

HLA typing Panel

Background

Human leukocyte antigen (HLA), the major histocompatibility complex (MHC) of humans, is located on the short arm of chromosome 6 and is an important part of the human immune system. Different complexes bind to various exogenous or endogenous antigenic fragments through their binding grooves, which further interact with different T cells to activate downstream immune responses. Therefore, the functions undertaken by HLA place demands on its own diversity: HLA genes are among the most polymorphic region of human genome. HLA antigen polymorphisms are associated with a variety of diseases, as well as with vaccine and drug targeted population screening, tissue and organ transplantation. The compatibility of HLA matching is a critical factor for successful organ, bone marrow, and stem cell transplantation. In addition, HLA genotypes in cancer patients as well as systemic mutations in tumors may affect the efficacy of immunotherapy. Therefore, accurate typing of HLA genes is of great importance.

Introduction

HLA typing Panel v1.0 targets a series of HLA genes and immune pathway genes, covering an approximately 40 Kb region of the genome. The Panel has been optimized for polymorphisms in the exonic region of the classical HLA gene to ensure balanced capture of alleles and support typing to the **third field level**.

HLA-A	HLA-B	HLA-C								
DMA	DMB	DOA	DOB	DPA1	DPB1	DQA1	DQA2	DQB1	DQB2	DRA
DRB1	DRB5									
B2M	CTNNB1	IFNGR1	JAK1	JAK2	MAPK1	PTEN				

HLA typing Panel v2.0 refers to the latest database (Version 3.50), and targets 11 HLA genes (Class I: HLA-A, B, C; Class II: HLA-DPA1, DPB1, DQA1, DQB1, DRB1/3/4/5). The probe covers the full-length genome sequence of all alleles and supports high-precision typing to the **fourth field level**.

Performance

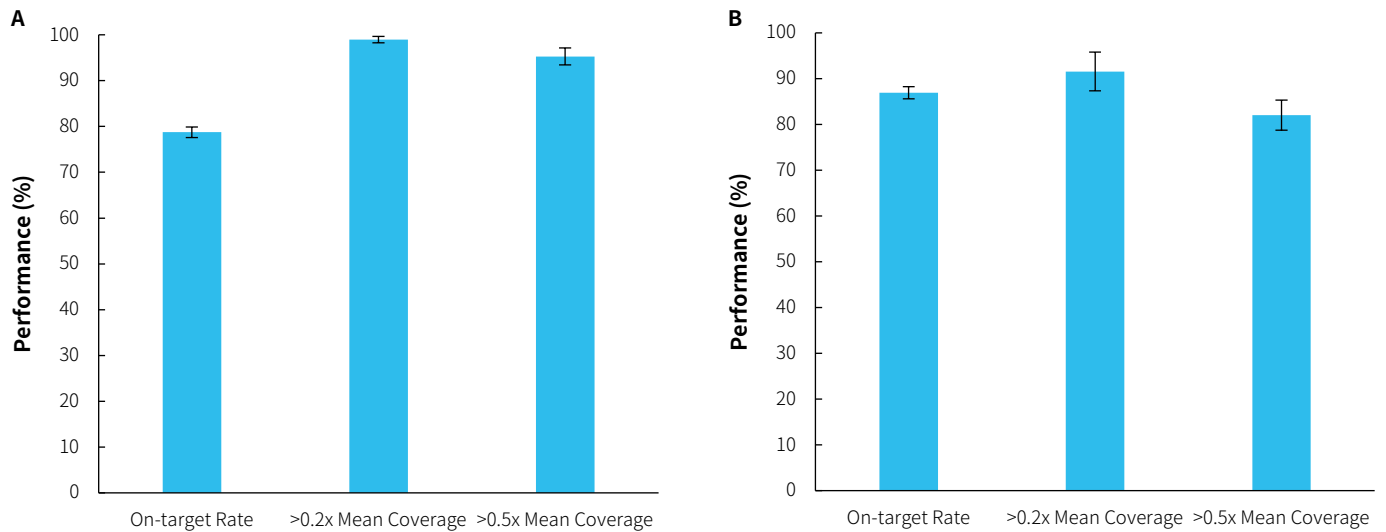


Figure 1. Capture performance of HLA typing Panel. Following targeted capture of standards using **A.** HLA typing Panel v1.0 and **B.** HLA typing Panel v2.0, respectively, sequencing was performed using Illumina® platform.

