

**The structural basis of chicken, swine and bovine CD8 $\alpha$  dimers provides insight into the co-evolution with MHC I in endotherm species**

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**Table S1. Contributions of CD8 $\alpha$  dimerization by residues in interface**

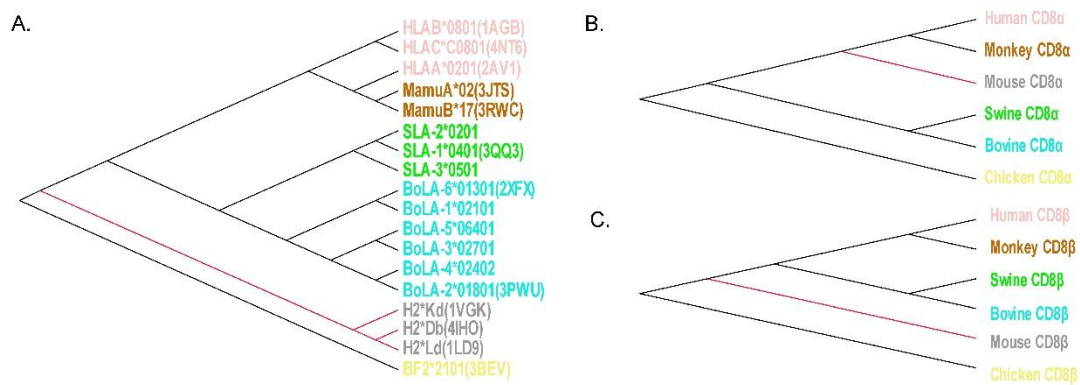
|               | Chicken |       |                        | Bovine  |       |                        | Swine   |       |                        |
|---------------|---------|-------|------------------------|---------|-------|------------------------|---------|-------|------------------------|
|               | Residue | VDW*  | BSA (Å <sup>2</sup> )* | Residue | VDW   | BSA (Å <sup>2</sup> )* | Residue | VDW   | BSA (Å <sup>2</sup> )* |
| conserved     | S41     | 5     | 13.74                  | S35     | 3     | 7.74                   | S34     | 4     | 11.84                  |
|               | F53     | 55    | 66.95                  | F49     | 58    | 74.02                  | F48     | 58    | 64.10                  |
|               | Y56     | 28    | 41.16                  | Y52     | 24    | 37.60                  | Y51     | 28    | 28.91                  |
|               | F100    | 16    | 35.34                  | F95     | 25    | 28.09                  | F93     | 6     | 9.54                   |
|               | N106    | 1     | 3.44                   | N101    | 2     | 17.67                  | N99     | 5, H* | 26.66                  |
|               | Y110    | 11    | 29.09                  | Y105    | 0     | 1.14                   | Y103    | 0     | 0                      |
|               | F111    | 51    | 89.67                  | F106    | 37    | 76.54                  | F104    | 54, H | 98.23                  |
|               | S112    | 0     | 1.84                   | S107    | 12, H | 9.62                   | S105    | 15    | 6.64                   |
| Total         |         | 167   | 281.23                 |         | 161   | 252.42                 |         | 170   | 245.92                 |
| Non-conserved | F34     | 0     | 1.10                   | H39     | 15    | 26.47                  | F3      | 0     | 0.15                   |
|               | L43     | 10    | 18.92                  | D43     | 4     | 7.90                   | L36     | 11    | 21.92                  |
|               | Q45     | 13    | 35.11                  | D44     | 16    | 11.25                  | Q38     | 13, H | 25.91                  |
|               | G49     | 4, H* | 9.68                   | P45     | 49    | 102.71                 | A43     | 21    | 50.71                  |
|               | K50     | 0     | 1.67                   | R46     | 74, H | 109.04                 | S44     | 23    | 13.00                  |
|               | L51     | 38    | 93.64                  | P47     | 33    | 61.65                  | K45     | H     | 96.39                  |
|               | H52     | 7     | 1.12                   | T48     | 3     | 0.17                   | P46     | 43    | 64.83                  |
|               | S58     | 0     | 0.17                   | K59     | 9     | 43.03                  | R56     | 6     | 15.77                  |
|               | A64     | 5     | 28.19                  | L60     | 2     | 3.19                   | K58     | 18    | 48.39                  |
|               | F65     | 6     | 16.07                  | A61     | 1     | 3.52                   | A60     | 0     | 1.67                   |
|               | Y66     | 5     | 7.53                   | E62     | 0     | 2.61                   | Y91     | 8     | 21.42                  |
|               | R67     | 21    | 52.77                  | Y93     | 16    | 16.53                  | S95     | 2     | 7.03                   |
|               | I102    | 3     | 22.71                  | S97     | 2     | 4.19                   | L97     | 1     | 32.22                  |
|               | N104    | 5     | 21.17                  | V99     | 0     | 4.86                   | S100    | 48    | 90.63                  |
|               | Q107    | 37    | 74.49                  | S102    | 29    | 63.46                  | V101    | 29    | 52.06                  |
|               | M108    | 37    | 81.42                  | I103    | 30    | 69.50                  | L102    | 38    | 94.99                  |
|               | L109    | 36    | 81.18                  | L104    | 39    | 93.93                  | N106    | 22, H | 28.01                  |
|               | S113    | 0     | 0.17                   | N108    | 18    | 13.53                  | F107    | 58    | 63.03                  |
|               |         |       | F109                   | 56      | 65.14 |                        |         |       |                        |
| Total         |         | 227   | 547.11                 |         | 402   | 702.68                 |         | 410   | 728.13                 |

