Viability Primary Screen IMPC_VIA_001

Purpose

To assess the postnatal viability, sub-viability, and lethality of homozygous mice during cohort production.

Experimental Design

- Monitor genotypes of Het X Het breeding units; score genotypes of at least 28 live pups, unless four or more hom pups are produced before this threshold is reached. (if other breeding strategies are used specify in the metadata and follow this convention HomXHet FemaleXMale)
- Definition of female age: "Female age earliest start/Female age oldest end" age of the youngest and oldest female mouse respectively when cohort breeding starts
- Age to be genotyped: P1-P28
- Record sex ratios of pups
- Collect and report all litters and genotype data: flag strains that produce no homozygote pups
- Identify and score lethals (defined as no homozygotes at genotype)
- Identify subviables (defined as <50% of expected homozygotes)
- If homozygous lethal: perform the embryonic lethal pipeline (if available)

Procedure

1. Monitor pup number, genotypes and sex ratios of Het X Het intercrosses set to generate cohorts for phenotyping. Score at least 28 live pups when genotyped, unless four or more hom pups are produced before this threshold is reached.
2. Identify strains that produce no homozygous/hemizygous male or female pups.
   a. Strains that produce NO homozygous pups will be considered LETHAL (complete preweaning lethality [MP: 0011100]).
   b. X-linked strains that produce NO hemizygous male pups and NO female homozygous pups will be considered LETHAL (complete preweaning lethality [MP: 0011100]).
   c. These will undergo embryonic lethal pipeline (if available)
3. Identify strains that produce less than normal numbers of homozygous/hemizygous male or female pups.
   a. Strains that produce <50% expected (#total pups * 0.125 (3 for 28) (4 for 29-36) (5 for 37-52) (See stats table in Notes)) homozygous pups will be considered SUBVIA BLE (partial preweaning lethality [MP: 0011110]).
   b. X-linked strains that produce <50% expected (#total pups* 0.125 (3 for 28) (4 for 29-36) (5 for 37-52) (See stats table in Notes)) hemizygous male pups and female homozygous pups will be considered SUBVIA BLE (partial preweaning lethality [MP: 0011110]).
   c. Some centers will proceed with secondary screening.
4. For lethal and subviable strains, heterozygous progeny will be sent for adult phenotyping.
Notes

All genotypes should be collected using validated assays. Line level calls will be rejected until 28 mice have been genotyped, unless four or more homopups are produced before this threshold is reached, in which case a viable call is valid.

Sub-viable significance table:

<table>
<thead>
<tr>
<th>Number genotyped</th>
<th>Pups observed</th>
<th>Formula (Excel)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>3</td>
<td>=BINOMDIST(3,28,0.25,1)</td>
<td>0.055135567</td>
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<tr>
<td>29</td>
<td>4</td>
<td>=BINOMDIST(4,29,0.25,1)</td>
<td>0.115324345</td>
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<td>30</td>
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<td>0.0978696</td>
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<td>31</td>
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<tr>
<td>32</td>
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<td>0.069757389</td>
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<tr>
<td>33</td>
<td>4</td>
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<tr>
<td>34</td>
<td>4</td>
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<tr>
<td>35</td>
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<td>36</td>
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</tbody>
</table>

Parameters and Metadata

**Total pups** IMPC_VIA_003_001 | v1.1

`simpleParameter`
% male WT IMPC_VIA_020_001 | v1.1

simpleParameter


Unit Measured: %

Derivation: div('IMPC_VIA_007_001', 'IMPC_VIA_010_001')

% female heterozygous IMPC_VIA_024_001 | v1.1

simpleParameter


Unit Measured: %

Derivation: div('IMPC_VIA_012_001', 'IMPC_VIA_014_001')

P-value for outcome call IMPC_VIA_032_001 | v1.2

simpleParameter
Total pups homozygous  
IMPC_VIA_006_001 | v1.0

Free Comment  
IMPC_VIA_016_001 | v1.0

Total male pups  
IMPC_VIA_010_001 | v1.0
Total female WT  IMPC_VIA_011_001 | v1.0
simpleParameter


Unit Measured: count

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Viability Outcome IMPC_VIA_001_001 | v1.1
simpleParameter


