

Landscape of immunoglobulin heavy chain γ gene class switch recombination in patients with adult T-cell leukemia–lymphoma

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Supplementary Information

Title:

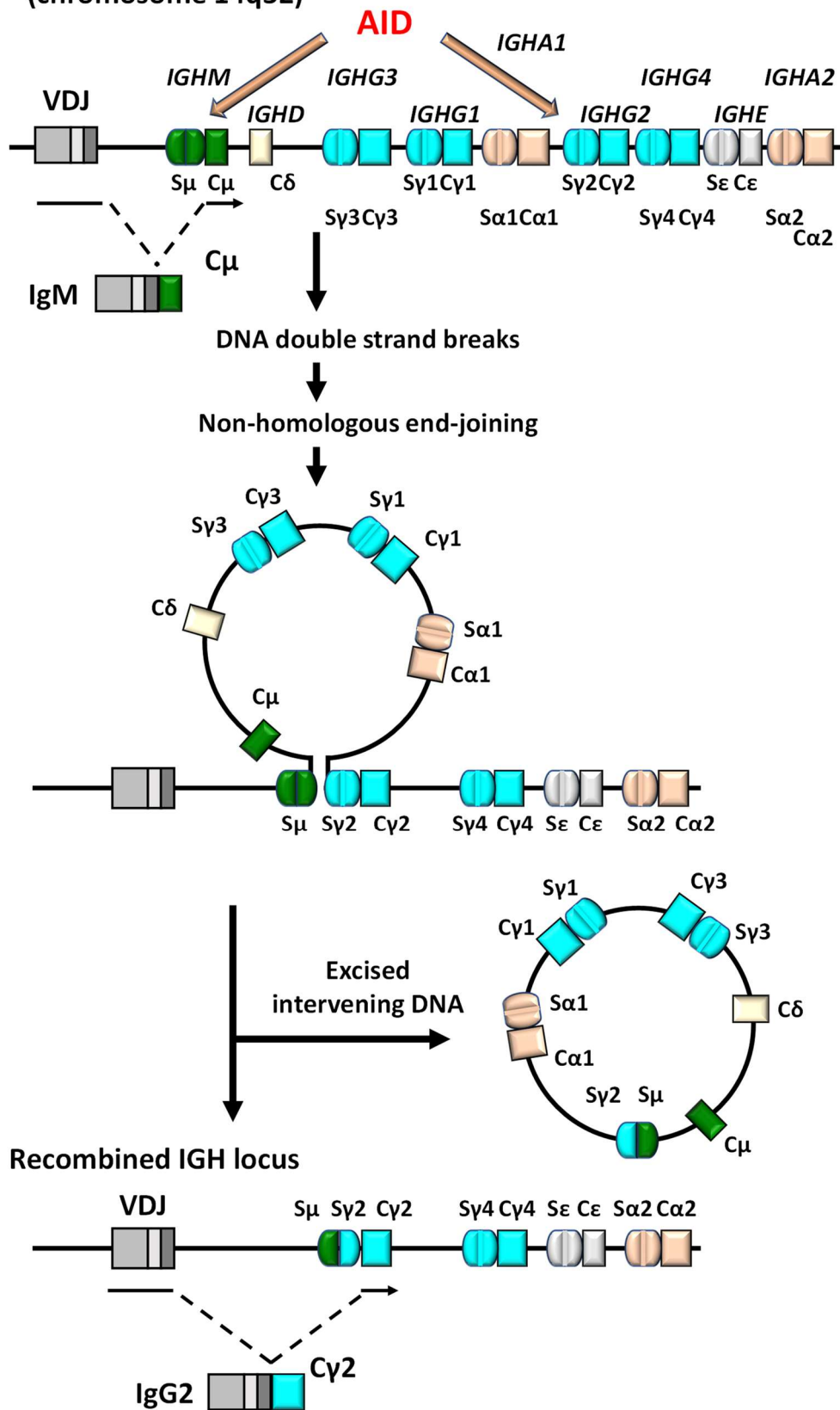
Landscape of *immunoglobulin heavy chain gamma* gene class switch recombination in patients with adult T-cell leukemia–lymphoma

Supplementary Table S1.**Univariate Cox proportional hazards analysis of OS according to the %CSR of *IGHG* in PBMC**

