Cell, Volume *183*

Supplemental Information

HLA-DR15 Molecules Jointly Shape an Autoreactive T Cell Repertoire in Multiple Sclerosis

Jian Wang, Ivan Jelcic, Lena Mühlenbruch, Veronika Haunerdinger, Nora C. Toussaint, Yingdong Zhao, Carolina Cruciani, Wolfgang Faigle, Reza Naghavian, Magdalena Foege, Thomas M.C. Binder, Thomas Eiermann, Lennart Opitz, Laura Fuentes-Font, Richard Reynolds, William W. Kwok, Julie T. Nguyen, Jar-How Lee, Andreas Lutterotti, Christian Münz, Hans-Georg Rammensee, Mathias Hauri-Hohl, Mireia Sospedra, Stefan Stevanovic, and Roland Martin

Table S1. Information of PBMC samples from healthy donors and RRMS patients for immunopeptidome analysis and proliferation testing, Related to Figures 1, 3, 4, 5, S1, S4, and S5

ID	Gender	Age[#]	Treatment	HLA-DRB1*	HLA-DRB3*	HLA-DRB4*	HLA-DRB5*
HD-1[†,ᵠ]	**F**	**49**	–	**15:01 / 15:01**	– / –	– / –	**01:01 / 01:01**
HD-2[†,ᵠ]	**M**	**41**	–	13:02 / **15:01**	03:01 / –	– / –	**01:01** / –
HD-3[†,ᵠ]	**M**	**22**	–	03:01 / **15:01**	01:01 / –	– / –	**01:01** / –
HD-4[ᵠ]	**N.A.**	**N.A.**	–	+[£]			+[£]
HD-5[ᵠ]	**N.A.**	**N.A.**	–	+[£]			+[£]
HD-6[ᵠ]	**N.A.**	**N.A.**	–	+[£]			+[£]
HD-7[ᵠ]	**N.A.**	**N.A.**	–	+[£]			+[£]
HD-8[ᵠ]	**N.A.**	**N.A.**	–	+[£]			+[£]
RRMS-1[†,ᵠ]	**F**	**25**	**nihil**	04:01 / **15:01**	– / –	01:01 / –	**01:01** / –
RRMS-2[†,ᵠ]	**F**	**49**	**nihil**	04:03 / **15:01**	– / –	01:01 / –	**01:01** / –
RRMS-3[†,ᵠ]	**M**	**27**	**nihil**	03:01 / **15:01**	01:01 / –	– / –	**01:01** / –
RRMS-4[ᵠ]	**F**	**26**	**nihil**	+/–			+/–
RRMS_NAT-1[†,ᵠ,§]	**M**	**54**	**Natalizumab**	**15:01 / 15:01**	– / –	– / –	**01:01 / 01:01**
RRMS_NAT-2[†,ᵠ,§]	**M**	**43**	**Natalizumab**	11:01 / **15:01**	02:01 / –	– / –	**01:01** / –
RRMS_NAT-3[†,ᵠ,§]	**M**	**25**	**Natalizumab**	01:01 / **15:01**	– / –	– / –	**01:01** / –
RRMS_NAT-4[ᵠ]	**M**	**29**	**Natalizumab**	+/–			+/–
RRMS_NAT-5[ᵠ]	**M**	**38**	**Natalizumab**	+/–			+/–
RRMS_NAT-6[ᵠ]	**F**	**35**	**Natalizumab**	+/–			+/–
RRMS_NAT-7[ᵠ]	**M**	**47**	**Natalizumab**	+/–			+/–
RRMS_NAT-8[ᵠ]	**F**	**23**	**Natalizumab**	+/–			+/–
RRMS_NAT-9[ᵠ]	**M**	**54**	**Natalizumab**	+/+			+/+
RRMS_NAT-10[ᵠ]	**M**	**50**	**Natalizumab**	+/–			+/–

[#]The age (in years) when the sample was collected

[†]Samples used for immunopeptidome analyses, B cells and monocytes isolation, and RNAseq