|               | Human   |       |                        | Monkey  |       |                        | Mouse   |       |                        |        |
|---------------|---------|-------|------------------------|---------|-------|------------------------|---------|-------|------------------------|--------|
|               | Residue | VDW*  | BSA (Å <sup>2</sup> )* | Residue | VDW   | BSA (Å <sup>2</sup> )* | Residue | VDW   | BSA (Å <sup>2</sup> )* |        |
| conserved     | S34     | 9     | 13.45                  | S34     | 3     | 14.15                  | S37     | 5     | 12.80                  |        |
|               | F48     | 74    | 65.73                  | F48     | 69    | 77.34                  | F52     | 58    | 61.22                  |        |
|               | Y51     | 28    | 27.72                  | Y51     | 21    | 29.28                  | Y55     | 22    | 30.17                  |        |
|               | F93     | 10    | 9.54                   | F93     | 8     | 7.19                   | F101    | 8     | 12.07                  |        |
|               | N99     | 18    | 16.57                  | N99     | 6, H* | 16.14                  | N107    | 3     | 4.05                   |        |
|               | Y103    | 5     | 6.25                   | Y103    | 6, H* | 18.49                  | Y111    | 0     | 2.62                   |        |
|               | F104    | 60    | 75.58                  | F104    | 50    | 83.42                  | F112    | 37    | 71.50                  |        |
|               | S105    | 10    | 10.01                  | S105    | 7     | 8.89                   | S113    | 6, H* | 11.16                  |        |
| Total         |         | 214   | 224.85                 |         | 170   | 254.90                 |         | 139   | 205.59                 |        |
| Non-conserved | S1      | 1     | 0                      | N1      | 1     | 4.55                   | L39     | 13    | 30.21                  |        |
|               | L36     | 12    | 19.41                  | L36     | 7     | 20.50                  | Q41     | 23, H | 34.06                  |        |
|               | Q38     | 51, H | 20.71                  | Q38     | 27    | 30.20                  | L47     | 21    | 66.20                  |        |
|               | R40     | 34    | 32.46                  | G41     | 26, H | 38.68                  | P48     | 49    | 93.63                  |        |
|               | G41     | 45    | 36.32                  | T42     | 32, H | 58.62                  | Q49     | 36, H | 63.95                  |        |
|               | A42     | 52    | 59.97                  | A43     | 33    | 52.05                  | P50     | 38    | 60.33                  |        |
|               | A43     | 14    | 15.98                  | A44     | 21, H | 15.40                  | T51     | 4     | 0.84                   |        |
|               | A44     | 18    | 2.28                   | R45     | 45    | 89.26                  | K62     | 1     | 10.16                  |        |
|               | S45     | 67    | 68.03                  | P46     | 31    | 73.97                  | T64     | 8     | 30.86                  |        |
|               | P46     | 47    | 60.80                  | T47     | 7     | 1.46                   | W65     | 0     | 1.84                   |        |
|               | T47     | 5     | 0                      | K58     | 20    | 42.33                  | D66     | 0     | 6.56                   |        |
|               | K58     | 38    | 51.92                  | A59     | 7     | 2.33                   | E67     | 11    | 40.25                  |        |
|               | A59     | 2     | 0.24                   | A60     | 4     | 6.03                   | Y99     | 27    | 43.00                  |        |
|               | A60     | 1     | 5.86                   | Q61     | 2     | 22.44                  | S103    | 4     | 3.70                   |        |
|               | E61     | 15    | 22.50                  | Y91     | 12    | 22.18                  | I105    | 2     | 35.82                  |        |
|               | Y91     | 18    | 16.62                  | S95     | 3     | 6.54                   | S108    | 45, H | 76.76                  |        |
|               | S95     | 5     | 9.96                   | L97     | 1     | 19.99                  | V109    | 26    | 51.20                  |        |
|               | A96     | 0     | 1.93                   | S100    | 34    | 69.14                  | M110    | 47    | 100.74                 |        |
|               | L97     | 1     | 31.54                  | I101    | 39    | 88.36                  | S114    | 11    | 10.80                  |        |
|               | S100    | 44    | 65.48                  | M102    | 45    | 94.79                  | V115    | 35, H | 59.85                  |        |
|               | I101    | 52    | 82.73                  | H106    | 28    | 36.72                  | P117    | 5     | 22.33                  |        |
|               | M102    | 58    | 116.5                  | F107    | 54    | 55.01                  |         |       |                        |        |
|               | H106    | 15    | 9.11                   |         |       |                        |         |       |                        |        |
|               | F107    | 89    | 71.09                  |         |       |                        |         |       |                        |        |
|               | Total   |       | 684                    | 801.44  |       | 479                    | 850.55  |       | 407                    | 843.09 |

