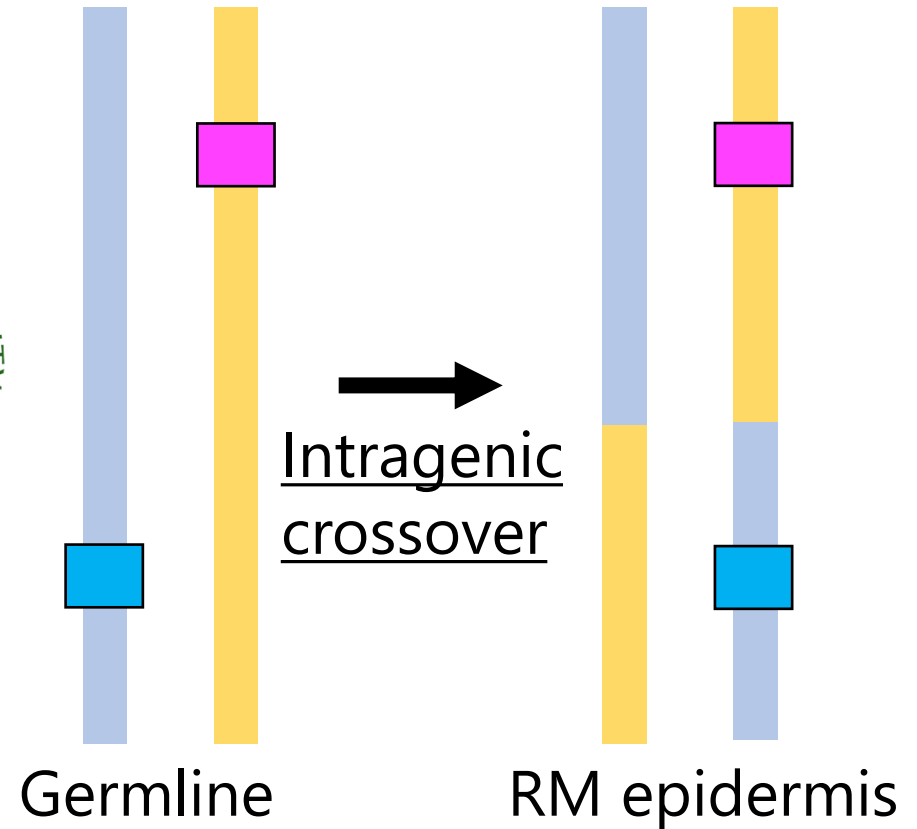
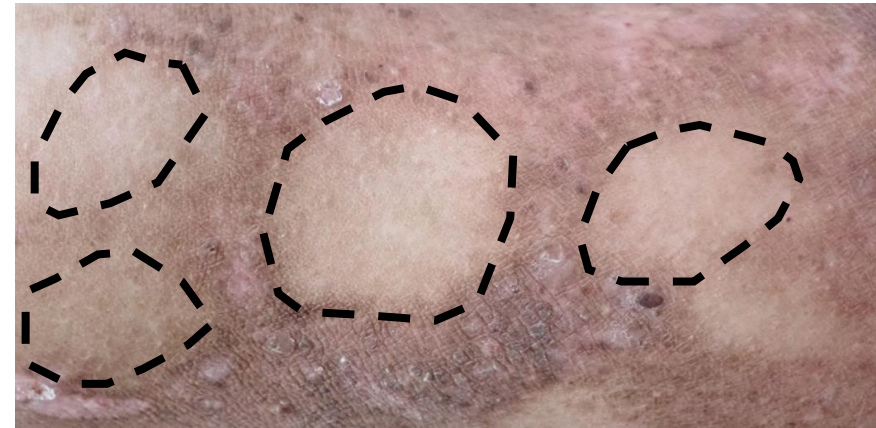


Revertant mosaicism

Ken Natsuga
Hokkaido Univ.
Sapporo, Japan

COI disclosure: Funding from J-TEC



Revertant mosaicism (RM)

Spontaneous
gene
correction at
somatic cells

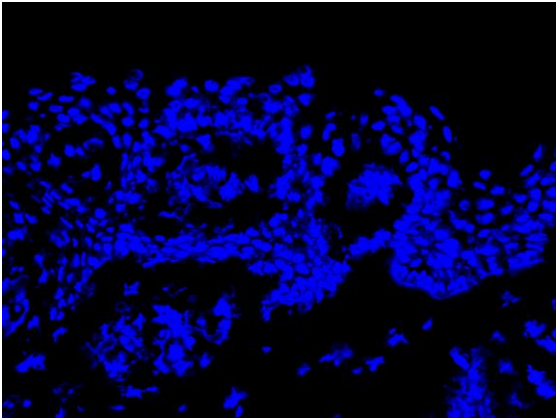


Clinical manifestations of RM

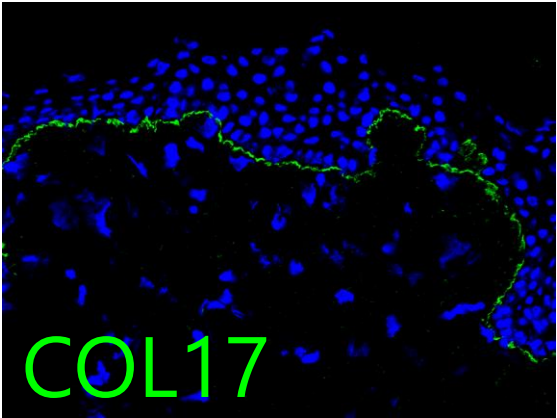
JEB



Non-RM



RM



Compound het. for c.1179del (p.Ala394Leufs*9) and c.4159C>T (p.Gln1387*) in *COL17A1*