Note: The standards are Class I and Class II UCLA DNA Reference Panel. The capture performance of HLA typing Panel v1.0 was reflected through calculated mean values and standard deviations of 24 Class I and 12 Class II; the capture performance of HLA typing Panel v2.0 was reflected through calculated mean values and standard deviations of 24 Class I and 24 Class II.

Table 1. Genotyping results for Class I by HLA typing Panel v1.0.

Class I UCLA DNA Reference Panel (Standard)		HLA-A		HLA-B		HLA-C	
C1-101	Expected	34:01:00		15:21	40:01:00	4:03	12:03
	Reported	A*34:01:01		B*15:21:01	B*40:01:02	C*04:03:01	C*12:03:01
C1-102	Expected	11:01	74:01:00	7:02	53:01:00	4:01	7:02
	Reported	A*11:01:01	A*74:01:01	B*07:02:01	B*53:01:01	C*04:01:01	C*07:02:01
C1-103	Expected	2:01	2:06	7:02	40:02:00	03:08/04	7:02
	Reported	A*02:01:01	A*02:06:01	B*07:02:01	B*40:02:01	C*03:08	C*07:02:01
C1-104	Expected	1:01	68:01:00	8:01	44:02:00	7:01	7:04
	Reported	A*01:01:01	A*68:01:02	B*08:01:01	B*44:02:01	C*07:01:01	C*07:04:01
C1-105	Expected	1:01	2:01	35:01:00	37:01:00	4:01	6:02
	Reported	A*01:01:01	A*02:01:01	B*35:01:01	B*37:01:01	C*04:01:01	C*06:02:01
C1-106	Expected	2:01	33:01:00	14:02	35:12:00	4:01	8:02
	Reported	A*02:642	A*33:01:01	B*14:02:01	B*35:12:01	C*04:01:01	C*08:02:01
C1-107	Expected	2:01		15:17	35:03:00	4:01	7:01
	Reported	A*02:01:01		B*15:17:01	B*35:03:01	C*04:01:01	C*07:01:02
C1-108	Expected	31:01:00	68:01:00	15:15	39:06:00	1:02	7:02
	Reported	A*31:01:02	A*68:01:02	B*15:15	B*39:06:02	C*01:02:01	C*07:02:01
C1-109	Expected	2:07	3:01	27:05:00	46:01:00	1:02	2:02
	Reported	A*02:07:01	A*03:01:01	B*27:05:02	B*46:01:01	C*01:02:01	C*02:02:02
C1-110	Expected	25:01:00	30:01:00	13:02	18:01	6:02	12:03
	Reported	A*25:01:01	A*30:01:01	B*13:02:01	B*18:01:01	C*06:02:01	C*12:03:01
C1-112	Expected	11:01:01	25:01:01	18:01:01	51:01:01	12:03:01	15:02:01
	Reported	A*11:01:01	A*25:01:01	B*18:01:01	B*51:01:01	C*12:03:01	C*15:02:01
C1-113	Expected	2:01:01	66:01:01	27:05:02	40:01:02	1:02:01	3:04:01
	Reported	A*02:01:01	A*66:01:01	B*27:05:02	B*40:01:02	C*01:02:01	C*03:04:01

Following targeted capture of standards using HLA typing Panel v1.0, sequencing was performed using Illumina® platform and typing analysis was performed using HLA-HD analysis software, with up to 100% accuracy. Among them, C1-106 samples were correctly typed as HLA-A02:642 according to the latest database.

Note: The standard is Class I UCLA DNA Reference Panel. The first row of each standard refers to the typing result for the standard and the second row refers to the data typing result using HLA typing Panel v1.0.

Table 2. Genotyping results for Class I by HLA typing Panel v2.0.

