CLAIMS

1. Computer-implemented method for prediction of an immune response after transplantation, wherein said immune response comprises T-cell-alloreactivity against human leukocyte antigens (HLA) that are mismatched between donor and recipient, said method comprising:

   - HLA-typing of a sample obtained from the donor and/or donor material and recipient and/or provision of HLA typing data from the donor and recipient to determine HLA-mismatches, and

   - Determination of the number of predicted indirectly recognized HLA epitopes (PIRCHES), wherein said PIRCHES are recipient- or donor-specific HLA-derived peptides from the mismatched recipient-HLA allele and are predicted to be presented by a shared (matched) HLA molecule,

   - wherein the likelihood of said immune response is increased with an increased number of PIRCHES.

2. Method according to any one of the preceding claims, wherein said recipient- or donor-specific HLA-derived peptides from the mismatched recipient-HLA allele are identified by a computer-implemented method for identifying the cleavage sites within said peptide of the human proteasome.

3. Method according to any one of the preceding claims, wherein said presentation of peptides by a shared (matched) HLA molecule is determined by a computer-implemented method for predicting the binding of said peptide to any given HLA molecule.

4. Method according to any one of the preceding claims, wherein said transplantation comprises transplantation of stem cells, independent of their origin.

5. Method according to any one of the preceding claims, wherein said transplantation comprises haematopoietic stem-cell transplantation (HSCT).

6. Method according to any one of the preceding claims, wherein said transplantation comprises cord blood or cord blood cell transplantation.

7. Method according to any one of the preceding claims, wherein said transplantation comprises kidney transplantation.

8. Method for selecting a cell or tissue preparation or organ for allogeneic transplantation comprising the method according to any one of the preceding claims.

9. Method for selecting and/or screening donor material for allogeneic transplantation with acceptable mismatches comprising the method according to any one of the preceding claims.

10. Method for prediction of therapeutic outcome of a transplantation comprising the method according to any one of the preceding claims.

11. Method for prediction of therapeutic outcome of a transplantation comprising the method according to any one of the preceding claims, wherein said therapeutic outcome is selected from the group consisting of patient survival, disease free survival and transplant-related mortality.

12. Method according to any one of the preceding claims, wherein said immune response comprises an antibody-mediated response.

13. Method according to any one of the preceding claims, wherein said immune response comprises an unwanted alloreactivity.

14. Method according to any one of the preceding claims, wherein said immune response comprises a wanted alloreactivity, whereby a wanted alloreactivity can be an anti-leukemic alloreactivity.

15. Method according to any one of the preceding claims, wherein said immune response leads to acute graft versus host disease (aGVHD) or chronic graft versus host disease (cGVHD).

16. Method according to any one of the preceding claims, wherein said immune response leads to de novo development of donor specific HLA IgG antibodies after kidney transplantation.

17. Method according to any one of the preceding claims, wherein said PIRCHES are between 5 to 20 amino acids in length, preferably 8 to 15 amino acids in length.

18. Method according to any one of the preceding claims, wherein said PIRCHES are nonameric (9 amino acids in length) peptides.

19. Method according to any one of the preceding claims, wherein said PIRCHES are presented by shared HLA class I (PIRCHE I) or by shared HLA class II (PIRCHE II).

20. Method according to any one of the preceding claims, wherein PIRCHE-I peptides have a predicted IC50 binding value of ≤10 µM, preferably ≤1000nM, more preferably ≤500nM.

21. Method according to any one of the preceding claims, wherein PIRCHE-II peptides have a predicted IC50 binding value of ≤20 µM, preferably ≤5 µM, more preferably ≤1000nM.

22. Method according to any one of the preceding claims, wherein HLA typing is carried out on HLA subtypes HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DQB1, HLA-DPB1, -DQA1, -DPA1, -G, -E, -F, MICA, MICB and/or KIR.

23. Method according to any one of the preceding claims, wherein HLA typing is carried out on HLA-A, -B, -C, -DRB1 and –DQB1.

24. Method according to any one of the preceding claims, wherein HLA typing comprises serological and/or molecular typing.

25. Method according to any one of the preceding claims, wherein HLA typing is carried out at high resolution level with sequence-based typing.

26. Method according to any one of the preceding claims, wherein HLA typing comprises sequencing of exon 1-7 for HLA class I alleles and exon 1-6 for HLA class II alleles.

27. Method according to any one of the preceding claims, wherein HLA typing comprises high resolution HLA-A, -B, -C, -DRB1 and –DQB1 typing of exons 2 and 3 for HLA class-I alleles and exon 2 for HLA class-II alleles.

28. Method for selecting and/or screening donor material for allogeneic transplantation with acceptable mismatches comprising the method according to any one of the preceding claims, wherein the method is carried out in advance of transplantation.

29. Method according to any one of the preceding claims, wherein donor material for allogeneic transplantation originates from a donor with at least one allelic match.

30. Method according to any one of the preceding claims, wherein donor material for allogeneic transplantation originates from a donor with 10/10 matches and an HLA-DP mismatch.

31. Method according to any one of the preceding claims, wherein donor material for allogeneic transplantation originates from a 9/10-matched unrelated donor.

32. Method according to any one of the preceding claims, wherein donor material for allogeneic transplantation is associated with a low risk of an unwanted immune response when the number of PIRCHE-I ≤3, preferably ≤2, more preferably ≤1.

33. Method according to any one of the preceding claims, wherein donor material for allogeneic transplantation is associated with a low risk of an unwanted immune response when the number of PIRCHE-II ≤4, preferably ≤3, more preferably ≤2.

34. Method according to any one of the preceding claims, wherein donor material for allogeneic transplantation is associated with a low risk of an unwanted immune response when the number of combined PIRCHE-I and PIRCHE-II ≤6, preferably ≤4, more preferably ≤2.

35. Method according to any one of the preceding claims, wherein HLA-DQB1 antigenic mismatches are interrogated.

36. Method according to any one of the preceding claims for predicting the best donor out of multiple HLA-mismatched donors.

37. Method according to any one of the preceding claims comprising additionally the analysis and comparison of multiple HLA-mismatched donors for the purpose of predicting alloreactivity between multiple donors, for example between two cord blood units and/or between a matched and an HLA-mismatched donor.