RDEB

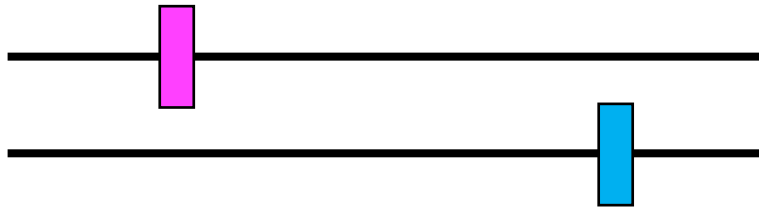
Clinically revertant skin



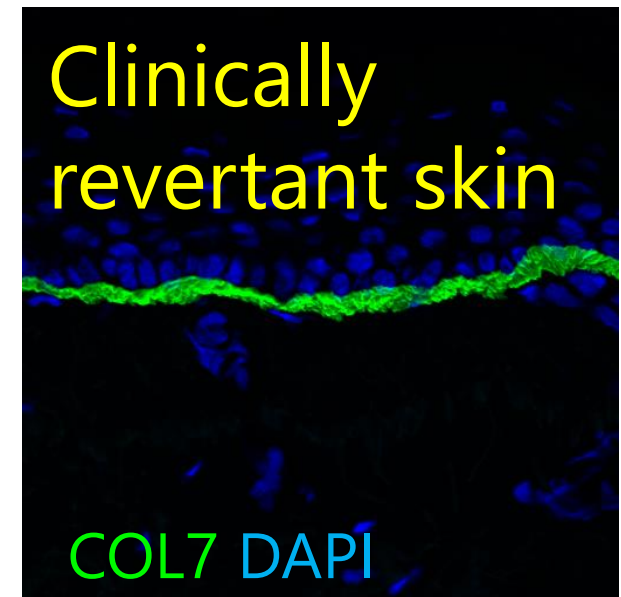
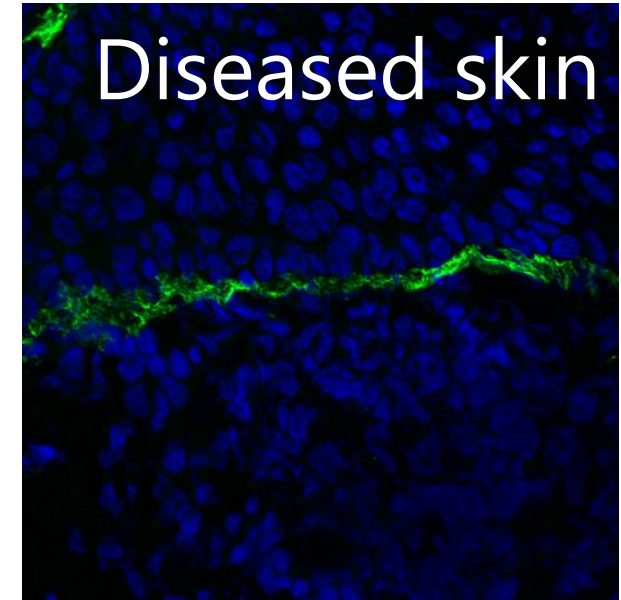
Difficulty in confirming RM

COL7A1

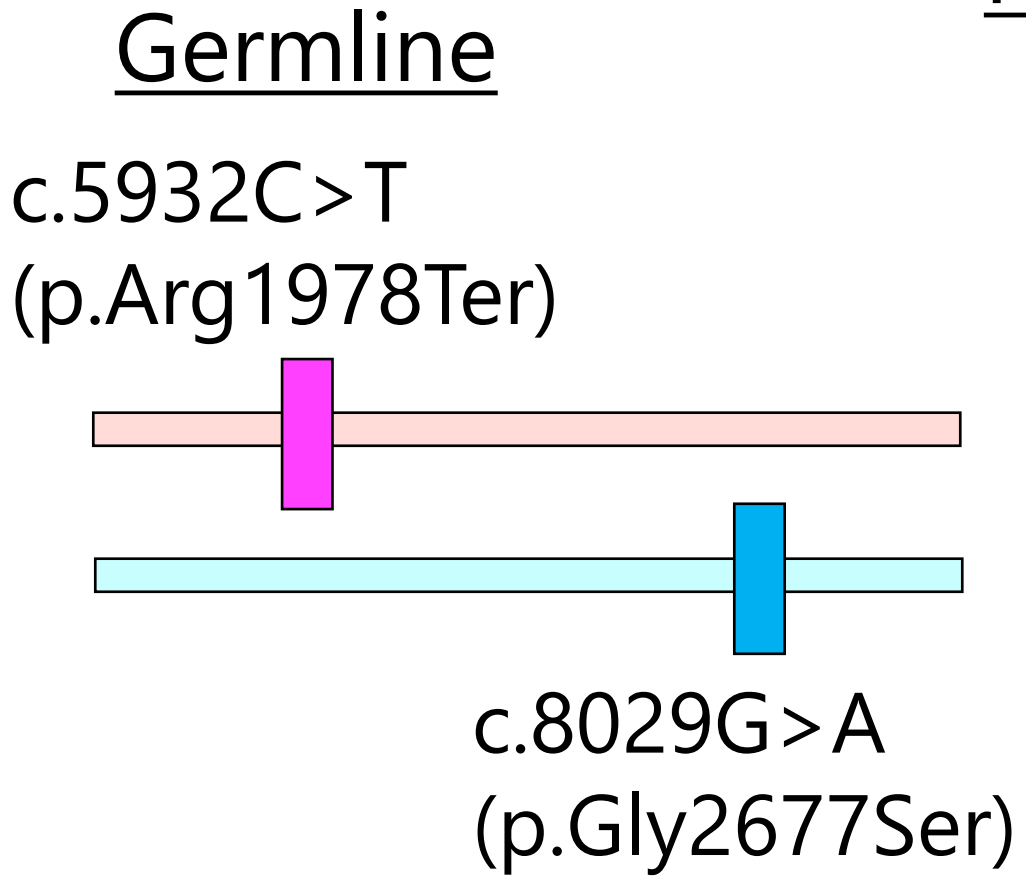
c.5932C>T
(p.Arg1978Ter;
Nonsense)