	%CSR of <i>IGHG</i>	Number	Hazard Ratio	95% CI	<i>P</i> value
30 percentile	≤ 5.000	24	1.000		Ref.
	> 5.000	57	0.898	(0.489-1.649)	0.728
38 percentile	≤ 6.400	31	1.000		Ref.
	> 6.400	50	0.674	(0.382-1.190)	0.173
46 percentile	≤ 8.000	37	1.000		Ref.
	> 8.000	44	0.569	(0.313-1.035)	0.065
54 percentile	≤ 8.880	44	1.000		Ref.
	> 8.880	37	0.598	(0.337-1.062)	0.079
62 percentile	≤ 9.363	50	1.000		Ref.
	> 9.363	31	0.541	(0.296-0.989)	0.046
70 percentile	≤ 10.600	57	1.000		Ref.
	> 10.600	24	0.639	(0.341-1.196)	0.161

CSR, class switch recombination; *IGHG*, immunoglobulin heavy chain gamma; CI, confidence interval; Ref, reference; OS, overall survival; PBMC, peripheral blood mononuclear cells

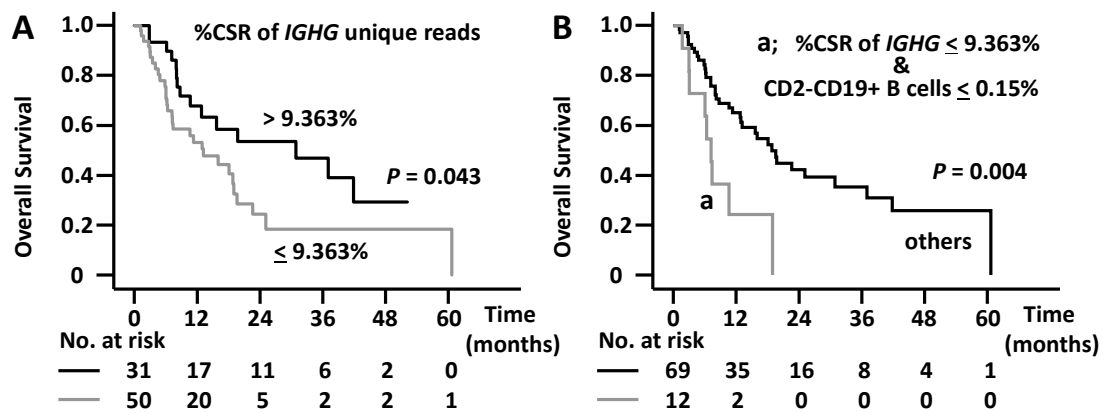
Immunoglobulin heavy chain (IGH) locus
(chromosome 14q32)



Supplementary Figure S1.

Supplementary Figure S1. Immunoglobulin heavy chain class switch recombination.

Class switch recombination (CSR) exchanges the gene encoding the *immunoglobulin heavy chain constant (IGHC)* region with one of a downstream *IGHC* genes. Human B cells initiate the switch from *IGHM* (*immunoglobulin heavy constant μ*)/*IGHD* (*immunoglobulin heavy constant δ*) to *IGHG3*, then to *IGHG1*, *IGHA1*, *IGHG2*, *IGHG4*, *IGHE*, and finally to *IGHA2* in the order corresponding to the genomic location of the *IGHC* genes. Activation-induced cytidine deaminase (AID) targets to the donor S_{μ} and one of the acceptor S regions located in the downstream ($S_{\gamma 2}$ in the figure example), and they are converted into DNA double strand breaks. Broken S regions are joined by non-homologous end-joining and the intervening DNA is excised as a circle. When CSR is completed, the originally expressed C_{μ} exons are replaced by $C_{\gamma 2}$ exons that are juxtaposed to the same *VDJ* exon. Eventually, IgM B cells switch to IgG2 B cells.



Supplementary Figure S2.

Supplementary Figure S2. Overall survival (OS) of adult T-cell leukemia-lymphoma (ATL) patients. (A) OS of patients with a higher %CSR of *IGHG* in PBMC (> 9.363%) was significantly longer than of those with a lower %CSR (median OS, 30.9 vs 13.2 months, $P = 0.043$). **(B)** OS of patients with both a lower %CSR and a lower percentage of CD2-CD19+ B cells within lymphocytes ($\leq 0.15\%$) was significantly worse than the other patients (median OS, 7.2 vs 18.8 months, $P = 0.004$).