Options: Homozygous - Viable, Homozygous - Lethal, Homozygous - Subviable, Hemizygous - Lethal, Hemizygous - Viable,

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Total pups heterozygous IMPC_VIA_005_001 | v1.0
simpleParameter


Unit Measured: count

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% pups WT IMPC_VIA_015_001 | v1.3
simpleParameter
Unit Measured: %
Derivation: div('IMPC_VIA_004_001', 'IMPC_VIA_003_001')

Total pups WT IMPC_VIA_004_001 | v1.1

Unit Measured: count

% pups heterozygous IMPC_VIA_018_001 | v1.2

Unit Measured: %
Derivation: div('IMPC_VIA_005_001', 'IMPC_VIA_003_001')

Time of dark cycle end IMPC_VIA_029_001 | v1.0
Total female heterozygous IMPC_VIA_012_001 | v1.0

Unit Measured: count

Additional Outcome IMPC_VIA_002_001 | v1.1

Options: Homozygous - Reduced Life Span, Homozygous - Sick Mouse,

Total female homozygous IMPC_VIA_013_001 | v1.0

Unit Measured: count
**Female age oldest end** IMPC_VIA_027_001 | v1.1  
procedureMetadata

- **Req. Analysis:** false  
- **Req. Upload:** false  
- **Is Annotated:** false

**Unit Measured:** Weeks

**Total female pups** IMPC_VIA_014_001 | v1.1  
simpleParameter

- **Req. Analysis:** false  
- **Req. Upload:** true  
- **Is Annotated:** false

**Unit Measured:** count

**% female homozygous** IMPC_VIA_025_001 | v1.1  
simpleParameter

- **Req. Analysis:** false  
- **Req. Upload:** false  
- **Is Annotated:** false

**Unit Measured:** %

**Derivation:** `div('IMPC_VIA_013_001', 'IMPC_VIA_014_001')`

**Age of pups at genotype** IMPC_VIA_030_001 | v1.1  
procedureMetadata
<table>
<thead>
<tr>
<th>Requirement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total male homozygous</strong></td>
<td>IMPC_VIA_009_001</td>
</tr>
<tr>
<td><strong>Additional Subviable Outcome</strong></td>
<td>IMPC_VIA_033_001</td>
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<tr>
<td><strong>Breeding Strategy</strong></td>
<td>IMPC_VIA_031_001</td>
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</table>
**Total male WT**  IMPC_VIA_007_001 | v1.0

*simpleParameter*

- **Req. Analysis:** false  
- **Req. Upload:** true  
- **Is Annotated:** false

**Unit Measured:** count

---

**% female WT**  IMPC_VIA_023_001 | v1.1

*simpleParameter*

- **Req. Analysis:** false  
- **Req. Upload:** false  
- **Is Annotated:** false

**Unit Measured:** %

**Derivation:** div('IMPC_VIA_011_001', 'IMPC_VIA_014_001')

---

**% male heterozygous**  IMPC_VIA_021_001 | v1.1

*simpleParameter*

- **Req. Analysis:** false  
- **Req. Upload:** false  
- **Is Annotated:** false

**Unit Measured:** %

**Derivation:** div('IMPC_VIA_008_001', 'IMPC_VIA_010_001')
Total male heterozygous  IMPC_VIA_008_001 | v1.0

simpleParameter


Unit Measured: count

-----------------------------------------------

Female age earliest start  IMPC_VIA_026_001 | v1.1

procedureMetadata


Unit Measured: Weeks

-----------------------------------------------

Average litter size  IMPC_VIA_017_001 | v1.0

simpleParameter


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% pups homozygous  IMPC_VIA_019_001 | v1.1

simpleParameter
Unit Measured: %

Derivation: \( \frac{\text{IMPC_VIA_006}_001}{\text{IMPC_VIA_003}_001} \)

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**% male homozygous** IMPC_VIA_022_001 | v1.1

Unit Measured: %

Derivation: \( \frac{\text{IMPC_VIA_009}_001}{\text{IMPC_VIA_010}_001} \)

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**Time of dark cycle start** IMPC_VIA_028_001 | v1.1

Unit Measured: %

Derivation: \( \frac{\text{IMPC_VIA_009}_001}{\text{IMPC_VIA_010}_001} \)