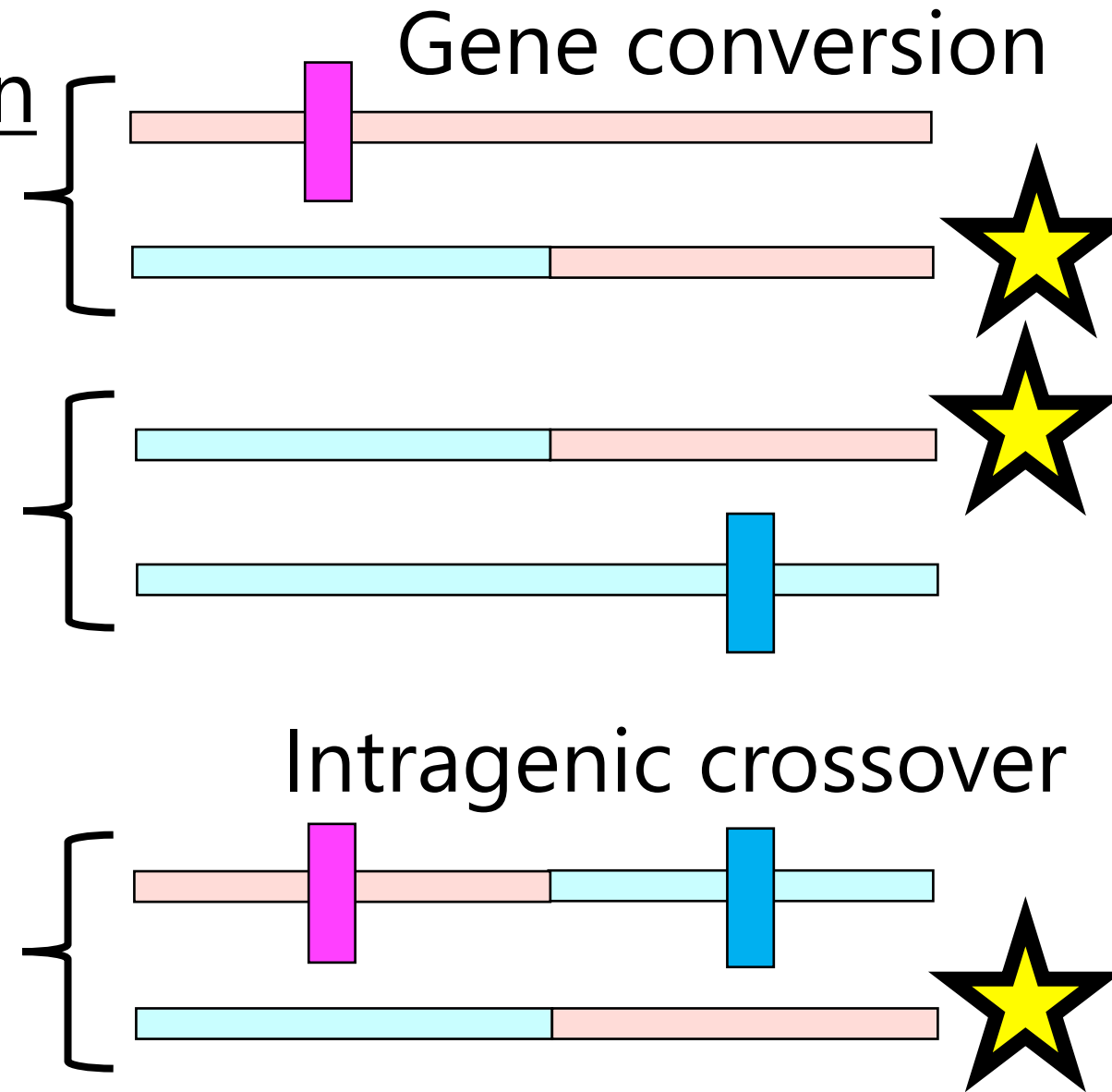
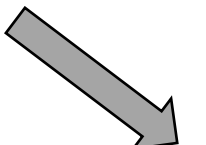
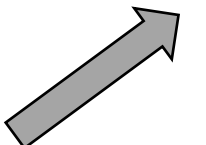
c.8029G>A
(p.Gly2677Ser;
Missense)



Homologous recombination?