Class I UCLA DNA Reference Panel (Standard)		HLA-A		HLA-B		HLA-C	
C1-201	Expected	02:01	80:01	14:01	44:03	04:01	08:02
	Reported	A*02:01:01:01	A*80:01:01:02	B*14:01:01:01	B*44:03:01:19	C*04:01:01:17	C*08:02:01:02
C1-202	Expected	01:03	69:01	51:01	73:01	15:05	16:02
	Reported	A*01:03:01:02	A*69:01:01:01	B*51:01:01:10	B*73:01:01:01	C*15:05:01:01	C*16:02:01:01
C1-203	Expected	24:02	34:01	38:02	48:01	07:02	08:01
	Reported	A*24:02:01:01	A*34:01:01:01	B*38:02:01:01	B*48:01:01:01	C*07:02:01:01	C*08:01:01:04
C1-204	Expected	02:06	24:02	51:01	54:01	01:02	14:02
	Reported	A*02:06:01:01	A*24:02:01:01	B*51:01:01:01	B*54:01:01:01	C*01:02:01:05	C*14:02:01:01
C1-205	Expected	29:02	32:01	35:01	44:03	04:01	16:01
	Reported	A*29:02:01:01	A*32:01:01:01	B*35:01:01:05	B*44:03:01:01	C*04:01:01:79	C*16:01:01:01
C1-206	Expected	02:01	26:01	37:01	58:01	03:02	06:02
	Reported	A*02:01:01:01	A*26:01:01:01	B*37:01:01:01	B*58:01:01:03	C*03:02:02:05	C*06:02:01:01
C1-207	Expected	66:01	74:01	42:01	58:02	06:02	17:01
	Reported	A*66:01:01:01	A*74:01:01:01	B*42:01:01:01	B*58:02:01:01	C*06:02:01:01	C*17:01:01:02
C1-208	Expected	03:01		14:02	47:01	06:02	08:02
	Reported	A*03:01:01:01	A*03:01:01:05	B*14:02:01:01	B*47:01:01:03	C*06:02:01:08	C*08:02:01:01
C1-209	Expected	03:01		07:02	41:02	07:02	17:03
	Reported	A*03:01:01:01	A*03:01:01:01	B*07:02:01:46	B*41:02:01:05	C*07:02:01:03	C*17:03:01:03
C1-210	Expected	30:02	36:01	50:01	53:01	04:01	06:02
	Reported	A*30:02:01:14	A*36:01:01:01	B*50:01:01:01	B*53:01:01:01	C*04:01:01:75	C*06:02:01:48
C1-211	Expected	02:01	34:02	15:03	81:01	04:01	18:01
	Reported	A*02:01:01:01	A*34:02:01:01	B*15:03:01:02	B*81:01:01:01	C*04:01:01:14	C*18:01:01:01
C1-212	Expected	02:06	33:03	56:01	58:01	03:02	07:02
	Reported	A*02:06:01:01	A*33:03:01:01	B*56:01:01:03	B*58:01:01:03	C*03:02:02:05	C*07:02:01:01
C1-213	Expected	02:06	11:01	51:01	52:01	08:02	12:02
	Reported	A*02:06:01:01	A*11:01:01:01	B*51:01:01:35	B*52:01:01:02	C*08:01:01:01	C*12:02:02:01
C1-214	Expected	02:06	11:01	15:12	35:03	03:04	04:01
	Reported	A*02:06:01:01	A*11:01:01:01	B*15:12:01	B*35:03:01:03	C*03:04:01:02	C*04:01:01:14
C1-215	Expected	02:07:01	33:03:01	46:01:01	58:01:01	01:02:01	03:02:02
	Reported	A*02:07:01:01	A*33:03:01:01	B*46:01:01:01	B*58:01:01:03	C*01:02:01:01	C*03:02:02:03
C1-216	Expected	11:01	24:02	40:02	44:02	02:02	05:01
	Reported	A*11:01:01:01	A*24:02:01:01	B*40:02:01:05	B*44:02:01:01	C*02:02:02:01	C*05:01:01:02
C1-217	Expected	26:01	30:02	08:01	15:03	03:04	04:01
	Reported	A*26:01:01:13	A*30:02:01:02	B*08:01:01:01	B*15:03:01:01	C*03:04:01:13	C*04:01:01:14
C1-218	Expected	02:01:01	66:02	44:02:01	57:03:01	05:01:01	06:02:01
	Reported	A*02:01:01:01	A*66:02	B*44:02:01:01	B*57:03:01:05	C*05:01:01:39	C*06:02:01:10
C1-219	Expected	01:01	31:01	35:01	51:02	08:01	15:05
	Reported	A*01:01:01:01	A*31:01:02:01	B*35:01:01:43	B*51:02:01:01	C*08:01:01:01	C*15:05:02:01
C1-220	Expected	02:01:01	26:01:01	14:01:01	55:01:01	03:03:01	08:02:01
	Reported	A*02:01:01:01	A*26:01:01:01	B*14:01:01:01	B*55:01:01:01	C*03:03:01:01	C*08:02:01:02
C1-221	Expected	02:06	24:02	27:04	39:01	07:02	12:02
	Reported	A*02:06:01:01	A*24:02:01:01	B*27:04:01	B*39:01:01:03	C*07:02:01:15	C*12:02:02:01
C1-222	Expected	02:01	68:02	15:16	35:05	04:01	14:02
	Reported	A*02:01:01:01	A*68:02:01:01	B*15:16:01:02	B*35:05:01:02	C*04:01:01:79	C*14:02:03
C1-224	Expected	03:01	32:01	37:01	57:01	06:02	
	Reported	A*03:01:01:01	A*32:01:01:01	B*37:01:01:01	B*57:01:01:04	C*06:02:01:01	C*06:02:01:48
C1-225	Expected	23:01:01	30:10	41:01:01		06:02:01	08:02:01
	Reported	A*23:01:01:01	A*30:10	B*41:01:01:01	B*41:01:01:01	C*06:02:01:01	C*08:02:01:01