\*VDW: Van der Waal force

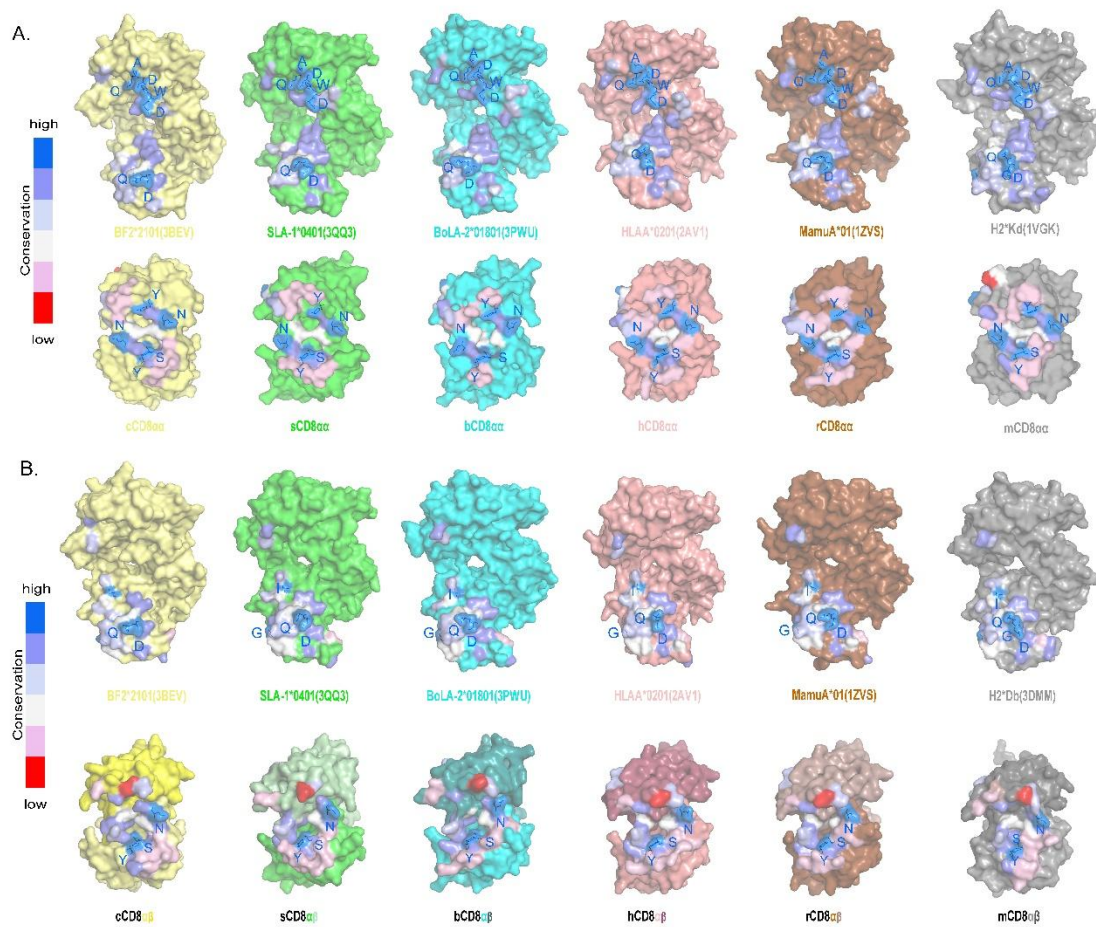
\*H: hydrogen bond

\*BSA: buried surface area



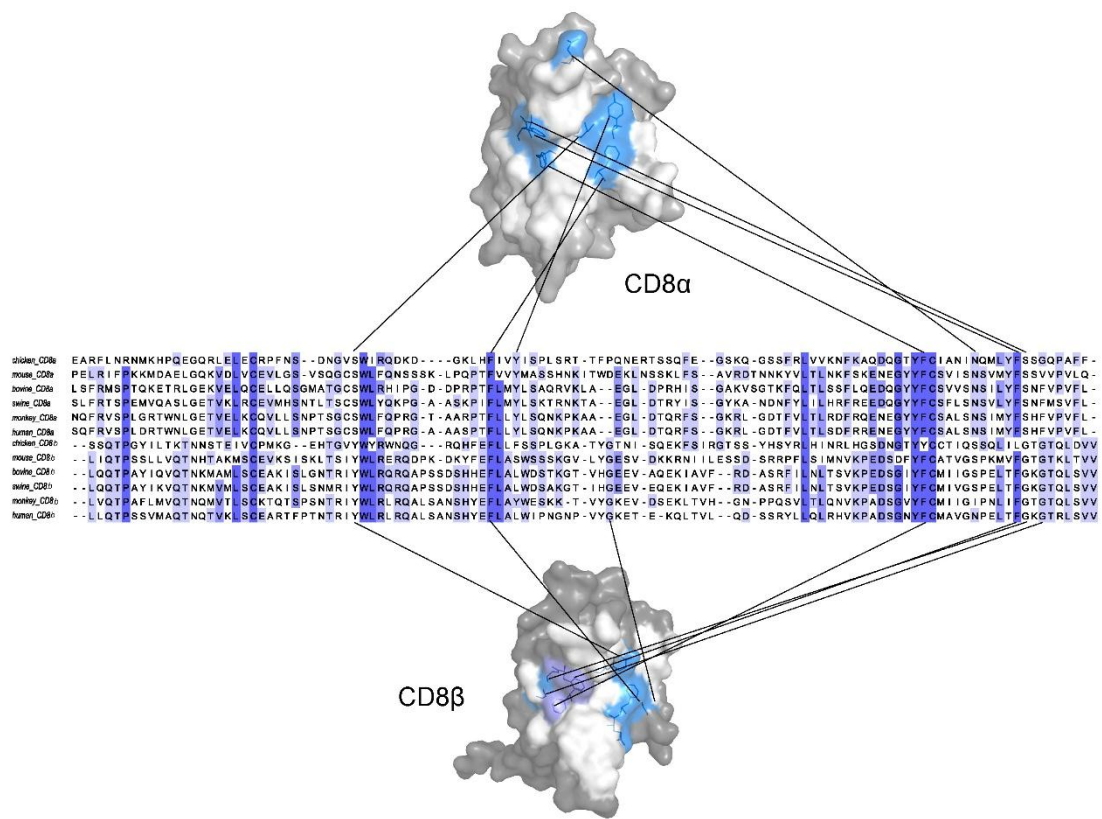
**Fig. S1. The phylogenetic trees of CD8 and MHC I molecules of six endotherm species with elucidated crystal structures.**

**A.** The phylogenetic trees of MHC I molecules from different six species. The MHC I alleles with known crystal structure were labelled by their PDB ID. **B.** The phylogenetic trees of CD8α molecules. **C.** The phylogenetic trees of CD8β molecules.



**Fig. S2. Residues and the conservation in the interfaces of chicken, swine, bovine, macaque, monkey and human CD8αα/CD8αβ and p/MHC I**

The completely conserved residues are labelled and shown in stick form. The interface between the CD8 dimers and MHC I are coloured differently according to the conservations of these residues in the six known CD8α structures. **A.** Interface of CD8αα and MHC I. **B.** Interface of CD8αβ and MHC I.



**Fig. S3. The conservation of residues on the CD8αβ interface**

Sequences of CD8α and CD8β are aligned to show their conservation. Residues on the interface of mouse CD8αβ are labelled with different colours to indicate their conservations. Residues in the structures were linked to their sequence positions by lines.