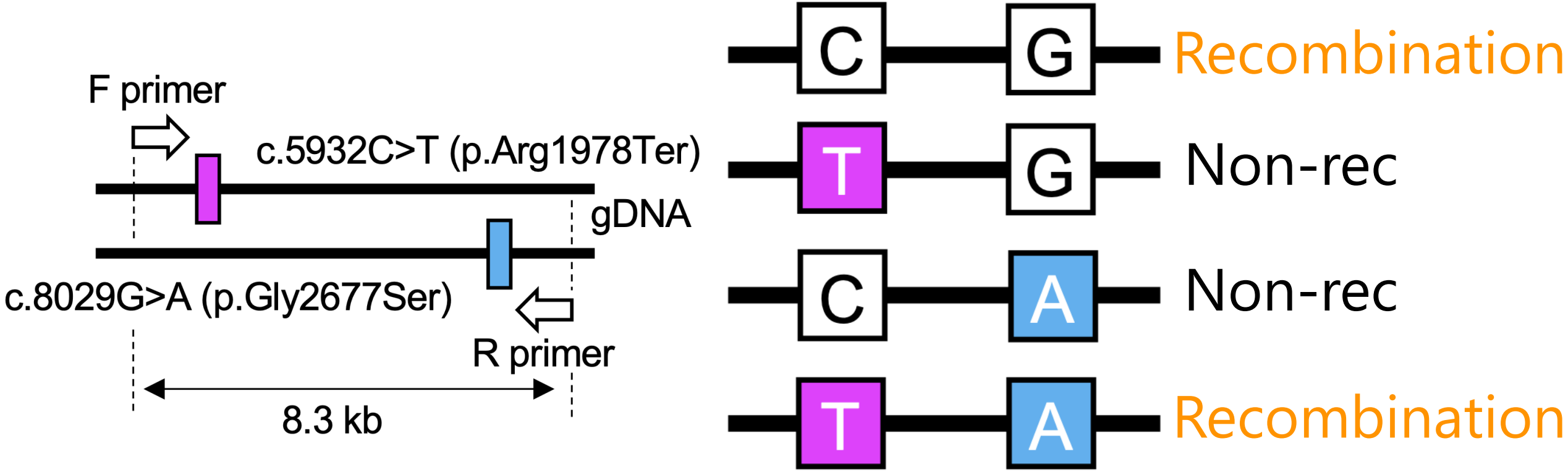


RM skin



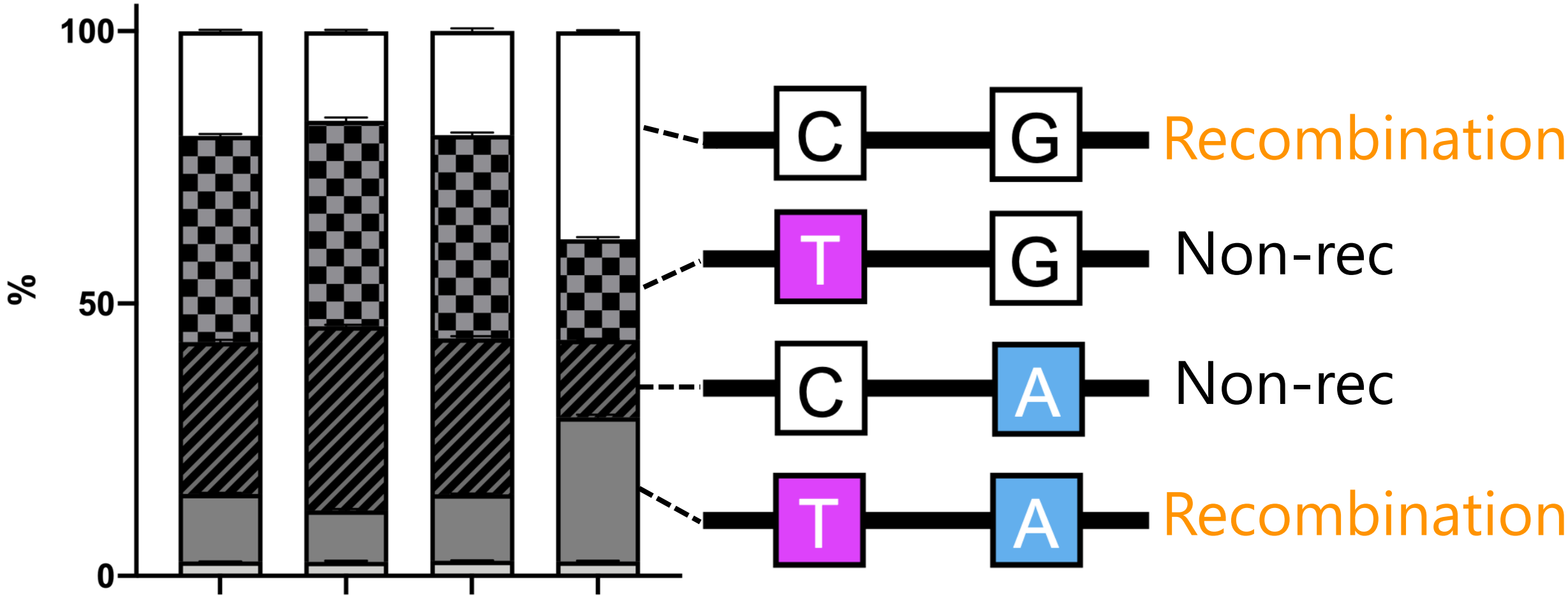
Detectable?