Libraries were prepared using 50 ng of gDNA and the NadPrep EZ DNA Library Preparation Kit v2, hybrid capture (6 plex) was completed using HLA typing Panel v2.0, followed by sequencing using NovaSeq 6000 PE150 with the data of approximately 0.5 Gb. Sequencing data were HLA typed using in-house tools.

Note: The standard is Class I UCLA DNA Reference Panel. The first row of each standard refers to the typing result for the standard and the second row refers to the data typing result using HLA typing Panel v2.0.

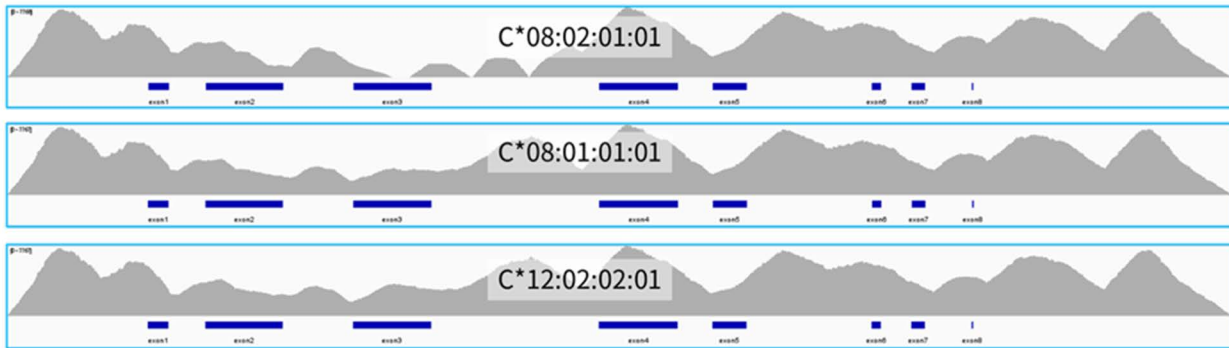


Figure 2. Coverage of reference sequence under non-mismatching conditions with targeted capture for C1-213 using HLA typing Panel v2.0. The sequence data for typing results was aligned to the reference sequence of the type. Individual results with differences in the second field level presented in the typing results of Class I using HLA typing Panel v2.0. After sequence alignment and inspection, it was found that the new typing results using HLA typing Panel v2.0 were more in line with the situation: The whole reference sequence showed continuous coverage under non-mismatching conditions; while the old results showed interruption of coverage, that is, the sequence composition here lacked support.

Note: C*08:02 (top) is the typing result provided by standard C1-213, with discontinuous coverage; C*08:01 (middle) is the new typing result, with continuous coverage; meanwhile, the coverage of another allele C*12:02 with consistent results (bottom) is shown.

Ordering Information

Product	Detail	Catalog#
HLA typing Panel v1.0, 16 rxn	16 rxn	1001622
HLA typing Panel v1.0, 96 rxn	96 rxn	1001621
HLA typing Panel v2.0, 16 rxn	16 rxn	1001952
HLA typing Panel v2.0, 96 rxn	96 rxn	1001951

Statement

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