

CLAIMS

1. Mammalian cell comprising a B2M/HLA-E gene wherein said mammalian cell comprises no other expressible B2M genes and has knock-ins of at least 4 HSV-TK genes at distinct and known locations.
2. The mammalian cell according to claim 1, wherein said mammalian cell comprises B2M/HLA-E*0101 and B2M/HLA-E*0103 genes.
3. The mammalian cell according to any of claims 1-2, wherein said mammalian cell is a stem cell.
4. The mammalian cell according to any of claims 1-2, wherein said mammalian cell is selected from the group consisting of a neural cell, a neuron, an interneuron cell, an oligodendrocyte, an astrocyte, a dopaminergic cell, an exosome cell, a cardiomyocyte, a retinal cell, a retinal pigment epithelium cell, a mesenchymal stem cell, a beta cell, a INS+ and NKX6.1+ double positive cell, a C-peptide+ and NKX6.1+ double positive cell, an insulin producing cell, an *in vitro* derived beta-like cell, a pancreatic endocrine cell, an endocrine cell, an immune cell, a T cell, a NK cell, a macrophage, a dendritic cell, an hepatocyte, a stellate cell, a fibroblast, a keratinocyte, a hair cell, an inner ear cell, an intestinal cell or organoid cell, a nephroid cell and a kidney-related cell.
5. The mammalian cell according to any of claims 1-4, wherein said mammalian cell is HLA-II deficient, for example CIITA deficient.
6. The mammalian cell according to any one of claims 1-5, wherein at least 2 HSV-TK genes are knock-in at safe genomic harbour sites.
7. The mammalian cell according to any of claims 1-6, wherein one HSV-TK gene is knocked-in at a safe harbour site and another HSV-TK gene is knocked-in to eliminate a CIITA allele.
8. A method for making an implantable mammalian cell, comprising the steps of:
 - providing a mammalian cell,

- knock-in of at least a B2M/HLA-E gene into said mammalian cell,
- inactivating the native B2M genes of said mammalian cell,
- knock-in of at least 4 HSV-TK genes at distinct and known locations,
- optionally differentiating said mammalian cell,

5 whereby said implantable mammalian cell is obtained.

9. The method according to claim 8, wherein said implantable mammalian cell has the cell surface phenotype of HLA-A/B/C^{-/-} HLA-E*0101⁺ HLA-E*0103⁺ cells.

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10. The method according to any of claims 8-9, wherein said mammalian cell is selected from the group consisting of a stem cell, a pluripotent cell or an iPS cell, an endocrine progenitor cell and a NGN3⁺/NKX2.2⁺ double positive cell

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11. The method according to any of claims 8-9, wherein said implantable mammalian cell is selected from the group consisting of a neural cell, a neuron, an interneuron cell, an oligodendrocyte, an astrocyte, a dopaminergic cell, an exosome cell, a cardiomyocyte, a retinal cell, a retinal pigment epithelium cell, a mesenchymal stem cell, a beta cell, a INS⁺ and NKX6.1⁺ double positive cell, a C-peptide⁺ and NKX6.1⁺ double positive cell, an insulin producing cell, an *in vitro* derived beta-like cell, a pancreatic endocrine cell, an endocrine cell, an immune cell, a T cell, a NK cell, a macrophage, a dendritic cell, an hepatocyte, a stellate cell, a fibroblast, a keratinocyte, a hair cell, an inner ear cell, an intestinal cell or organoid cell, a nephroid cell and a kidney-related cell.

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12. The method according to any of claims 8-11, wherein said knock-ins of 4 HSV-TK genes are at locations on 2 different chromosomes.

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13. The method according to any one of claims 8-12, wherein at least 2 HSV-TK genes are knocked-in at safe genomic harbour sites.

14. The use of a mammalian cell according to any one of claims 1-7 for the prevention, treatment or cure of a chronic disease.

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15. The use according to claim 14, wherein said disease is selected from the group consisting of diabetes, type 1 diabetes, type 2 diabetes, dry macular degeneration, retinitis pigmentosa, neurological disease, Parkinson's disease, heart disease, chronic heart failure and chronic kidney disease.