RM detection by gDNA PCR



*Nanopore sequencing

Failure of PCR-guided RM detection

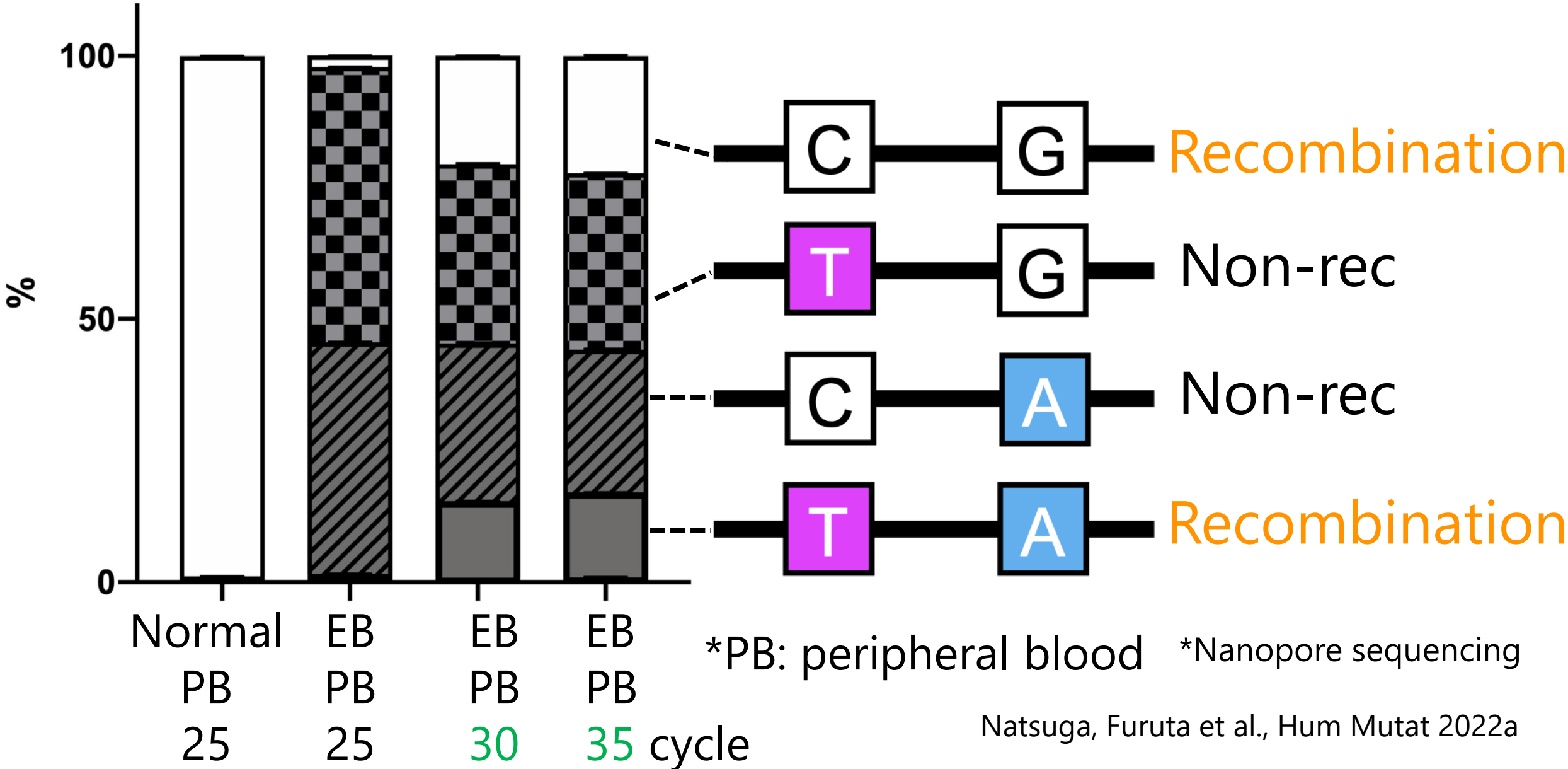


Non-RM der epi RM der **RM epi**

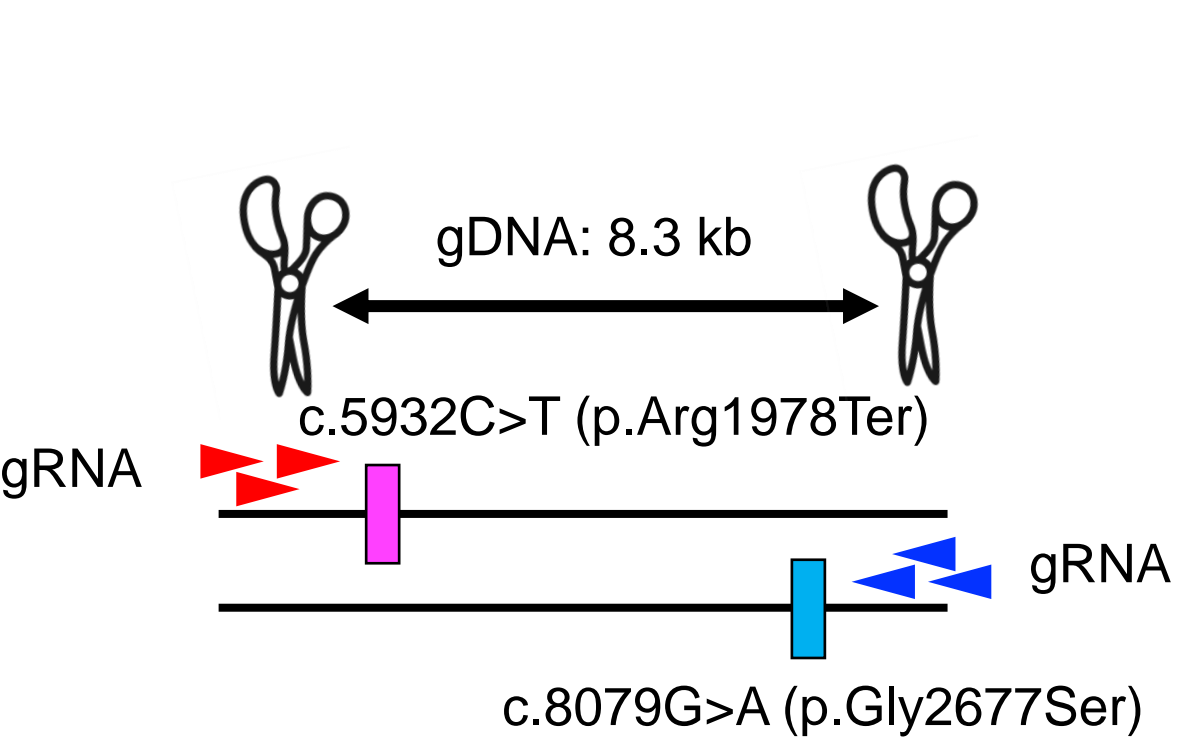
*Nanopore sequencing

Natsuga, Furuta et al., Hum Mutat 2022a

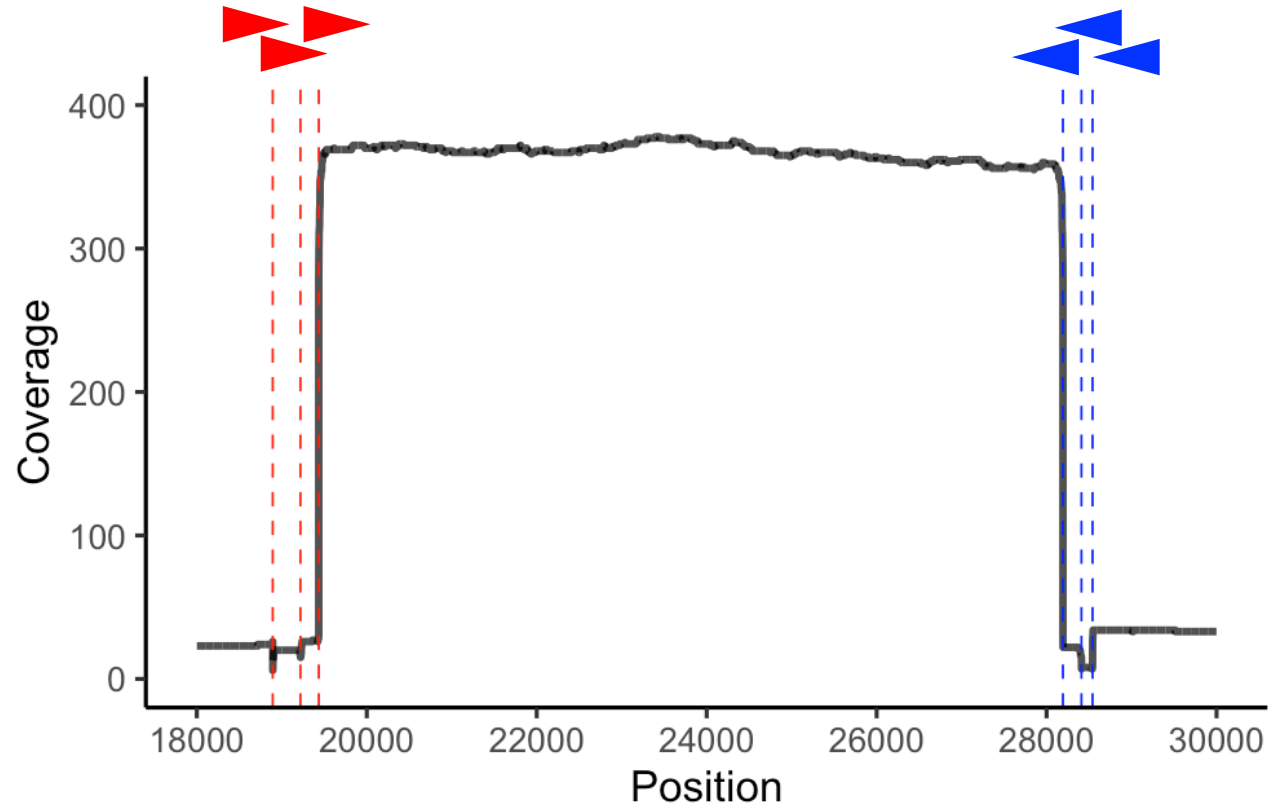