[ᵠ]Samples used for proliferation testing

[§]Samples used for T cell cloning

[£]Determined by flow cytometer using fluorochrome-conjugated anti-DR2a and DR2b-specific antibodies

N.A., not available

Table S4. Information of thymic and MS brain tissues for immunopeptidome analysis, Related to Figure 2

ID	Gender	Age[#]	Feature	HLA-DRB1*15:01	HLA-DRB5*01:01
Thymus_1[†]	M	4 days	Immunologically healthy children undergoing cardiac surgery	+/–	+/–
Thymus_2[†, §]	M	6 months	Immunologically healthy children undergoing cardiac surgery	+/–	+/–
Thymus_3[†, §]	M	2 months	Immunologically healthy children undergoing cardiac surgery	+/–	+/–
Thymus_4[†, §]	M	6 months	Immunologically healthy children undergoing cardiac surgery	+/–	+/–
MS brain_1[†]	M	48 years	White matter lesion with high inflammation	+/–	+/–
MS brain_2[†]	F	53 years	White matter lesion with high inflammation	+/–	+/–
MS brain_3[†]	M	46 years	White matter lesion with high inflammation	+/–	+/–
MS brain_4[†]	F	45 years	White matter lesion with high inflammation	+/–	+/–

[#]The age when the sample was collected

[†]Samples used for immunopeptidome analyses

[§]Samples used for TECs isolation and RNAseq

Table S5. Information of selected HLA-DR-SPs for analysis of $CD4^+$ T cell reactivity, Related to Figure 3

The five most common HLA-DR-SPs presented by DR2a and DR2b on B cells were selected and synthesized for further functional testing. The name of the peptides is composed by the source protein and the location of the peptide sequence within the source protein. The HLA-DR-SP pool included all five individual HLA-DR-SPs.

Name	Sequence	Source protein
HLA-DRB1$_{(57-70)}$	**DRYFYNQEESVRFD**	**HLA-DRB1*15:01**
HLA-DRB1$_{(72-86)}$	**DVGEFRAVTELGRPD**	**HLA-DRB1*15:01**
HLA-DRB5$_{(72-86)}$	**DVGEYRAVTELGRPD**	**HLA-DRB5*01:01**
HLA-DRB1/5$_{(184-199)}$	**FQTLVMLETVPRSGEV**	**HLA-DRB1*15:01 / HLA-DRB5*01:01**
HLA-DRA$_{(70-85)}$	**LEEFGRFASFEAQGAL**	**HLA-DRA*01:01**
HLA-DR-SPs pool	**HLA-DRB1$_{(57-70)}$ + HLA-DRB1$_{(72-86)}$ + HLA-DRB5$_{(72-86)}$ + HLA-DRB1/5$_{(184-199)}$ + HLA-DRA$_{(70-85)}$**	

Table S6. Information of source samples of CSF-infiltrating CD4$^+$ T cells, Related to Figure 4

ID	Gender	Age[#]	Disease	Treatment	HLA-DRB1*15:01	HLA-DRB5*01:01
Donor 1	**M**	**45**	**RRMS**	**nihil**	+/–	+/–
Donor 2	**M**	**22**	**RRMS**	**nihil**	+/–	+/–
Donor 3	**F**	**27**	**RRMS**	**nihil**	+/–	+/–
Donor 4	**F**	**34**	**RRMS**	**nihil**	+/–	+/–
Donor 5	**M**	**22**	**RRMS**	**nihil**	+/–	+/–
Donor 6	**F**	**37**	**RRMS**	**nihil**	+/–	+/–
Donor 7	**M**	**27**	**RRMS**	**nihil**	+/–	+/–
Donor 8	**F**	**37**	**RRMS**	**nihil**	+/–	+/–
Donor 9	**F**	**34**	**RRMS**	**nihil**	+/–	+/–

[#]The age (in years) when the sample was collected