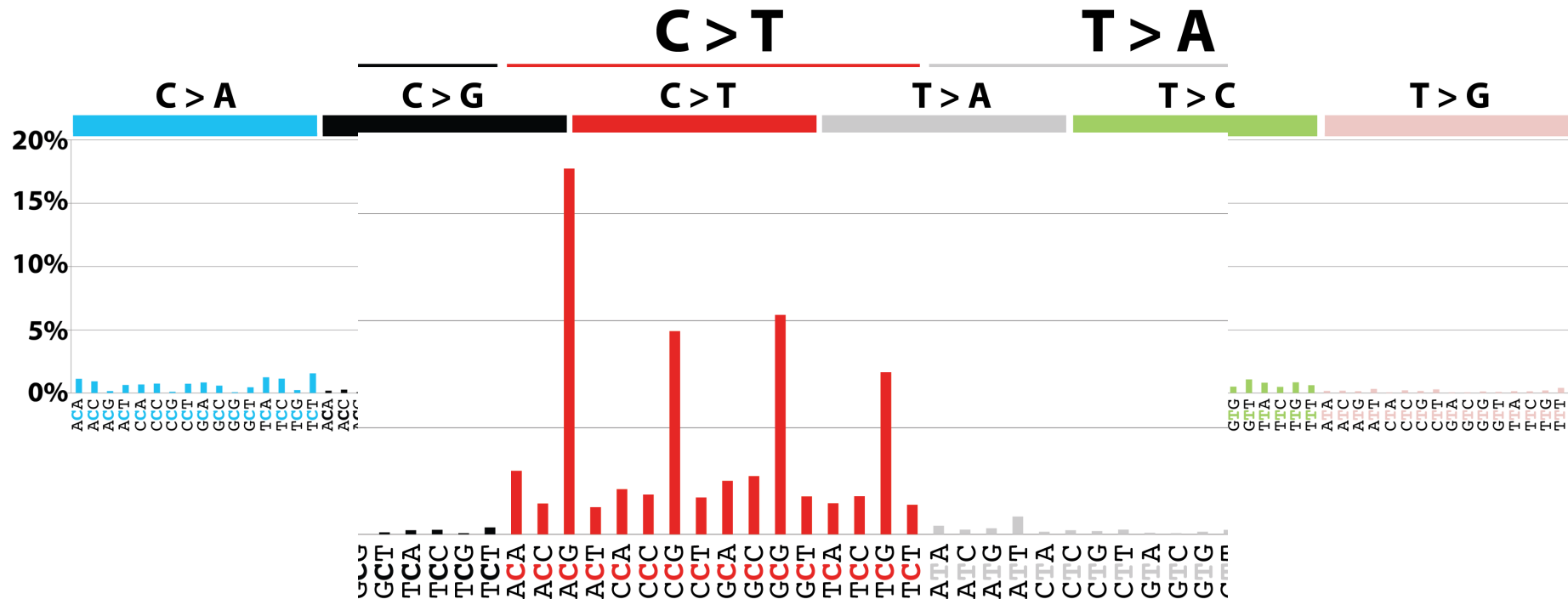
ATA>AGA
ATC>AGC
ATG>AGG
ATT>AGT
CTA>CGA
CTC>CGC
CTG>CGG
CTT>CGT
GTA>GGA
GTC>GGC
GTG>GGG
GTT>GGT
TTA>TGA
TTC>TGC
TTG>TGG
TTT>TGT

96 mutation classes

Patterns of mutations are defined by base substitutions and context

Six classes of single-base mutations
Reported by pyrimidine

Adding 5' and 3' adjacent bases
96 possibilities considering context



Each mutational process generate a specific mutational signature



Tobacco smoking



Cause of ~80% of lung cancers