PCR-induced artificial recombination



CRISPR/Cas9-guided sequencing



COL7A1



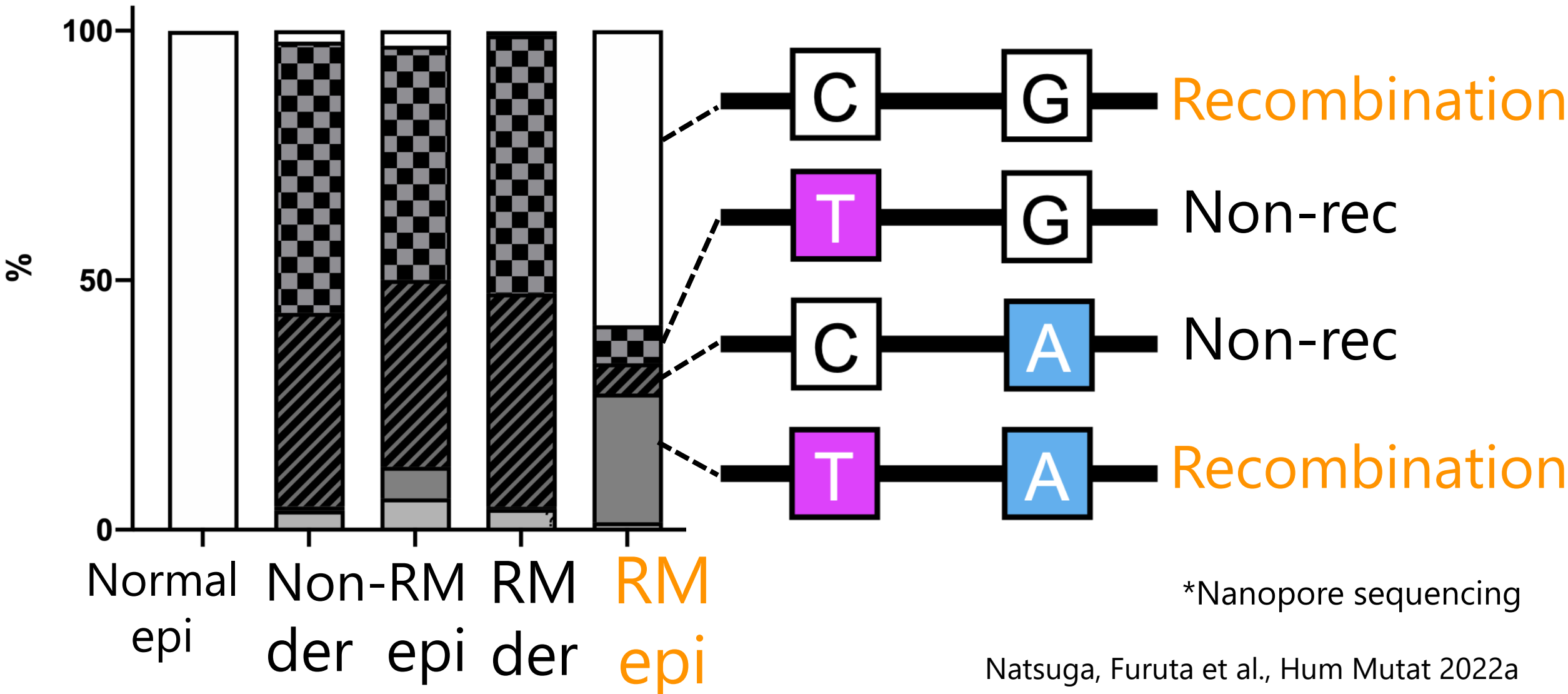
Devoid of PCR

Normal human peripheral blood

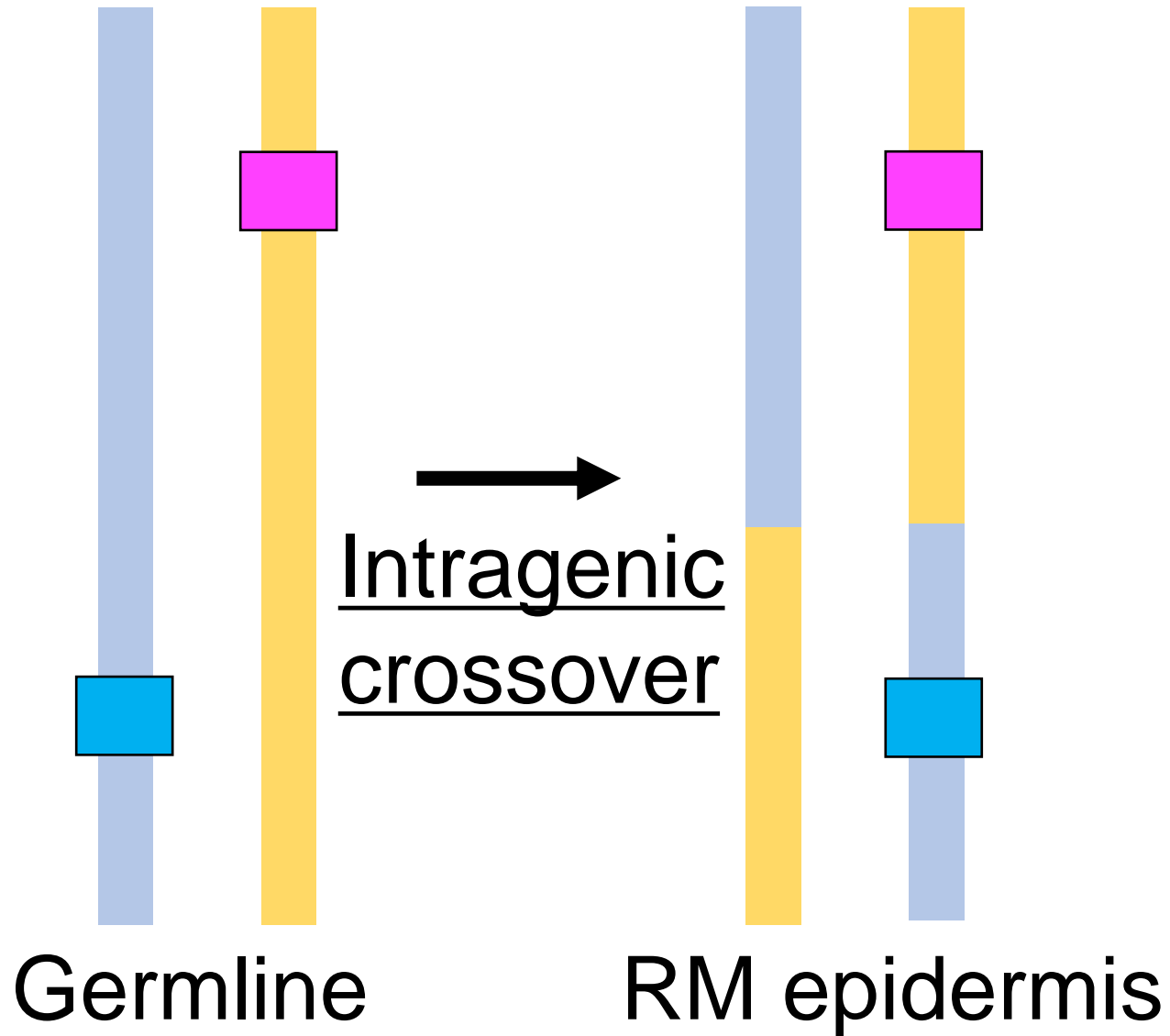
*Nanopore sequencing

Gilpatrick et al., Nat Biotechnol 2020
Natsuga, Furuta et al., Hum Mutat 2022a

CRISPR/Cas9-guided sequencing



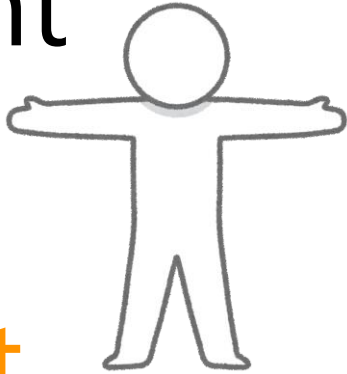
RM detection by Cas9-guided seq



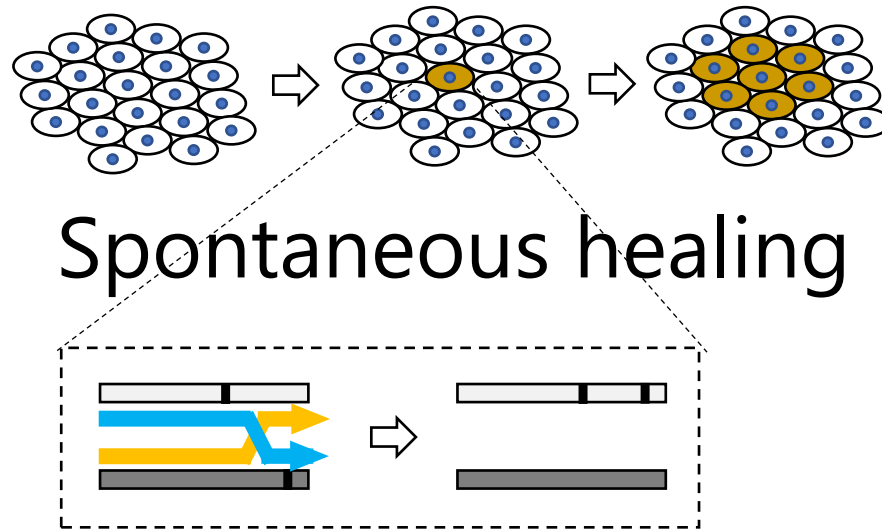
Useful for selecting
donor sites for
EB autograft

Epidermal autograft from RM skin

EB patient

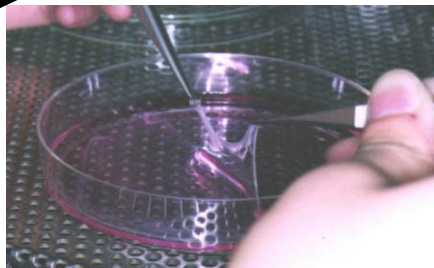
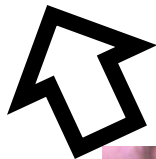


Autograft

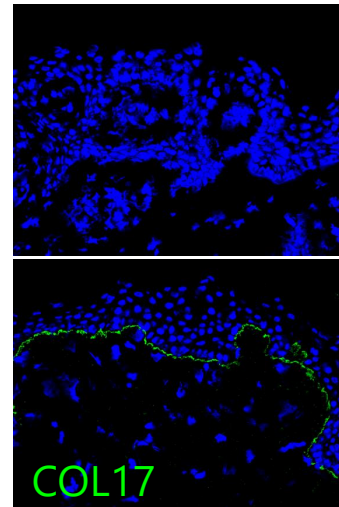


Clonal expansion

RM

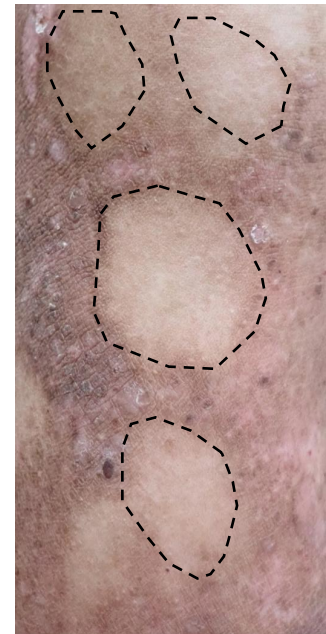


Cultured epidermal sheet



Non-RM

RM



For JEB and DEB (in Japan, 2019-)

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(-2021)

